

REQUEST FOR AUTHORISATION OF A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE COMMUNITY

For official use:

| | | |
|---|---|---|
| Date of receiving the request: | Date of request for additional information: | Grounds for non acceptance / negative opinion : |
| Date of request for information to make it valid: | | Give date: |
| Date of valid application : | Date of receipt of additional / amended information : | Authorisation / positive opinion: |
| Date of start of procedure : | | Give date: |
| Competent authority registration number : | | Withdrawal of application : |
| Ethics Committee registration number : | | Give date : |

A: Trial identification

A1. National Competent Authority:

UK - MHRA

A2. European Clinical Trials Database (EudraCT) number:

2015-002340-14

A3. Full title of the trial:

Randomized, Embedded, Multifactorial, Adaptive Platform trial for Community-Acquired Pneumonia (COVID-19)

A3-1. Title of the trial for lay people, in easily understood, i.e. non-technical, language

REMAP-CAP: Randomised, Embedded, Multi-factorial Adaptive Platform Trial for community acquired pneumonia (COVID-19)

A3-2. Name or abbreviated title of the trial where available:

REMAP-CAP(COVID-19)

A4. Sponsor's protocol:

Number:

Version: 3.0

Date: 10/07/2019

A5-1. ISRCTN number, if available :

A5-2. US NCT number:

NCT02735707

A5-3. Who Universal Trial Reference Number (UTRN)

U1111-1189-1653

A5-4. Other Identifiers:

| Name | Identifier |
|--------------------|-------------|
| ClinicalTrials.gov | NCT02735707 |

A6. Is this a resubmission?☐ Yes ☒ No**A7. Is the trial part of a Paediatric Investigation Plan?**☐ Yes ☒ No ☐ Not Answered**B: Identification of the sponsor responsible for the request****B1. Sponsor****SP1****Contact person**

Name of organisation University Medical Centre Utrecht
Given name clementina
Family name okundaye
Address Heidelberglaan 100 (Room number: Str. 3.116), 3584 CX Utrecht, The Netherlands
Town/city Utrecht
Post code 3584 CX
Country Netherlands
Telephone 0887555196
Fax 0887568099
E-mail eu.remapcap@umcutrecht.nl

B2. Legal Representative for the purpose of this CTIMP.

A legal representative must be appointed for a clinical trial of an investigational medicinal product (CTIMP) if the sponsor is not established in the UK or on the MHRA approved country list (please refer to question specific guidance).

Legal Representative 1**Contact person**

Name of organisation University Medical Centre Utrecht

| | |
|-------------|--|
| Given name | Albert |
| Family name | Vermaas |
| Address | Heidelberglaan 100, 3584 CX Utrecht, The Netherlands |
| Town/city | Utrecht |
| Post code | 3584 CX |
| Country | Netherlands |
| Telephone | |
| Fax | |
| E-mail | A.M.Vermaas@umcutrecht.nl |

B3. Status of the sponsor: Non-Commercial

B.4 Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):

| | |
|----------------------|--|
| Name of organisation | |
| Country | |

B.5 Contact point designated by the sponsor for further information on the trial:

| | |
|----------------------------------|---------------------------------|
| Name of organisation | ICNARC |
| Functional name of contact point | Farah Al-Beidh |
| Street Address | 24 Napier House, High Holborn |
| Town/city | London |
| Post code | WC1V 6AZ |
| Country | United Kingdom |
| Telephone | 02033110211 |
| Fax | |
| E-mail | farah.al-beidh04@imperial.ac.uk |

C: Applicant identification

C1. Request for the competent authority

C1-1. Who is responsible for the Clinical Trial Authorisation Application?

Sponsor

C1-4. Complete the details of the applicant below even if they are provided elsewhere on the form:

Contact person

Person or organisation name: UMC Utrecht
Contact person Given name Wilma
Contact person Family name van Bentum-Puijk
Address Heidelberglaan 100
Town/city Utrecht
Post code 3584 CX
Country Netherlands
Telephone 310887555196
Fax 310887568099
E-mail EU.remapcap@umcutrecht.nl

C1-5. Do you want a xml file copy of the CTA form data saved on EudraCT?

☐ Yes ☒ No ☐ Not Answered

C2.Request for ethics committee**C2-1. Who is responsible for the Clinical Trial Authorisation Application?**

.....

C2-5. Complete the details of the applicant below even if they are provided elsewhere on the form

Person or organisation name:
Title:
Forename/Initials:
Surname:
Middlename:
Address:
Town/city:
Post code:
Country:
Telephone:
Fax:
E-mail:

Part D: Investigational Medicinal Products**D: Information on the IMPs**

Information on each "bulk product" before trial-specific operations (blinding, trial specific packaging and labelling) should be provided in this section for each investigational medicinal product (IMP) being tested including each comparator, if applicable. If the trial is performed with several products please create a separate set of the following questions for each product. If the product is a combination product please give separate information for each active substance.

Click on the first row and enter details of the product in the following screens. When you have completed the details, click on the navigate button or the "See All" link and return to this section to enter details of the next product. When you have completed details of all products please move to question D7 using the navigation screen.

D. Investigational medicinal products

- PR1 [ceftriaxone](#)
- PR2 [moxifloxacin](#)
- PR3 [levofloxacin](#)
- PR4 [piperacilin-tazobactam](#)
- PR5 [ceftaroline](#)
- PR6 [amoxicillin-clavulanate](#)
- PR7 [azithromycin](#)
- PR8 [clarithromycin](#)
- PR10 [hydrocortisone](#)
- PR11 [interferon beta-1a](#)
- PR12 [anakinra](#)
- PR13 [Lopinavir/Ritonavir Mylan](#)
- PR15 [hydroxychloroquine](#)
- PR16 [tocilizumab](#)
- PR17 [Sarilumab](#)
- PR18 [Heparin](#)
- PR20 [Sarilumab unlicensed](#)
- PR21 [Kaletra 80mg/20mg Oral Solution](#)
- PR22 [Ascorbic Acid](#)
- PR23 [simvastatin](#)
- PR24 [Aspirin](#)
- PR25 [Clopidogrel](#)
- PR26 [Prasugrel](#)

PR27 [ticagrelor](#)

PR28 [Pascorbin](#)

PR29 [Ramipril](#)

PR30 [Lisinopril](#)

PR31 [perindopril](#)

PR32 [enalapril](#)

PR33 [captopril](#)

PR34 [losartan](#)

PR35 [valsartan](#)

PR36 [candesartan](#)

PR37 [irbesartan](#)

PR38 [Repagermanium](#)

PR39 [cysteamine bitartrate](#)

PR41 [Casirivimab / imdevimab \(Ronapreve\)](#)

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR1**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP if the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

ceftriaxone

EV Product Code

Name of the MA holder:

RANBAXY (UK)

MA number (if MA granted by a Member State):

PL 14894 / 0342

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any

brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

| | |
|--|--|
| D.3.1 Product name where applicable | ceftriaxone |
| D.3.2 Product code where applicable | ceftriaxone |
| D.3.3 ATC codes, if officially registered | J01DD04 |
| D.3.4 Pharmaceutical form (use standard terms) | Powder for infusion |
| D.3.4.1 Is this a specific paediatric formulation? | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | 1-2g daily of ceftriaxone, once a day infusion for as many days as is clinically necessary |

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | ceftriaxone has a well established safety profile in patients with pneumonia. As in normal clinical care patients will be prescribed 1-2mg / day for as long as is clinically necessary |
| D.3.6.1 Specify per day or total: | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | 1-2 g gram(s) |
| D.3.6.1 Route of administration (relevant to the first dose): | Intravenous use |
| D.3.6.2 Maximum dose allowed | 4g/day |
| D.3.6.2 Specify per day or total | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 4 g gram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |

D.3.7 Routes of administration for this IMP

Intravascular use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): ceftriaxone sodium

CAS number: 73384-59-5

Current sponsor code:

Other descriptive name:

Full Molecular formula C18-H18-N8-O7-S3

Chemical/biological description of the Active Substance

Strength

Concentration unit: g gram(s)

Concentration type: equal

Concentration number (only use both fields for range): 1

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Ceftriaxone

inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR2**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

moxifloxacin

EV Product Code

Name of the MA holder:

Bayer

MA number (if MA granted by a Member State):

PL 00010/0291

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable moxifloxacin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J01MA14

D.3.4 Pharmaceutical form (use standard terms) Solution for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 400mg daily of moxifloxacin, for as many days as is clinically necessary

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial 400mg daily of moxifloxacin, for as many days as is clinically necessary

D.3.6.1 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit) 400 mg
milligram(s)

D.3.6.1 Route of administration (relevant to the first dose): Intravenous use

D.3.6.2 Maximum dose allowed 400mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 400 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): moxifloxacin hydrochloride

CAS number: 354812-41-2

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₁H₂₄FN₃O₄

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 1.6

D3-11. Type of IMP

Does the IMP contain an active substance:

