**FAQs**

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| **Question** | **Answer** |
| **Site Admin** | |
| 1. Do pharmacists need to be GCP trained | The study (research) pharmacist listed on the delegation log need to be GCP trained. Clinical pharmacists on the wards / ICU do not. |
| 1. Who can prescribe REMAP-CAP treatments? | The study pharmacist should be listed on the delegation log, and GCP trained. This pharmacist can oversee the prescribing for the study but the prescribing clinicians do not need to be listed on the delegation log or GCP trained. |
| 1. Can we confirm do all pharmacists need GCP or just pharmacists within the clinical trials team set up | Only those dealing with the drug supply for the trial, the research pharmacist. Other clinical pharmacists in the hospital or ICU do not. |
| 1. Our site might struggle to open baloxavir as our drug administers are not GCP trained | As this is a clinically approved drug (used in routine practice), the administers of the drug are not required to be on the delegation log or GCP trained.  Staff should still receive appropriate medication training for Baloxavir. For instance, this drug is **NOT** given daily due to its longer half life. |
| 1. Can anyone obtain consent if they are delegated to do so on the delegation log? | Yes, if the PI has delegated the responsibility of taking consent to a doctor or nurse either can obtain consent as long as they are appropriately trained. |
| 1. Is deferred consent approved for this study? | Yes, this was more relevant for ICUs but if a ward patient lacks capacity the same deferred consent model can be applied. Please ensure the patient has the opportunity to consent and speak to NOK first if possible. Always seek retrospective consent once the patient regains capacity. |
| 1. Can we adapt the consent form? Remove parts that we are not participating in? | Yes, we have designed the consent forms so that you can remove domains/interventions that your site is not participating in, and we can also remove treatments once they are no longer available. |
| 1. Do clinicians who are confirming eligibility need to be on the delegation log? | Yes, clinicians confirming eligibility should be listed. |
| 1. Can ACCPs confirm eligibility? | Yes, they can, but these would need to be listed on the delegation log, as this study is a CTIMP medical oversight is required. |
| 1. Does AM037 include updates to the PIS/ICF | Yes, and we have taken the opportunity to streamline these too so hopefully they are easier and simpler to use. |
| 1. Who can sign off Co-PI’s in different departments | The lead PI can sign off the Co-PI’s |
| 1. If a site is already open but we are not opening the Paeds department would that be considered a new site | No, a new site would be defined as a new site contract. If a current contract with a Trust stands and a department is added this is considered in addition to the current site and not a new site. |
| 1. Is the new mCTA on the website | For new sites we will provide new contracts but for existing sites we will generate variations/appendix as needed including the new funding arrangements. |
| 1. Do open sites who are moving to the wards receive a site set up fee | The new site set up fee covers contract negotiations and pharmacy checks, therefore if a site is already open and moving into the ward a site set up fee would not apply.  There is an additional site fee for existing sites when they expand to the new influenza domains. |
| 1. Will a new eligibility checklist be distributed | Yes, this is available on our website |
| 1. Is there training available for local teams | Yes, please see our website, we have training slides, the webinar recordings and training logs. |
| 1. Can we run the study only on the intensive care unit or do we need to agree to the ward elements as well? | Yes, you can focus on ICU only. We would encourage sites to expand to wards as many patients with flu are going to be on the ward and treating early is likely to be most effective. If not practical let us know. |
| 1. For the eCRF are we using spinnaker | Yes |
| 1. Can we co-enrol with ASPECT | Yes |
| 1. Can we co-enrol with any observational studies | Yes, REMAP-CAP can co-enrol with any observational studies |
| 1. Can we co-enrol with MARCH? | Yes, we can co-enrol with MARCH, we cannot co-enrol MARCH patients in the cysteamine domain in REMAP-CAP but all other domains. |
| 1. Can we co-enrol with RECOVERY? | RECOVERY are only recruiting patients with influenza in Scotland. Patients with influenza enrolled to RECOVERY influenza interventions should not be enrolled in REMAP-CAP.  A patient with COVID and influenza could be enrolled to both COVID treatments in RECOVERY and influenza treatments in REMAP-CAP |
| 1. Who completes the day 180 follow up calls with the patients? | The site teams complete these calls, the time for this was factored in to the SoECAT and the per patient fee. |
| 1. Are the current PIS/ICF available in other languages? | No, we do not currently have translations of these. We are looking into developing these and will inform sites in the future once they are available. |