- Of chemical origin? ☒ Yes ☐ No ☐ Not Answered
- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Moxifloxacin inhibits bacterial type II topoisomerases (DNA gyrase and topoisomerase IV) that are required for bacterial DNA replication, transcription and repair

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR3**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

levofloxacin

EV Product Code

Name of the MA holder:

Amneal Pharma Europe Ltd

MA number (if MA granted by a Member State):

PL 42357/0192

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Ireland

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable levofloxacin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J01MA12

D.3.4 Pharmaceutical form (use standard terms) Solution for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 500 mg once or twice daily for as many days as is clinically necessary (typically 5-10 days)

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | 500 mg once or twice daily |
| D.3.6.1 Specify per day or total: | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | 1000 mg milligram(s) |
| D.3.6.1 Route of administration (relevant to the first dose): | Intravenous use |

| | |
|---|---|
| D.3.6.2 Maximum dose allowed | 1000 mg /day |
| D.3.6.2 Specify per day or total | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 1000 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): levofloxacin hemihydrate

CAS number: 100986-85-4

Current sponsor code:

Other descriptive name:

Full Molecular formula C18H20FN3O4

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 5

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. As a fluoroquinolone antibacterial agent, levofloxacin acts on the DNA-DNA-gyrase complex and topoisomerase IV.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR4**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

piperacilin-tazobactam

EV Product Code

Name of the MA holder:

Hospira UK Limited

MA number (if MA granted by a Member State):

PL 04515/0374

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable piperacilin-tazobactam

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J01C R05

D.3.4 Pharmaceutical form (use standard terms) Powder for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 4g piperacillin / 0.5g tazobactam given every 6-8 hours
Piperacillin/tazobactam 4 g / 0.5 g is administered by intravenous infusion (over 30 minutes) for as many days as is clinically necessary (typically 5-10 days)

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | Piperacillin/tazobactam 16g / 2g |
| D.3.6.1 Specify per day or total: | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | 16 / 2.0 ^g gram(s) |
| D.3.6.1 Route of administration (relevant to the first dose): | Intravenous use |

| | |
|---|---|
| D.3.6.2 Maximum dose allowed | Piperacillin/tazobactam 16 g / 2.0 g |
| D.3.6.2 Specify per day or total | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 16 / 2.0 ^g gram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravascular use (Noncurrent) |

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

| | |
|--|--------------|
| Name of active substance (INN or proposed INN if available): | Piperacillin |
| CAS number: | 61477-96-1 |
| Current sponsor code: | |
| Other descriptive name: | |
| Full Molecular formula | C23H27N5O7S |
| Chemical/biological description of the Active Substance | |
| Strength | |
| Concentration unit: | g gram(s) |
| Concentration type: | equal |
| Concentration number (only use both fields for range): | 4 |

Active Substance 2

| | |
|--|------------|
| Name of active substance (INN or proposed INN if available): | tazobactam |
| CAS number: | 89786-04-9 |
| Current sponsor code: | |

Other descriptive name:

Full Molecular formula C10H12N4O5S

Chemical/biological description of the Active Substance

Strength

Concentration unit: g gram(s)

Concentration type: equal

Concentration number (only use both fields for range): 0.5

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not AnsweredCombination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not AnsweredRadiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not AnsweredImmunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not AnsweredPlasma derived medicinal product? ☐ Yes ☒ No ☐ Not AnsweredExtractive medicinal product? ☐ Yes ☒ No ☐ Not AnsweredRecombinant medicinal product? ☐ Yes ☒ No ☐ Not AnsweredMedicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not AnsweredHerbal medicinal product? ☐ Yes ☒ No ☐ Not AnsweredHomeopathic medicinal product? ☐ Yes ☒ No ☐ Not AnsweredAnother type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Piperacillin, a broad spectrum, semisynthetic penicillin exerts bactericidal activity by inhibition of both septum and cell-wall synthesis.

Tazobactam, a beta-lactam structurally related to penicillins, is an inhibitor of many beta-lactamases which commonly cause resistance to penicillins and cephalosporins but it does not inhibit AmpC enzymes or metallo beta-lactamases. Tazobactam extends the antibiotic spectrum to those bacteria that have acquired resistance to piperacillin

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ *As defined in Article 2(1)(b) of Regulation 1394/2007/EC*

⁽⁶⁾ *Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR5**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

ceftaroline

EV Product Code

Name of the MA holder:

Pfizer Ireland Pharmaceuticals

MA number (if MA granted by a Member State):

EU/1/12/785/001

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Ireland

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable ceftaroline

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J01DI02

D.3.4 Pharmaceutical form (use standard terms) Powder for concentrate for solution for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 600mg, every 12 hours for as long as is required

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial 600mg, every 12 hours

D.3.6.1 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit) 1200 mg
milligram(s)

D.3.6.1 Route of administration (relevant to the first dose): Intravenous use

D.3.6.2 Maximum dose allowed 1200mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 1200 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): ceftaroline fosamil acetic acid solvate monohydrate

CAS number: 400827-46-5

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₄H₂₅N₈O₁₀PS₄

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 30

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. In vitro studies have shown that ceftaroline is bactericidal and able to inhibit bacterial cell wall synthesis in methicillin-resistant Staphylococcus aureus (MRSA) and penicillin non-susceptible Streptococcus pneumoniae (PNSP) due to its affinity for the altered penicillin-binding proteins (PBPs) found in these organisms

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR6**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

amoxicillin-clavulanate

EV Product Code

Name of the MA holder:

Sandoz Ltd

MA number (if MA granted by a Member State):

PL 04416/0634

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable amoxicillin-clavulanate

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J01CR02

D.3.4 Pharmaceutical form (use standard terms) Powder for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 1000 mg/ 200 mg every 6-8 hours for as many days as is clinically necessary (typically 5-10 days)

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | 1000 mg/ 200 mg every 6-8 hours |
| D.3.6.1 Specify per day or total: | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | 4000 / 800 mg milligram(s) |
| D.3.6.1 Route of administration (relevant to the first dose): | Intravenous use |

| | |
|---|---|
| D.3.6.2 Maximum dose allowed | total daily dose of 3000 mg amoxicillin and 600 mg clavulanic acid |
| D.3.6.2 Specify per day or total | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 4000/800 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): sodium amoxicillin

CAS number: 26787-78-0

Current sponsor code:

Other descriptive name:

Full Molecular formula C₁₆H₁₉N₃O₅S

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 1000

Active Substance 2

Name of active substance (INN or proposed INN if available): potassium clavulanate

CAS number: 61177-45-5

Current sponsor code:

Other descriptive name:

Full Molecular formula C8H8NO5.K

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 200

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not AnsweredCombination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not AnsweredRadiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not AnsweredImmunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not AnsweredPlasma derived medicinal product? ☐ Yes ☒ No ☐ Not AnsweredExtractive medicinal product? ☐ Yes ☒ No ☐ Not AnsweredRecombinant medicinal product? ☐ Yes ☒ No ☐ Not AnsweredMedicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not AnsweredHerbal medicinal product? ☐ Yes ☒ No ☐ Not AnsweredHomeopathic medicinal product? ☐ Yes ☒ No ☐ Not AnsweredAnother type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Amoxicillin is a semisynthetic penicillin that inhibits one or more enzymes in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death. Clavulanic acid inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ *Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR7**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

azithromycin

EV Product Code

Name of the MA holder:

Aspire Pharma Ltd

MA number (if MA granted by a Member State):

PL 35533/0026

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable azithromycin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J01FA10

D.3.4 Pharmaceutical form (use standard terms) Powder for solution for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 500 mg administered as a single intravenous daily dose for up to 14 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial 500 mg administered as a single intravenous daily
 D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered
 D.3.6.1 Specify total dose (number and unit) 500 mg
 milligram(s)
 D.3.6.1 Route of administration (relevant to the first dose): Intravenous use

D.3.6.2 Maximum dose allowed 500 mg administered as a single intravenous daily
 D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered
 D.3.6.2 Specify total dose (number and unit) 500 mg
 milligram(s)
 D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): azithromycin dihydrate
 CAS number: 83905-01-5
 Current sponsor code:
 Other descriptive name:
 Full Molecular formula C38H72N2O12
 Chemical/biological description of the Active Substance
 Strength
 Concentration unit: mg/ml milligram(s)/millilitre
 Concentration type: equal
 Concentration number (only use both fields for range): 100

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. The mechanism of action of azithromycin is based upon the suppression of bacterial protein synthesis by means of binding to the ribosomal 50s sub-unit and inhibition of peptide translocation.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR8**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

clarithromycin

EV Product Code

Name of the MA holder:

Mercury Pharmaceuticals Ltd.,

MA number (if MA granted by a Member State):

PL 12762/0404

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable clarithromycin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J01FA09

D.3.4 Pharmaceutical form (use standard terms) Powder for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 1.0 gram daily of Clarithromycin powder for concentrate for solution for infusion for upto 14 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial 1.0 gram daily of Clarithromycin powder for concentrate for solution for infusion.

D.3.6.1 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit) 1 g
gram(s)

D.3.6.1 Route of administration (relevant to the first dose): Intravenous use

D.3.6.2 Maximum dose allowed 1.0 gram daily of Clarithromycin powder for concentrate for solution for infusion.

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 1 g
gram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): clarithromycin

CAS number: 81103-11-9

Current sponsor code:

Other descriptive name:

Full Molecular formula C38H69NO13

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 2

D3-11. Type of IMP

Does the IMP contain an active substance:

- Of chemical origin? ☒ Yes ☐ No ☐ Not Answered
- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. The mechanism of action of clarithromycin is based on the inhibition of the protein biosynthesis by its binding to the 50S subunit of the bacterial ribosome.

The 14(R)-hydroxy metabolite of clarithromycin, a product of the metabolism of the parent substance which is found in humans, also has an antibacterial effect.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR10**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

hydrocortisone

EV Product Code

Name of the MA holder:

Pfizer

MA number (if MA granted by a Member State):

PL 00057/1050

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☐ No ☒ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☐ No ☒ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable hydrocortisone

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered H02AB09

D.3.4 Pharmaceutical form (use standard terms) Powder for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Intravenous Hydrocortisone, 50 milligrams (mg) every 6 hours for up-to 7 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial Intravenous Hydrocortisone, 50 milligrams (mg) every 6 hours for up-to 7 days

D.3.6.1 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit) 200 mg milligram(s)

D.3.6.1 Route of administration (relevant to the first dose): Intravenous use

D.3.6.2 Maximum dose allowed 200mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 200 mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): hydrocortisone sodium succinate

CAS number: 125-04-2

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₅H₃₄NaO₈

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 133.7

D3-11. Type of IMP

Does the IMP contain an active substance:

- Of chemical origin? ☒ Yes ☐ No ☐ Not Answered
- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.

Corticosteroids exhibit anti-inflammatory, antipruritic, and vasoconstrictive properties. At the cellular level, corticosteroids induce peptides called lipocortins. Lipocortins antagonize phospholipase A2, an enzyme which causes the breakdown of leukocyte lysosomal membranes to release arachidonic acid. This action decreases the subsequent formation and release of endogenous inflammatory mediators including prostaglandins, kinins, histamine, liposomal enzymes and the complement system

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR11**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

interferon beta-1a

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable interferon beta-1a

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered L03AB07

D.3.4 Pharmaceutical form (use standard terms) Solution for injection in pre-filled syringe

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol IFN-β1a will be administered once daily for 6 days or until ICU discharge, whichever occurs first.

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit) 10 µg microgram(s)

D.3.6.1 Route of administration (relevant to the first dose): Intravenous bolus use (Noncurrent)

D.3.6.2 Maximum dose allowed IFN-β1a 10 µg will be diluted in 1 mL of sterile water. The diluted IFN-β1a will be administered as an intravenous bolus injection via a central or peripheral line. The injection will be followed with a 5 mL flush of sterile saline.

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 10 µg microgram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous bolus use (Noncurrent)

D.3.7 Routes of administration for this IMP

Intravenous bolus use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): interferon beta-1a.

CAS number: 145258-61-3

Current sponsor code:

Other descriptive name: Rebif

Full Molecular formula C908H1408N246O252S7

Chemical/biological description of the Active Substance

Strength

Concentration unit: µg microgram(s)

Concentration type: equal

Concentration number (only use both fields for range): 10

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☐ Yes ☒ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☒ Yes ☐ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☒ Yes ☐ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. interferon beta-1a is an immunostimulant. Interferons are a group of endogenous glycoproteins endowed with immunomodulatory, antiviral and antiproliferative properties.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR12**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

anakinra

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable anakinra

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered L04AC03

D.3.4 Pharmaceutical form (use standard terms) Solution for injection/infusion in pre-filled syringe

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol A loading dose of 300 mg will be administered, followed by maintenance doses of 100 mg of anakinra administered every 6 hours. Anakinra will be administered four times daily until the patient has been breathing without receiving inv mech vent

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day ☒ per day ☐ total ☐ Not Answered or total:

D.3.6.1 Specify total dose (number and unit) 600 mg milligram(s)

D.3.6.1 Route of administration (relevant to the first dose): Intravenous use

D.3.6.2 Maximum dose allowed A loading dose of 300 mg will be administered, followed by maintenance doses of 100 mg of anakinra administered every 6 hours. In patients with creatinine clearance of less than 30 ml/min or receiving RRT anakinra will be dosed every 12hrs

D.3.6.2 Specify per day ☒ per day ☐ total ☐ Not Answered or total

D.3.6.2 Specify total dose (number and unit) 600 mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous bolus use (Noncurrent)

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Anakinra

CAS number: 143090-92-0

Current sponsor code:

Other descriptive name: Interleukin-1 receptor antagonist anakinra

Full Molecular formula C759H1186N208O232S10

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 100

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☐ Yes ☒ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☒ Yes ☐ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☒ Yes ☐ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anakinra is an immunosuppressant, it neutralises the biologic activity of interleukin-1 α (IL-1 α) and interleukin-1 β (IL-1 β) by competitively inhibiting their binding to interleukin-1 type I receptor (IL-1RI). Interleukin-1 (IL-1) is a pivotal pro-inflammatory cytokine mediating many cellular responses including those important in synovial inflammation.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR13**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Lopinavir/Ritonavir Mylan

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Lopinavir/Ritonavir Mylan

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J05AR10

D.3.4 Pharmaceutical form (use standard terms)

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Maximum duration of 14 Days.
Lopinavir/ritonavir will be administered for a minimum of 5 days, including if discharged from ICU before the end of study day 5.

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day ☒ per day ☐ total ☐ Not Answered or total:

D.3.6.1 Specify total dose (number and unit) 800/200 mg milligram(s)

D.3.6.1 Route of administration (relevant to the first dose): Enteral use (Noncurrent)

D.3.6.2 Maximum dose allowed Dosing will be Lopinavir/ritonavir 400/100 mg, administered by the enteral route every 12 hours. The preferred method of administration is two 200/50 mg tablets swallowed whole. In patients with a gastric tube-5ml of 80/20 mg per ml suspension.

D.3.6.2 Specify per day ☒ per day ☐ total ☐ Not Answered or total

D.3.6.2 Specify total dose (number and unit) 800/200 mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

Gastroenteral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Lopinavir

CAS number: 192725-17-0

Current sponsor code:

Other descriptive name:

Full Molecular formula C37H48N4O5

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 400

Active Substance 2

Name of active substance (INN or proposed INN if available): ritonavir

CAS number: 155213-67-5

Current sponsor code:

Other descriptive name:

Full Molecular formula C37H48N6O5S2

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 100

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not AnsweredCombination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not AnsweredRadiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not AnsweredImmunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not AnsweredPlasma derived medicinal product? ☐ Yes ☒ No ☐ Not AnsweredExtractive medicinal product? ☐ Yes ☒ No ☐ Not AnsweredRecombinant medicinal product? ☐ Yes ☒ No ☐ Not AnsweredMedicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not AnsweredHerbal medicinal product? ☐ Yes ☒ No ☐ Not AnsweredHomeopathic medicinal product? ☐ Yes ☒ No ☐ Not AnsweredAnother type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Lopinavir provides the antiviral activity of lopinavir/ritonavir. Lopinavir is an inhibitor of the HIV-1 and HIV-2 proteases. Inhibition of HIV protease prevents cleavage of the gag-pol polyprotein resulting in the production of immature, non-infectious virus.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR15**

Investigational medicinal product category:

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

hydroxychloroquine

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable hydroxychloroquine

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered P01B A02

D.3.4 Pharmaceutical form (use standard terms) Coated tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 7 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 1600mg / day -The loading dose will be 800 mg, administered 6-hourly, until 2 doses have been administered. Subsequently, starting 12 hours after the first loading dose, the dose will be 400 mg administered 12-hourly for 12 doses.

D.3.6.2 Specify per day or total: ☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 6400 mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Oral use

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): hydroxychloriquine

CAS number: 747-36-4

Current sponsor code:

Other descriptive name:

Full Molecular formula C18H26ClN3O

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/g milligram(s)/gram

Concentration type: equal

Concentration number (only use both fields for range): 200

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not AnsweredCombination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not AnsweredRadiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not AnsweredImmunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not AnsweredPlasma derived medicinal product? ☐ Yes ☒ No ☐ Not AnsweredExtractive medicinal product? ☐ Yes ☒ No ☐ Not AnsweredRecombinant medicinal product? ☐ Yes ☒ No ☐ Not AnsweredMedicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not AnsweredHerbal medicinal product? ☐ Yes ☒ No ☐ Not AnsweredHomeopathic medicinal product? ☐ Yes ☒ No ☐ Not AnsweredAnother type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.

Hydroxychloroquine is a racemic mixture consisting of an R and S enantiomer.

Hydroxychloroquine is an aminoquinoline like chloroquine. It is a commonly prescribed medication in the treatment of uncomplicated malaria and rheumatoid arthritis

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered*(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable**(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended**(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC**(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR16**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**☐ Yes ☒ No ☐ Not Answered**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**☐ Yes ☒ No ☐ Not Answered**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP**D3-1.**

D.3.1 Product name where applicable tocilizumab

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered L04AC07.