| 1. How will monitoring be organised? Will ward and ICU teams be visited together or separately. | The sponsor and REMAP-CAP team are currently updating the monitoring plan and will provide an update as soon as confirmed. **Update: ICU, wards and paeds will be monitored separately. Unless it is easier for the site to join these visits.** |
| 1. We would usually collect personal information such as address and next of kin, is this information needed for the trial? | We will only ask for information as described in the patient information sheet to be provided on the database. This does not include the patients address or next of kin. |
| 1. Are you collecting any documents such as financial disclosure forms or GP letters? | No. |
| 1. If we cannot reach a patient or family member for consent is there a set timeframe that we should try to get consent within? | We do not have a set timeframe for this. We rely on the site’s professional judgement on the number of times they deem appropriate to reach out to the patient or family member. We ask that you make sure you document all attempts/ conversations that are had around consent. |
| **Influenza inclusion** | |
| 1. Does a patient have to be flu positive before we can randomize? | Yes |
| 1. Would a point of care test from A&E be sufficient in confirming influenza? | Yes |
| 1. For the ‘no antivirals intervention’ the guidance states that no antiviral should be given for 28 days, what happens if an antiviral is given in this time? | We keep the patient in the study but raise a protocol deviation. |
| 1. Do we need to ringfence hospital stock? | We are not mandating sites to ringfence stock for your business-as-usual hospital clinical stock, pharmacists may choose to do this as part of their processes, but we are not mandating this.  For drug stock supplied specifically for REMAP-CAP e.g. baloxavir, this does need to be ring-fenced for the trial |
| 1. Do you require us to capture subtypes of influenza | This is not mandatory, however if your site does run tests for subtypes this could be helpful and so please do enter the subtype if known on the eCRF. |
| 1. Are we including incidental influenza? | No, please only include patients who are acutely unwell due to influenza not incidental cases. |
| 1. Would all participants have to have CAP as well as influenza to be eligible for the influenza platform? | The whole platform is CAP rather than influenza, but we are focusing on influenza this winter. Only influenza patients are included from the ward right now. |
| 1. Can you clarify the moderate vs severe state? | Severe state = patient is in ICU AND receiving respiratory and/or support.  Moderate state = all other patients:-  in ICU receiving no cardio or respiratory support, all patients not in ICU. |
| 1. If patients are randomised in moderate and move to severe state can they be re-randomised? | No, patients can only be randomised in each domain once.  If they are randomised to a domain in a moderate state and later move to severe state and are now eligible for a new severe state domain they can be randomised to this new domain as this is a different domain. |
| 1. The corticosteroid domain says it’s for “patients admitted to hospital with CAP, including patients with suspected or proven influenza”. Does this mean patients with bacterial pneumonia with no suspicion of flu can be recruited to the corticosteroid domain? | This is possible with the current corticosteroid domain but we are focusing on recruiting patients with flu on the ward at this time. |
| 1. Do we need to have confirmed radiological evidence for patients for eligibility | No, the patient must be acutely unwell because of flu |
| 1. If we do not have equipoise for the ‘no oseltamivir’ option can we amend the interventions per patient? | No, patients must be balanced at each site for the analysis, we cannot adjust for individual patients and so you must decide which interventions are available for all patients and not select per patient. |
| 1. Can patients be recruited from the Emergency Department? | Yes, as long as they are being admitted to hospital. The earlier the better but they will need to be flu positive which is not always known while in ED. But currently we realise patients could spend a long time in ED |
| 1. Is baseline or randomisation classed as day 1? | Once the patient is randomised, this is day 1. Prior to randomisation is baseline |
| 1. How much supplemental oxygen does a patient need to be on to be recruited, i.e., 0.5 litres/1 litre of O2 via nasal specs, would these patients be classed as too well to participate? | Any level, there is no set criteria. They would be eligible even on low flow oxygen in the steroid domain. |
| 1. Is co-infection an exclusion criteria? | It is not a specific exclusion to the platform but would be for individual interventions. |
| 1. Our ICU likes to prescribe hydrocortisone for high vasopressor use, would that be an exclusion criteria? | For ICU patients, we have the two doses of steroids or the shock only intervention. If your ICU believes it to be unacceptable to give steroids in these patients with shock you can just select the interventions which work best for you. |