D.3.4 Pharmaceutical form (use standard terms) Solution for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol The recommended dose is 8 mg/kg with the option to repeat a dose in 12 hours.

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial The recommended dose is 8 mg/kg with the option to repeat a dose

| | |
|--|---|
| in 12 hours. | |
| D.3.6.1 Specify per day or total: | <input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | Intravenous use |
| D.3.6.2 Maximum dose allowed | |
| The recommended dose is 8 mg/kg (800mg) with the option to repeat a dose in 12 hours. Max would therefore be 16mg/kg (1600mg) | |
| D.3.6.2 Specify per day or total | <input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 1600 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |
| D.3.7 Routes of administration for this IMP | |
| Intravenous use | |

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): tocilizumab

CAS number: 375823-41-9

Current sponsor code:

Other descriptive name: RoActemra

Full Molecular formula C6428H9976N1720O2018S42

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/kg milligram(s)/kilogram

Concentration type: equal

Concentration number (only use both fields for range): 4 8

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☐ Yes ☒ No ☐ Not Answered

- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☒ Yes ☐ No ☐ Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Interleukin (IL)-6 plays essential roles not only in the immune response, but also in haematopoiesis and the central nervous system.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR17**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**☐ Yes ☒ No ☐ Not Answered**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**☐ Yes ☒ No ☐ Not Answered**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP**D3-1.**

D.3.1 Product name where applicable Sarilumab

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered L04AC14

D.3.4 Pharmaceutical form (use standard terms) Solution for infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol a single dose of 400mg sarilumab will be administered.

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial a single dose of 400mg sarilumab

| | |
|---|---|
| D.3.6.1 Specify per day or total: | <input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| D.3.6.2 Maximum dose allowed | a single dose of 400mg sarilumab |
| D.3.6.2 Specify per day or total | <input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 400 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): sarilumab
 CAS number: 1189541-98-7
 Current sponsor code:
 Other descriptive name:
 Full Molecular formula C6388H9918N1718O1998S44
 Chemical/biological description of the Active Substance
 Strength
 Concentration unit: mg milligram(s)
 Concentration type: equal
 Concentration number (only use both fields for range): 200

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☐ Yes ☒ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☒ Yes ☐ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.

Sarilumab is a human recombinant IgG1 antibody that binds to both forms of interleukin 6 receptors (IL-6R), thus inhibiting the IL-6-mediated signaling

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) *Complete sections D.4, D.5, D.6. and D.7, as applicable*

(2,3) *As defined in Annex 1 part IV of Directive 2001/83/EC as amended*

(4) *As defined in Article 2(1)(b) of Regulation 1394/2007/EC*

(6) *Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR18**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 29831/0110

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Heparin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered B01AB05

D.3.4 Pharmaceutical form (use standard terms)

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

D.3.6.2 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

D.3.6.2 Route of administration (relevant to the maximum dose):

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Heparin

CAS number: 37270-89-6

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₆H₄₂N₂O₃₇S₅

Chemical/biological description of the Active Substance

Strength

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☐ Yes ☒ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☒ Yes ☐ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. heparin is used to prevent embolisms in patients with atrial fibrillation and as an adjunct antithrombin therapy in patients with unstable angina and/or non-Q wave myocardial infarctions who are on platelet glycoprotein (IIb/IIIa) receptor inhibitors. Additionally, it is used to prevent clotting during dialysis and surgical procedures, maintain the patency of intravenous injection devices and prevent in vitro coagulation of blood transfusions and i

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR20**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☐ Yes ☒ No ☐ Not Answered

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☐ Yes ☒ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP**D3-1.**

| | |
|--|--|
| D.3.1 Product name where applicable | Sarilumab unlicensed |
| D.3.2 Product code where applicable | |
| D.3.3 ATC codes, if officially registered | L04AC14 |
| D.3.4 Pharmaceutical form (use standard terms) | Solution for infusion |
| D.3.4.1 Is this a specific paediatric formulation? | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | A single dose of 400mg sarilumab |

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | A single dose of 400mg sarilumab |
| D.3.6.1 Specify per day or total: | <input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| D.3.6.2 Maximum dose allowed | A single dose of 400mg sarilumab |
| D.3.6.2 Specify per day or total | <input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 400 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): sarilumab

CAS number: 1189541-98-7

Current sponsor code:

Other descriptive name:

Full Molecular formula C6388H9918N171801998S44

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 200

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☐ Yes ☒ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☒ Yes ☐ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Sarilumab is a human recombinant IgG1 antibody that binds to both forms of interleukin 6 receptors (IL-6R), thus inhibiting the IL-6-mediated signaling

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR21**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Kaletra 80mg/20mg Oral Solution

EV Product Code

Name of the MA holder:

Abbvie

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

South Africa

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

| | |
|--|---|
| D.3.1 Product name where applicable | Kaletra 80mg/20mg Oral Solution |
| D.3.2 Product code where applicable | |
| D.3.3 ATC codes, if officially registered | J05AR10 |
| D.3.4 Pharmaceutical form (use standard terms) | Oral liquid |
| D.3.4.1 Is this a specific paediatric formulation? | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | Maximum duration of 14 Days. Lopinavir/ritonavir will be administered for a minimum of 5 days, including if discharged from ICU before the end of study day 5. |

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial Dosing will be Lopinavir/ritonavir 400/100 mg, administered by the enteral route every 12 hours. In patients with a gastric tube-5ml of 80/20 mg per ml suspension.

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed Dosing will be Lopinavir/ritonavir 400/100 mg, administered by the enteral route every 12 hours. In patients with a gastric tube-5ml of 80/20 mg per ml suspension.

D.3.6.2 Specify per day or total ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 400/100 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Lopinavir

CAS number: 192725-17-0

Current sponsor code:

Other descriptive name:

Full Molecular formula C37H48N4O5

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 400

Active Substance 2

Name of active substance (INN or proposed INN if available): ritonavir

| | |
|---|-----------------|
| CAS number: | 155213-67-5 |
| Current sponsor code: | |
| Other descriptive name: | |
| Full Molecular formula | C37H48N6O5S2 |
| Chemical/biological description of the Active Substance | |
| <i>Strength</i> | |
| Concentration unit: | mg milligram(s) |
| Concentration type: | equal |
| Concentration number (only use both fields for range): | 100 |

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not AnsweredCombination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not AnsweredRadiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not AnsweredImmunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not AnsweredPlasma derived medicinal product? ☐ Yes ☒ No ☐ Not AnsweredExtractive medicinal product? ☐ Yes ☒ No ☐ Not AnsweredRecombinant medicinal product? ☐ Yes ☒ No ☐ Not AnsweredMedicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not AnsweredHerbal medicinal product? ☐ Yes ☒ No ☐ Not AnsweredHomeopathic medicinal product? ☐ Yes ☒ No ☐ Not AnsweredAnother type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Lopinavir provides the antiviral activity of lopinavir/ritonavir. Lopinavir is an inhibitor of the HIV-1 and HIV-2 proteases. Inhibition of HIV protease prevents cleavage of the gag-pol polyprotein resulting in the production of immature, non-infectious virus.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR22**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Ascorbic Acid

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Ascorbic Acid

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered A11G A01

D.3.4 Pharmaceutical form (use standard terms) Solution for injection/infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Maximum duration of 4 days. 50mg/kg of estimated / measured body weight will be administered every 6 hours for 16 doses (200mg/kg/day, 96 hour course) or up until hospital discharge

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | 200mg/kg |
| D.3.6.1 Specify per day or total: | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| D.3.6.2 Maximum dose allowed | 200mg/kg/day |
| D.3.6.2 Specify per day or total | <input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 200 mg/kg milligram(s)/kilogram |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Intravenous use |

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Ascorbic Acid

CAS number:

Current sponsor code:

Other descriptive name: Vitamin C

Full Molecular formula C₆H₈O₆

Chemical/biological description of the Active Substance

Strength

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Ascorbic acid, a water-soluble vitamin, is essential for formation of collagen and intercellular material, and therefore necessary for the development of cartilage, bone, teeth and for the healing of wounds. It is also essential for the conversion from folic acid to folinic acid, facilitates iron absorption from the gastro-intestinal tract and influences haemoglobin formation and erythrocyte maturation.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR23**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

simvastatin

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable simvastatin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C10A A01

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Maximum 28 days. simvastatin will be administered once daily until study day 28 or ICU discharge, whichever comes first.

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | 80mg/ day |
| D.3.6.1 Specify per day or total: | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| D.3.6.2 Maximum dose allowed | 80mg / day |
| D.3.6.2 Specify per day or total | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 2240 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): | Enteral use (Noncurrent) |

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): simvastatin

CAS number: 79902-63-9

Current sponsor code:

Other descriptive name:

Full Molecular formula C25H38O5

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 40

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Simvastatin is indicated for the treatment of hyperlipidemia to reduce elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), and triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C)

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR24**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Aspirin

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Aspirin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered B01AC06

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Aspirin will be administered daily as an enteral dose of 75mg or 100mg per day, till the end of study day 14 or hospital discharge, whichever occurs first.