| **IMP** | |
| 1. Will there be a new pharmacy guide | The pharmacy guide was generated during covid as there were many interventions and so the guide was generated to help pharmacists. The domain specific appendix and administration guides contain all the information pharmacists require. |
| 1. Tamiflu is standard of care in some Trusts, can we still participate in the Oseltamivir treatment of the Antiviral domain? | There are two responses to this:-   1. There is uncertainty about evidence for Tamiflu (oseltamivir) in hospitalized patients and certainly no RCT evidence to support its use. Therefore we encourage randomisation including no-antiviral treatment so that we learn if it is useful or not in this population 2. If the site does not have equipoise for the ‘no oseltamivir’ intervention, the site can still participate in this treatment option but select 5 days and 10 days and not the ‘no oseltamivir’ option. |
| 1. The dose of Oseltamivir in the DSA does not match the BNF guidelines for children | There is limited evidence in this area, based on the evidence we have provided one suggested dose from a previous RCT, as a guide. As per the DSA please follow your standard practice in the first instance. |
| 1. Do patients need to be weaned off steroids | No, as this is a short course no need for weaning, it can just be stopped after the course is completed. |
| 1. If the patient receives 2 doses of Oseltamivir in the community are they excluded from this domain? | The patient would be excluded from the antiviral domain as they have already been treated with an anti-viral drug. |
| 1. Do you require a specific formulation of oseltamivir | No, you can use any formulation you would usually use, capsules, suspension or capsule contents dissolved in water. |
| 1. Oseltamivir and corticosteroids will be used from routine stock. Do they require any clinical trial specific labelling? | No, these do not require any trial specific labelling as they are used in routine clinical practice. |
| 1. The protocol states that the treatment should continue once the course is complete or hospital discharge, can we discharge the patient with the treatment to finish the course? | It is not required to send the patient home with treatment to finish the course. If you choose to do so, please ensure the correct course duration is provided i.e. no more than 5 or 10 days depending on the allocation |
| 1. How do we get Baloxavir | Baloxavir will be provided by Roche for free to sites. Sites can request the order form from the [ukremap-cap@icnarc.org](mailto:ukremap-cap@icnarc.org) address. Sites must be open to the antiviral domain before ordering. |
| 1. Do we have to follow the baloxavir dosing in the DSA or can we follow our local policy | The dosing information in the DSA is provided as guidance, sites can choose to follow their local policy if they wish as long as they give the dose over the correct duration. |
| 1. Does Baloxavir require accountability? | Accountability is required at pharmacy level on inventory/accountability logs, but not at ward level. |
| 1. How should we document returns or expired/unused stock | Baloxavir that has been dispensed for a patient does not have to be returned from wards to pharmacy for counting or logging on an accountability log - these should be disposed of by the research team on the ward as they would for other drugs used in the clinical areas. If pharmacy have any unused or expired Baloxavir, pharmacy should email [ukremap-cap@icnarc.org](mailto:ukremap-cap@icnarc.org) for permission to destroy then file a copy of the destruction certificate in the pharmacy site file. |
| 1. The licensed dose for baloxavir is a single dose, what is the rationale for using 2 or 3? | Hospitalised patients are classed as ‘complicated influenza’ and therefore we recommend a second dose. Baloxavir has a half life of 79hrs. Therefore if the patient is still unwell on day 4 give another dose, if not and has been discharged home, do not give a dose on day 4. |
| 1. When do we give baloxavir at day 7? | This is at local clinical discretion. In previous trials if the patient is still unwell a third dose on day 7 has been given. |
| 1. It is our normal practice to discharge patients home with a course of oseltamivir, can we still do this? | Yes, this is fine as long as the patient does not exceed the randomized duration i.e., no more than 5 days or 10 days depending on the intervention. |
| 1. When will Tocilizumab and Baricitinib be available in the study | This will require another amendment which we hope to submit in 2023. |
| 1. Can you clarify what samples we need to take? | Only nasal swabs are required as part of the influenza stratum. These will be provided to your site once open, with pre-packaged safe boxes for return. |
| 1. How long will it take you to send swabs to sites | We will send the swabs to sites in Jan 2023 |