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

Maximum dose would be 100mg / day for 14day
-1400mg

D.3.6.2 Specify per day or total

☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

1400 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose):

Gastroenteral use

D.3.7 Routes of administration for this IMP

Gastroenteral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Acetylsalicylic acid

CAS number: 50-78-2

Current sponsor code:

Other descriptive name:

Full Molecular formula $C_9H_8O_4$

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 75 100

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Also known as Aspirin, acetylsalicylic acid (ASA) is a commonly used drug for the treatment of pain and fever due to various causes. Acetylsalicylic acid has both anti-inflammatory and antipyretic effects. This drug also inhibits platelet aggregation and is used in the prevention of blood clots stroke, and myocardial infarction

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR25**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Clopidogrel

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Clopidogrel

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered B01AC04

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Clopidogrel will be administered daily as an enteral dose of 75mg per day up to the end of study day 14 or hospital discharge, whichever comes first

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed maximum dose would be 75mg for 14 days -1050mg

D.3.6.2 Specify per day or total ☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 1050 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Gastroenteral use

D.3.7 Routes of administration for this IMP

Gastroenteral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): clopidogrel

CAS number: 113665-84-2

Current sponsor code:

Other descriptive name:

Full Molecular formula C₁₆H₁₆ClNO₂S·HCl

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 75

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Clopidogrel is indicated to reduce the risk of myocardial infarction for patients with non-ST elevated acute coronary syndrome (ACS), patients with ST-elevated myocardial infarction, and in recent MI, stroke, or established peripheral arterial disease

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR26**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Prasugrel

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Prasugrel

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered B01AC22

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Prasugrel will be administered daily by the enteral route as follows. If <75yrs old/>60kg : loading dose of 60mg followed by daily 10mg. If >75yrs/<60kg; loading dose of 60mg followed by daily 5mg up to 14 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

Maximum dose would be 60mg and 10mg for 13days

D.3.6.2 Specify per day or total

☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

190 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose):

Gastroenteral use

D.3.7 Routes of administration for this IMP

Gastroenteral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): prasugrel

CAS number: 150322-43-3

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₀H₂₀FNO₃S

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 5 60

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Prasugrel, a thienopyridine derivative, is a platelet activation and aggregation inhibitor structurally and pharmacologically related to clopidogrel

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR27**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

ticagrelor

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable ticagrelor

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered B01AC24

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Ticagrelor will be administered by the enteral route 60mg twice daily till the end of study day 14 or hospital discharge whichever occurs first

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 60mg twice daily for 14 days =1680

D.3.6.2 Specify per day or total: ☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 1680 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Gastroenteral use

D.3.7 Routes of administration for this IMP

Gastroenteral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): ticagrelor

CAS number: 274693-27-5

Current sponsor code:

Other descriptive name:

Full Molecular formula C23H28F2N6O4S

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 120

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☐ Yes ☒ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Ticagrelor is indicated to reduce the risk of cardiovascular death, myocardial infarction, and stroke in patients with acute coronary syndrome or a history of myocardial infarction. Ticagrelor is also indicated to reduce the risk of a first myocardial infarction or stroke in high risk patients with coronary artery disease

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR28**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Pascorbin

EV Product Code

Name of the MA holder:

PASCOE

MA number (if MA granted by a Member State):

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Germany

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

| | |
|--|--|
| D.3.1 Product name where applicable | Pascorbin |
| D.3.2 Product code where applicable | |
| D.3.3 ATC codes, if officially registered | A11GA |
| D.3.4 Pharmaceutical form (use standard terms) | Solution for infusion |
| D.3.4.1 Is this a specific paediatric formulation? | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | 50mg/kg IV every 6 hours for 16 doses |

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

200 mg/kg
milligram(s)/kilogram

D.3.6.1 Route of administration (relevant to the first dose):

Intravenous use

D.3.6.2 Maximum dose allowed

200mg/kg

D.3.6.2 Specify per day or total

☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

200 mg/kg
milligram(s)/kilogram

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Ascorbic Acid

CAS number: 50-81-7

Current sponsor code:

Other descriptive name:

Full Molecular formula C₆H₈O₆

Chemical/biological description of the Active Substance

Strength

Concentration unit: g gram(s)

Concentration type: equal

Concentration number (only use both fields for range): 7.5

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Ascorbic acid, a water-soluble vitamin, is essential for formation of collagen and intercellular material, and therefore necessary for the development of cartilage, bone, teeth and for the healing of wounds. It is also essential for the conversion from folic acid to folinic acid, facilitates iron absorption from the gastro-intestinal tract and influences haemoglobin formation and erythrocyte maturation.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR29**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 16363/0357

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Ramipril

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09AA05

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 10mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 10 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Ramipril

CAS number: 87333-19-5

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₃H₃₂N₂O₅

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: up to

Concentration number (only use both fields for range): 2.5 10

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Ramipril inhibits the RAAS system by binding to and inhibiting ACE thereby preventing the conversion of angiotensin I to angiotensin II. As plasma levels of angiotensin II fall, less activation of the G-protein coupled receptors angiotensin receptor I (AT1R) and angiotensin receptor II (AT2R) occurs.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR30**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 0142/0468

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Lisinopril

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09AA03

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 DAYS

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit) mg
milligram(s)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 20mg/day

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 20 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): lisinopril

CAS number: 76547-98-3

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₁H₃₁N₃O₅

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 5 10

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Lisinopril is an angiotensin converting enzyme inhibitor (ACEI) used to treat hypertension, heart failure, and myocardial infarction. Lisinopril and captopril are the only ACEIs that are not prodrugs. It functions by inhibition of angiotensin converting enzyme as well as the renin angiotensin aldosterone system. ACEIs are commonly used as a first line therapy in the treatment of hypertension, along with thiazide diuretics or beta blockers.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR31**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 0142/0468

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable perindopril

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09AA04

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 8mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 8 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): perindopril

CAS number: 82834-16-0

Current sponsor code:

Other descriptive name:

Full Molecular formula C₁₉H₃₂N₂O₅

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 2 8

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Perindopril is a nonsulfhydryl prodrug that belongs to the angiotensin-converting enzyme (ACE) inhibitor class of medications. It is rapidly metabolized in the liver to perindoprilat, its active metabolite, following oral administration. Perindoprilat is a potent, competitive inhibitor of ACE, the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII).

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR32**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 16363/0066

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable enalapril

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09AA02

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 DAYS

D.3.6 Dose allowed

| | |
|--|---|
| D.3.6.1 First dose for first-in-human clinical trial | |
| D.3.6.1 Specify per day or total: | <input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| | |
| D.3.6.2 Maximum dose allowed | 20mg |
| D.3.6.2 Specify per day or total | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 20 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent) | |

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): enalapril

CAS number: 75847-73-3

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₀H₂₈N₂O₅

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 2.5 20

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Enalapril is a prodrug belonging to the angiotensin-converting enzyme (ACE) inhibitor drug class that works on the renin-angiotensin-aldosterone system, which is responsible for the regulation of blood pressure and fluid and electrolyte homeostasis.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR33**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 20075/0308

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable captopril

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09AA01

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 Days

D.3.6 Dose allowed

| | |
|--|---|
| D.3.6.1 First dose for first-in-human clinical trial | |
| D.3.6.1 Specify per day or total: | <input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| D.3.6.2 Maximum dose allowed | |
| | 50mg x3 daily |
| D.3.6.2 Specify per day or total | <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 150 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent) | |

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): captopril

CAS number: 62571-86-2

Current sponsor code:

Other descriptive name:

Full Molecular formula C9H15NO3S

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 18.75 150

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII). ATII regulates blood pressure and is a key component of the renin-angiotensin-aldosterone system (RAAS). Captopril may be used in the treatment of hypertension.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR34**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 00025/0374

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable losartan

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09CA01

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 Days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 50mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 50mg mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): losartan

CAS number: 114798-26-4

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₂H₂₃ClN₆O

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 25 50

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Losartan is an angiotensin II receptor blocker (ARB) used to treat hypertension. Angiotensin-converting enzyme (ACE) inhibitors are used for a similar indication but are associated with a cough.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR35**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 00101/0651

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable valsartan

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09CA03

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 160mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 160 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): valsartan

CAS number: 137862-53-4

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₄H₂₉N₅O₃

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 80 160

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Valsartan belongs to the angiotensin II receptor blocker (ARB) family of drugs, which also includes telmisartan, candesartan, losartan, olmesartan, and irbesartan. ARBs selectively bind to angiotensin receptor 1 (AT1) and prevent the protein angiotensin II from binding and exerting its hypertensive effects, which include vasoconstriction, stimulation and synthesis of aldosterone and ADH, cardiac stimulation, and renal reabsorption of sodium, among others

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR36**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

16189/0007

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable candesartan

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09CA06

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 16 mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 16 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): candesartan

CAS number: 139481-59-7

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₄H₂₀N₆O₃

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 4 18

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Candesartan is an angiotensin-receptor blocker (ARB) that may be used alone or with other agents to treat hypertension.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR37**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

EV Product Code

Name of the MA holder:

MA number (if MA granted by a Member State):

PL 16363/0371

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable irbesartan

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered C09CA04

D.3.4 Pharmaceutical form (use standard terms) Tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 150mg

D.3.6.2 Specify per day or total: ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 150 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Enteral use (Noncurrent)

D.3.7 Routes of administration for this IMP

Enteral use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): irbesartan

CAS number: 138402-11-6

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂₅H₂₈N₆O

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: range

Concentration number (only use both fields for range): 75 150

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Irbesartan is an angiotensin receptor blocker (ARB) indicated to treat hypertension or diabetic nephropathy. It can also be used as part of a combination product with hydrochlorothiazide for patients not well controlled or not expected to be well controlled on monotherapy.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR38**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☒ Yes ☐ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☐ Yes ☒ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP**D3-1.**

| | |
|--|--|
| D.3.1 Product name where applicable | Repagermanium |
| D.3.2 Product code where applicable | DMX-200 |
| D.3.3 ATC codes, if officially registered | |
| D.3.4 Pharmaceutical form (use standard terms) | Capsule |
| D.3.4.1 Is this a specific paediatric formulation? | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| D.3.5 Maximum duration of treatment of a subject according to the protocol | Fixed dose, twice daily for 10 days |

D.3.6 Dose allowed

| | |
|---|---|
| D.3.6.1 First dose for first-in-human clinical trial | |
| D.3.6.1 Specify per day or total: | <input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.1 Specify total dose (number and unit) | |
| D.3.6.1 Route of administration (relevant to the first dose): | |
| | |
| D.3.6.2 Maximum dose allowed | 240mg / day for 10 days |
| D.3.6.2 Specify per day or total | <input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered |
| D.3.6.2 Specify total dose (number and unit) | 2400 mg milligram(s) |
| D.3.6.2 Route of administration (relevant to the maximum dose): Gastroenteral use | |

D.3.7 Routes of administration for this IMP

Oral use

Gastroenteral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): DMX-200 (Repagermanium)

CAS number: 12758-40-6

Current sponsor code:

Other descriptive name: Repagermanium

Full Molecular formula C₆H₁₀Ge₂O₇

Chemical/biological description of the Active Substance hydrophilic small molecule and an organometallic compound of germanium

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 120

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. CCR2 inhibition may blunt excessive monocyte recruitment and mitigate associated injurious maladaptive sequelae of lung tissue inflammation and thrombosis in severe COVID-19

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR39**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☐ Yes ☒ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☒ Yes ☐ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☐ Yes ☒ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP**D3-1.**

D.3.1 Product name where applicable cysteamine bitartrate

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered A16AA04

D.3.4 Pharmaceutical form (use standard terms) Concentrate for solution for injection/infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 1500mg
5mg/kg 3 times a day for 10 days

D.3.6.2 Specify per day or total ☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 5 mg/kg
milligram(s)/kilogram

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Cysteamine bitartrate

CAS number: 27761-19-9

Current sponsor code:

Other descriptive name:

Full Molecular formula C₂H₇NS

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 200

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Cysteamine converts cystine to cysteine and cysteine-cysteamine mixed disulfides. This drug participates in a thiol-disulfide interchange reaction with lysosomes, leading to cysteine exit from the lysosome in patients diagnosed with cystinosis.

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR41**

Investigational medicinal product category:

Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

Casirivimab / imdevimab (Ronapreve)

EV Product Code

Name of the MA holder:

Roche Products

MA number (if MA granted by a Member State):

PLGB 00031/0925

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

☐ Yes ☒ No ☐ Not Answered

D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Casirivimab / imdevimab (Ronapreve)

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J06BD

D.3.4 Pharmaceutical form (use standard terms) Solution for injection/infusion

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol one 60 minute infusion

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 4g of Casirivimab 4 g of imdevimab (combined dose of 8g) injected into a 250ml PVC or PO infusion of 0.9% saline of 5% Dextrose and infused over 60min

D.3.6.2 Specify per day or total ☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 8 g gram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Casirivimab / imdevimab

CAS number:

Current sponsor code:

Other descriptive name: Ronapreve

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 120

D3-11. Type of IMP

Does the IMP contain an active substance:

- Of chemical origin? ☐ Yes ☒ No ☐ Not Answered
- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☒ Yes ☐ No ☐ Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☒ Yes ☐ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Casirivimab (IgG1κ) and imdevimab (IgG1λ) are two recombinant human monoclonal antibodies which are unmodified in the Fc regions. Casirivimab and imdevimab bind to non-overlapping epitopes of the spike protein receptor binding domain (RBD) of SARS-CoV-2 with dissociation constants KD = 45.8 pM and 46.7 pM, respectively. Casirivimab, imdevimab and casirivimab and imdevimab together blocked RBD binding to the human ACE2 receptor with IC50 values of 56.4 pM, 165 pM and 81.8 pM, respectively.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D8. Information on placebo (if relevant; repeat as necessary)**D8. Is there a placebo:**

☐ Yes ☒ No ☐ Not Answered

D9. Sites responsible for final QP release for distribution to investigators.**D9-1. IMPs and placebos for which no responsible site needs to be identified.**

This section is used to identify IMPs and placebos which:

- Have an MA in the EU **and**
- Are sourced from the EU market **and**
- Are used in the trial without modification (eg not overencapsulated) **and**
- The packaging and labeling is carried out for local use only as per article 9.2 of the Directive 2005/28/EC (GCP Directive).

If all the conditions above are met, then select below the IMPs and placebos to which this applies.

Finished IMP
PR1

Finished IMP
PR2

Finished IMP
PR3

Finished IMP
PR4

Finished IMP
PR5

Finished IMP
PR6

Finished IMP
PR7

Finished IMP
PR8

Finished IMP
PR10

Finished IMP
PR11

Finished IMP
PR12

Finished IMP
PR13

Finished IMP
PR20

Finished IMP
PR21

Finished IMP
PR28

Finished IMP
PR38

Index of Sites where the qualified person certifies batch release

In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medicinal Products in the European Union

D9-2. Who is responsible in the Community for the certification of the finished IMP or placebo?

This section is dedicated to finished IMPs, i.e. medicinal products randomised, packaged, labelled and certified for use in the clinical trial. If there is more than one site or more than one IMP is certified, use extra pages and give each IMP its number from section D1 or D7. In the case of multiple sites indicate the product certified by each site.

RS1

Both

Name of the organisation: Aesica Queenborough Limited

Address: Queenborough

Town/city: kent

Post code: ME11 5EL

Country: United Kingdom

Give the manufacturing authorisation number
35/20.2.8/0255

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
PR21

RS3

Both

Name of the organisation: Sanofi- Aventis Research and Development

Address: 371 Rue du Professeur Joseph Blayac

Town/city: Montpellier

Post code: 34184

Country: France

Give the manufacturing authorisation number

M18 /076

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
PR20

IMP
PR17

Placebo
PL1

RS4

Both

Name of the organisation: Mawdsleys

Address Mawdsley Brooks & Co. Ltd, Quest 22, Quest Park, Wheatley Hall Road,

Town/city Doncaster

Post code DN2 4LT

Country United Kingdom

Give the manufacturing authorisation number

German MA number: 6727989.00.00

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
PR28

RS5

Both

Name of the organisation: Fischer Clinical Services GmbH

Address Weil am Rhein

Town/city Baden-Wuerttemberg

Post code 79576

Country Germany

Give the manufacturing authorisation number

DE_BW_01_MIA_2021_0022

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
PR38

Placebo
PL1

RS6

Both

Name of the organisation: Biotec Services International Ltd
Address Trading as PCI Pharma Services, Biotec House, Central Park
Town/city Western Avenue, Bridgend Industrial Estate
Post code Bridgend, CF31
Country

Give the manufacturing authorisation number

MIA-IMP 19819

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

Placebo
PL1

RS7

Both

Name of the organisation: Fisher Clinical services UK LTD
Address Langhurstwood road
Town/city Horsham
Post code RH12 4QD
Country United Kingdom

Give the manufacturing authorisation number

If no authorisation, give the reasons:

DMX-200 is an IMP and does not have an MA

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
PR38

E: Design of the Trial.**E.1 Medical Condition or Disease under Investigation****E1-1. Medical condition or disease under investigation ⁽¹⁾**

Specify the medical condition(s) to be investigated (free text) :
 Community acquired pneumonia, including COVID-19 disease
 Medical condition in easily understood language
 Community acquired pneumonia, including COVID-19 disease
 Identify the therapeutic area
 Diseases [C] - Respiratory Tract Diseases [C08]

⁽¹⁾ In the case of healthy volunteer trials, the intended indication for the product under development should be provided.