| 1. Can sites still recruit even without the swabs | Yes, the information we obtain from the swabs are not part of our primary outcome. Please do continue to recruit patients before the swabs arrive. |
| 1. Do we need to store swabs in the fridge/freezer | Swabs can be stored at room temperature. |
| 1. How many days can we keep the swab at room temperature (if required) | Up to 5 days. We therefore suggest sites to send them back to us twice a week. If they have one patient, please collect day 1 and day 3 samples and then send them back. |
| 1. Is there a time window for sampling? What do we do if day 3 falls on a weekend? Miss the swab? | Please take the swab as close to the timepoint as possible. If you miss the timepoint, please take the swab ASAP afterwards and enter the correct date. Alternatively take the swab upto 24 hours early |
| 1. Our pharmacists do not work weekends, are we able to dispense Baloxavir out of hours so they are available on the wards when we need it? | Yes, this is fine. Please make sure that it is kept in a secure location and that doses are only given on the correct days. |
| 1. Is there a specified time interval between administration of Baloxavir marboxil and enteral feed, calcium, zinc, iron/ other polyvalent cation containing medicines/supplements | The recommendation is to avoid concomitant administration because of the risk of complex formation between baloxavir and bivalent cation in the GI tract, which may reduce the absorption. Ideally, morning vs evening administration would be good; if not possible 4-5h apart. |
| **Paediatrics** | |
| 1. For the ‘within 48hrs of ICU criterion’ would this start at critical care retrieval only or admission to a PICU? | PICU admission time, as the difference is not likely to be many hours. |
| 1. What is the rationale of discontinuing at discharge if randomised into 10 days arm? | Adults tend to stay longer than children, and this was designed with adults in mind initially, there are some patients who do spend longer time in hospital, if you don’t want to participate in 10 day arm and prefer to just participate in the 5 day arm, this is fine |
| 1. Can you dissolve baloxavir in something that tastes nice   **UPDATE** | The company only have data for Ora-Blend which is difficult to get hold of in the UK. The volume is the main issue.  **Due to the lack of availability of ORA-Blend please only include severe patients (with NG tube) in the baloxavir intervention for now.** |
| 1. If baloxavir liquid is not made available what guidance is available regarding NG administration   **UPDATE** | Roche has provided instructions and this will be made available to sites. Essentially disperse one tablet in 100mL and give the required volume.  **As above, please only randomise severe patients (in ICU) to baloxavir for now due to the volume issue.** |
| 1. Should fluid restricted patients be excluded from baloxavir? | At the moment yes, for patients on the ward or that have fluid restrictions please exclude these from baloxavir at the moment due to the volume issue. We hope that by next winter we will have a solution for this. |
| 1. How do we handle inhaled zanamivir? | Inhaled zanamivir is not permissible as per the protocol. If the clinician plans to give zanamivir to the patient as is immunocompromised for example then the patient should be excluded for the following reason ‘not in best interest to randomise patient’ |
| 1. If the patient requires hydrocortisone on admission due to the signs of shock and later turns out to be flu positive, would the patient be eligible? | If you intend to give the patient steroids they would not be eligible to be randomised to that domain. |
| 1. Is dosing for baloxavir in adolescents ≥ 12yrs of age, is this based on actual body weight | Yes |
| 1. Fixed duration dexamethasone intervention (0.15mg/Kg to max dose of 6mg/day for 10 days), is this given IV or enterally – does this refers to dexamethasone base? | We advise that you use the same preparations as you would for patients with COVID-19. |
| 1. Can dosing for children can be according to local policy/SmPC rather that the dose given in the protocol of 4mg/kg/day. | Yes, we have provided guidance in case you do not have a local policy |
| 1. There are different dose recommendation in the protocol to the pharmacy manual. | Please follow the DSA in the first instance, the pharmacy manual provides more detail but the information is the same. |
| 1. The adult CRF uses the Apache II scoring tool in ICU. Do you have a specific paediatric tool you would like us to use, or is this a local decision | Our eCRF has been updated for paediatric patients both the pSOFA and ICU PIM3 score are applicable. |
| 1. How would we tell the difference between acute influenza infection and viral load from a nasal vaccination (up to 6 weeks ? ) should this be an exclusion criteria / or is there a way to tell the difference ? | It is uncommon that we detect flu virus in this way and so we need to be pragmatic about this, if the patient has and requires treatment for flu then include them in the study. |
| 1. What age are patients classified as adults? | Anyone aged 12+ in REMAP-CAP is classed as an adult. |