E1-2. MedDRA information ⁽²⁾**MR1**

| | |
|---------------------|--|
| Version | 14.0 |
| Level | LLT |
| Classification Code | 10010120 |
| Term | Community acquired pneumonia |
| SOC | 10021881 - Infections and infestations |

⁽²⁾ Applicants are encouraged to provide the MedDRA lower level term (LLT) if applicable and classification code.

E1-3. Is any of the conditions being studied a rare disease? ⁽³⁾

☐ Yes ☒ No ☐ Not Answered

⁽³⁾ Refer to "Points to consider on the calculation and reporting of the prevalence of a condition for Orphan drug designation": COM/436/01
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/09/WC500003773.pdf

E2. Objective of the trial**E2-1. What is the principal research question/objective? Please put this in language comprehensible to a lay person.**

The primary objective of the REMAP is to identify the effect of a range of interventions to improve outcome of adult patients with severe community acquired pneumonia, who are admitted to ICU. This is defined by all cause mortality at 90 days from the date of enrolment into the trial.

E2-2. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to a lay person.

The secondary objectives are to determine the effect of the interventions on:

- ICU Mortality
- ICU length of stay
- Hospital length of stay
- Ventilator free day censored at 28 days
- Organ failure free days censored at 28 days
- Survival at 6 months

Health Related quality of life at 6 months including EQ5D5L and WHODAS.

Secondary Antibiotic Domain-specific endpoints(censored at day 90):

1. Multi-resistant organisms (MRO) colonization/infection: Isolation of multi-drug resistant (MDR) bacteria from clinical or screening specimens
2. C. difficile illness based on detection from feces using current standard of care diagnostics used at site
3. Serious adverse event (SAE) as defined in CORE protocol

Secondary Macrolide Domain-specific endpoints (censored at day 90):

1. Serious ventricular arrhythmia (including ventricular fibrillation) or sudden unexpected death in hospital.
2. Serious Adverse Events (SAE) as defined in CORE protocol

E2-3. Is there a sub-study?

☐ Yes ☒ No ☐ Not Answered

E3. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Current participant inclusion criteria:

Non-pandemic participants:

1. Adult patient admitted to an ICU for severe CAP within 48 h of hospital admission with both of the following:
 - 1.1. Symptoms or signs or both that are consistent with lower respiratory tract infection (for example, acute onset of dyspnea, cough, pleuritic chest pain)
 - 1.2. Radiological evidence of new-onset consolidation (in-patients with pre-existing radiological changes, evidence of new infiltrate)
2. Requiring organ support with one or more of:
 - 2.1. Non-invasive or invasive ventilatory support
 - 2.2. Receiving infusion of vasopressor or inotropes or both

Pandemic participants:

1. Adult patient with confirmed or suspected pandemic infection

E4. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Exclusion criteria

1. Healthcare-associated pneumonia:
 - a) Prior to this illness, has been an in-patient in any healthcare facility within the last 30 days
 - b) Resident of a nursing home or long term care facility
2. Death is deemed imminent or inevitable during this hospital admission AND one or more of the patient, substitute decision maker or attending physician are not committed to full active treatment
3. Previous participation in this REMAP within the last 90 days

Patients will be deemed eligible for each treatment domain if they don't meet any of the following domain specific exclusion criteria

Antibiotic Domain

1. Received more than 48 hours of intravenous antibiotic treatment for this index illness
2. More than 24 hours has elapsed since becoming eligible for this domain
3. Known hypersensitivity to all of the study drugs in the site randomization schedule
4. A specific antibiotic choice is indicated
5. The treating clinician believes that participation in the domain would not be in the best interests of the patient

Macrolide Duration Domain (if randomised to a beta-lactam plus macrolide intervention within the Antibiotic Domain)

1. The treating clinician believes that participation in the domain would not be in the best interests of the patient

Corticosteroid Domain

1. An indication to prescribe systemic corticosteroids for a reason other than community-acquired pneumonia (CAP) (or severe sepsis) such as chronic corticosteroid use before admission, acute severe asthma, or suspected or proven Pneumocystis jiroveci pneumonia
2. Have received an immunomodulatory dose of systemic corticosteroid therapy for more than 24 hours prior to the

time of enrolment. An immunomodulatory dose is defined as >20mg of hydrocortisone, >5mg prednisone, >4mg methylprednisolone or >0.8mg dexamethasone per 24 hours.

3. The treating clinician believes that participation in the domain would not be in the best interests of the patient. Further domain specific eligibility criteria may apply depending on the domain in question. Please refer to the respective Domain Specific Appendix to the protocol for details

E5-1. What is the primary outcome measure for the study?(max 5000 characters)

The primary outcome for all domains will be the occurrence of death at 90 days post enrolment.

In patients recruited who are suspected to have COVID-19 disease the primary outcome will be "number of days alive and not admitted to ICU up to day 21

Any death before hospital discharge is recorded as -1 on this ordinal scale. All patients who never receive organ failure support while admitted to an ICU will be coded as 22.

Timepoint(s) of evaluation of this end point (max 800 characters)

The occurrence of death will be collected between day 1 and day 90 from the time of enrolment into the trial until end of the hospital admission.

The protocol will usually identify a single primary end point but there may be a co-primary end point in some cases and/or a number of secondary end points.

E5-2. Secondary end point(s) (max 5000 characters)

1. ICU mortality censored at 90 days
2. ICU length of stay censored at 90 days
3. Ventilator free days censored at 28 days
4. Organ failure free days censored at 28 days
5. proportion of intubated patients who receive a tracheostomy censored at 28 days
6. Hospital length of stay censored at 90 days after enrolment
7. Destination at time of hospital discharge
8. Readmission to the index ICU during the index hospitalization in the 90 days following enrolment
9. Survival at 6 months after enrolment
10. HRQoL at 6 months after enrolment using the EQ5D
11. Disability status measured at 6 months after enrolment using the WHODAS

Secondary Antibiotic Domain-specific endpoints(censored at day 90):

1. Multi-resistant organisms (MRO) colonization/infection: Isolation of multi-drug resistant (MDR) bacteria from clinical or screening specimens
2. C. difficile illness based on detection from feces using current standard of care diagnostics used at site
3. Serious adverse event (SAE) as defined in CORE protocol

Secondary Macrolide Domain-specific endpoints (censored at day 90):

1. Serious ventricular arrhythmia (including ventricular fibrillation) or sudden unexpected death in hospital.
2. Serious Adverse Events (SAE) as defined in CORE protocol

Timepoint(s) of evaluation of this end point (max 800 characters)

90 days or 6 months after enrolment as applicable.

E6. What is the scope of the trial?

- | | | | |
|-----------------|--------------------------------------|-------------------------------------|------------------------------------|
| Diagnosis | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Prophylaxis | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Therapy | <input checked="" type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Not Answered |
| Safety | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Efficacy | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacokinetic | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacodynamic | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Bioequivalence | <input checked="" type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Not Answered |

Dose Response ☒ Yes ☐ No ☐ Not Answered

Pharmacogenetic ☐ Yes ☒ No ☐ Not Answered

Pharmacogenomic ☐ Yes ☒ No ☐ Not Answered

Pharmacoeconomic ☐ Yes ☒ No ☐ Not Answered

Others ☐ Yes ☒ No ☐ Not Answered

Specify:

E7-1. Trial type and phase⁽¹⁾

Human pharmacology (Phase I) ☐ Yes ☒ No ☐ Not Answered

Therapeutic exploratory (Phase II) ☐ Yes ☒ No ☐ Not Answered

Therapeutic confirmatory (Phase III) ☐ Yes ☒ No ☐ Not Answered

Therapeutic use (Phase IV) ☒ Yes ☐ No ☐ Not Answered

⁽¹⁾ The descriptions of the trial types provided are those recommended in preference to Phases. See page 5 of Community guideline CPMP/ICH/291/95. The development of a new indication after initial approval of a medicine should be considered as a new development plan.

E8. Design of the Trial.**E8-1. Is the trial design controlled?**

☒ Yes ☐ No ☐ Not Answered

Specify:

Randomised ☒ Yes ☐ No ☐ Not Answered

Open ☒ Yes ☐ No ☐ Not Answered

Single blind ☐ Yes ☒ No ☐ Not Answered

Double blind ☐ Yes ☒ No ☐ Not Answered

Parallel group ☐ Yes ☒ No ☐ Not Answered

Cross over ☐ Yes ☒ No ☐ Not Answered

Other ☒ Yes ☐ No ☐ Not Answered

Specify the design of the trial
randomised, embedded, multifactorial, adaptive platform trial

E8-2. If controlled, specify the comparator:

Other medicinal product(s) ☒ Yes ☐ No ☐ Not Answered

Placebo ☐ Yes ☒ No ☐ Not Answered

Other ☐ Yes ☒ No ☐ Not Answered

Number of treatment arms in the trial

24

E8-3. Single site in the Member State concerned (see also section G):

☐ Yes ☒ No ☐ Not Answered

E8-4. Multiple sites in the Member State concerned (see also section G):

☒ Yes ☐ No ☐ Not Answered

Number of sites anticipated in Member State concerned

40

E8-5. Multiple Member States

☒ Yes ☐ No ☐ Not Answered

Number of sites anticipated in the Community.

100

E8-6. Trial being conducted both within and outside the EEA

☒ Yes ☐ No ☐ Not Answered

Trial conducted completely outside EEA

☐ Yes ☒ No ☐ Not Answered

Specify the countries in which trial sites are planned

United Kingdom

Netherlands

Germany

Belgium

Portugal

Croatia

Hungary

Romania

Australia

New Zealand

Ireland

Canada

Bosnia and Herzegovina

Austria

Spain

Greece

Italy

Israel

Serbia

United States

Estonia

Specify the number of sites anticipated outside of the EEA

100

E8-7. Will a data monitoring committee (DMC) be convened?

☒ Yes ☐ No ☐ Not Answered

E8-8.

Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial.

If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition.

The study will end when the required numbers of patients have been recruited, the final follow up visit data for the last patient has collected and the databases have been locked.

The design features of this trial create a 'perpetual' trial whose main objective is to continuously update best patient treatment for the life time of the REMAP, but current EU funding is provided until 2021.

E8-9. How long do you expect the study to last? ⁽¹⁾

In all countries concerned by the trial

Years: 2 Months: 5 Days: 22

In the MS concerned

Years: 3 Months: 1 Days: 31

⁽¹⁾ From the first inclusion until the last visit of the last subject.

E8-10. Recruitment start date

Recruitment start date in MS

01/06/2018

In any country

10/02/2016

⁽¹⁾ If not provided in the protocol.

F: Population of Trial Subjects**F1. What is the age span of the trial subjects?**

| | | |
|--------------------------------|--|------------------------------|
| Less than 18 years | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered | Approx no of participants: 0 |
| Adult (18-64 years) | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered | Approx no of participants: 0 |
| Elderly (geater than 65 years) | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered | Approx no of participants: 0 |

The number of participants will be initial estimates. Applicants will not be required to update this information nor do they constitute an authorisation or restriction on the inclusion of these numbers of patients in the trial.

F2. What is the gender of the trial subjects?

Female ☒ Yes ☐ No ☐ Not Answered

Male ☒ Yes ☐ No ☐ Not Answered

F3. Please select the categories of the trial subjects:

| | |
|--|--|
| Healthy volunteers | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Patients | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| Specific vulnerable populations | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| Women of childbearing potential not using contraception | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| Women of child bearing potential using contraception | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| Pregnant women | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| Nursing women | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| Emergency situations | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| Subjects incapable of giving consent personally | <input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered |
| If yes, please specify: Patients admitted with community acquired pneumonia and COVID-19 infection will most often need treatment started in a life-threatening emergency and will be unable to provide informed consent at this time due to reduced mental capacity. | |
| Others | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |

F4. Planned number of subjects to be included:

In the member state 6000

For a multinational trial:

In the European community: 4000

In the whole clinical trial: 8000

F5. Plans for treatment or care after a subject has ended his/her participation in the trial. If it is different from the expected normal treatment, please specify:

Not applicable. The interventions will be provided to the patients for the period that they are in the intensive care

unit/hospital.

G1. and G2. Investigator Details**G1. National coordinating investigator (for a multicentre trial) or principal investigator (for a single centre trial)**

- ☒ National coordinating investigator
☐ Principal investigator

Given name Anthony
 Family name Gordon
 Qualification (MD...) MD, FRCA, FFICM
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 Institution department name Surgery & Cancer
 Street address Fulham Palace Road
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 Post Code W6 8RF
 Country United Kingdom
 Telephone 02033130657
 Fax 02078316879
 E-mail anthony.gordon@imperial.ac.uk

G2. Other principal Investigators (for a multicentre trial)**IN2**

Given name David
 Family name Rogerson
 Qualification (MD...) MD
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IN3

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Fax
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IN4

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IN5

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IN6

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IN7

Given name Christopher
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| | |
|-----------------------------|--|
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IN8

| | |
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| Town/city | |
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IN10

| | |
|-----------------------------|---|
| Given name | Jason |
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| Fax | |
| E-mail | Dr.cupitt@bfwhospitals.nhs.uk |

IN11

| | |
|-----------------------------|--|
| Given name | Daniel |
| Family name | Conway |
| Qualification (MD...) | MD |
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| Institution department name | |
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IN14

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IN15

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IN16

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IN18

Given name Henrik
 Family name Reschreiter

| | |
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IN19

| | |
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| Telephone | |
| Fax | |
| E-mail | |

IN20

| | |
|-----------------------------|--------------------------------------|
| Given name | Andrew |
| Family name | Walden |
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IN21

| | |
|-----------------------------|--|
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| Family name | Roy |
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IN22

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IN23

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IN24

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IN25

Given name Prad

| | |
|-----------------------------|--------------------------------------|
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IN26

| | |
|-----------------------------|--|
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IN27

| | |
|-----------------------------|---|
| Given name | David |
| Family name | Golden |
| Qualification (MD...) | MD |
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| Institution department name | |
| Street address | MAIDSTONE HOSPITAL |
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| Telephone | |
| Fax | |
| E-mail | david.golden@nhs.net |

For multi-centre trials where the CI is also a local PI, please list the CI as a PI at G2 (single-centre).

G3. Central Technical Facility Details

G3. Central technical facilities to be used in the conduct of the trial. *Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised.*

Organisation

Central technical facility organisation name
 Central technical facility organisation department
 Contact person Given name
 Contact person Family name
 Street address
 Town/city
 Post code
 Country
 Work Telephone
 Fax
 E-mail

Enter the details of any duties subcontracted to this central technical facility in this trial:

| | | | |
|---|---------------------------|-------------------------------------|------------------------------------|
| Routine clinical pathology testing | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Clinical chemistry | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Clinical haematology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Clinical microbiology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Histopathology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Serology / endocrinology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Analytical chemistry | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| ECG analysis / review | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Medical image analysis/ review - X-ray, MRI, ultrasound, etc. | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Primary/ surrogate endpoint test | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Other | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |

Network organisation details

G4. Network organisation details

Organisation
 Contact person Given name
 Contact person Middle name
 Contact person Family name
 Street address
 Town/city
 PostCode
 Country
 Telephone number
 Fax number

E-mail

Activities carried out by the network

G5. Organisations to whom the sponsor has transferred trial related duties and functions**G5. Subcontractor organisations.***Enter details of central CRO facilities supplying services for at least this Member State.*

| | |
|----------------------------|-----------------------------------|
| Organisation | Mawdsleys |
| Department | Trial Management |
| Contact person Given name | Samatha |
| Contact person Family name | Howcroft |
| Street address | Mawdsley Brooks & Co |
| Town/city | Doncaster |
| PostCode | DN2 4LT |
| Country | United Kingdom |
| Telephone number | |
| Fax | |
| E-mail | Samantha.Howcroft@mawdsleys.co.uk |

Enter the details of any duties/ functions subcontracted to this sponsor's subcontractor facility in this trial

| | |
|---|--|
| All tasks of the sponsor: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Monitoring: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Regulatory (e.g. preparation of applications to CA and Ethics Committee): | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Investigator recruitment: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| IVRS ⁽¹⁾ - treatment randomisation: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Data management: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| E-data capture: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| SUSAR reporting: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Quality assurance auditing: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Statistical analysis: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Medical writing: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |
| Other duties subcontracted: | <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered |

H: Ethics Committee

H1-1. Type of application

Please tick the Ethics Committee box and give information of the Ethics committee concerned.

Ethics committee ☒

H2-1. Limited Name and address of ethics committee:

Organisation London - Surrey Borders Research Ethics Committee

Work Address

PostCode

Country

Fax

H2-2. Date of submission:

23/03/2018

H2-3. Current status of Ethics Committee Opinion at the time of submission to the National Competent Authority:

☐ To be requested ☐ Pending ☒ Given

If "Given", please specify:

Date of opinion: 18/04/2018

State opinion: ☒ Accepted ☐ Not Accepted

I: Signature Of The Applicant In The Member State

I1. I hereby confirm that /confirm on behalf of the sponsor (tick which is applicable) that:

- ☒ The information provided is complete;
- ☒ The attached documents contain an accurate account of the information available;
- ☒ the clinical trial will be conducted in accordance with the protocol;
- ☒ The clinical trial will be conducted, and SUSARs and result-related information will be reported, in accordance with the applicable legislation.

I2. Applicant of the request for the competent authority (as stated in section C.1):

This section was signed electronically by Ms Clementina Okundaye on 17/02/2022 12:09.

Job Title/Post: JrPM REMAP-CAP
Organisation: University Medical Centre Utrecht
Email: c.okundaye@umcutrecht.nl

J: Checklist

J3. For details of the documents required for applications to the MHRA in the UK please see
**[http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/
Applyingforaclinicaltrialauthorisation/Whattosend/index.htm](http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Applyingforaclinicaltrialauthorisation/Whattosend/index.htm)**