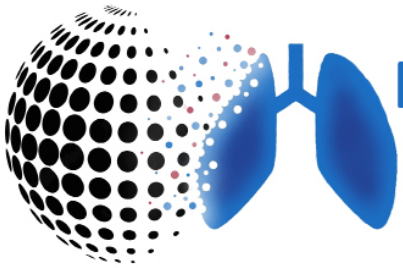

REMAP-CAP
Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia

Pharmacy Guide

REMAP-CAP: Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia

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REMAP-CAP Pharmacy Guide Version 5 dated 24th April, 2026

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1. INFLUENZA IMMUNE MODULATION DOMAIN

1.1. Tocilizumab

1.1.1. Presentation

The following preparations are available:

- Tocilizumab 400mg/20mL vial and 200mg/10mL vial (RoActemra® /Actemra®)
- Tocilizumab 80mg/4mL vial (RoActemra® /Actemra®)

1.1.2. Storage

Tocilizumab vials should be protected from light and heat. Keep the container in the outer carton to protect it from light. Store vials at 2°C to 8°C. Refrigerate. Do not freeze.

1.1.3. Warnings

Tocilizumab does not contain any antimicrobial agent; therefore, care must be taken to ensure the sterility of the prepared solution.

The product is for single use in one patient only. Discard any residue.

The prepared infusion solution is physically and chemically stable in 0.9% w/v sodium chloride solution at 30°C for 24 hours. To reduce microbiological hazard, the prepared infusion should be used immediately. If storage is necessary, hold at 2°C to 8°C for not more than 24 hours.

The occupational hazard of intermittent low-dose exposure to tocilizumab is not known. To minimize exposure, gloves and surgical mask should be worn when preparing this medication. Please refer to local protocol or guidelines on this matter.

Do not prepare if pregnant or trying to conceive.

1.1.4. Dosing

Tocilizumab will be administered intravenously at a dose of 8mg/kg based on measured or estimated body weight, with a total dose not exceeding 800 mg. In children weighing less than 30kg, the tocilizumab dose will be 12mg/kg.

Doses should be rounded to the nearest 10mg (which represents the nearest 0.5mL measurable volume).

1.1.5. Duration of therapy

A single dose of tocilizumab will be administered.

1.1.6. Preparation and administration

This infusion may be made in an aseptic environment or at the bedside, depending on local regulations. It is recommended that the tocilizumab infusion is prepared in 100mL sodium chloride 0.9% bag; however, for patients under 30kg, a 50mL sodium chloride 0.9% infusion bag may be used instead at the discretion of the treating clinician.

1. Calculate the volume (mL) required for the dose
    a. For adults and children weighing 30kg or more, the prescribed dose is 8 mg/kg estimated or measured body weight, with a maximum dose of 800 mg.
    b. For children < 30kg the prescribed dose is 12mg/kg estimated or measured body weight
    c. Round dose to the nearest 10mg (0.5 mL)
2. Withdraw this volume from a 100mL sodium chloride 0.9% infusion bag.
3. Discard the volume withdrawn from the sodium chloride 0.9% infusion bag. This will ensure that the final volume is 100mL after the drug has been added
4. Withdraw the required volume of tocilizumab solution for the patient dose
5. Add the tocilizumab solution to the 100mL sodium chloride 0.9% infusion bag
6. Gently invert the bag to mix, do not shake
7. Inspect the bag. Only bags which are clear to opalescent, colorless to pale yellow and free of visible particles can be infused
8. Prime the line with the tocilizumab infusion then administer infusion intravenously over 60 minutes via a central or peripheral line

a. The recommended infusion speed must be 10mL per hour for 15 minutes and then increased to 130mL per hour for the next 45 minutes.

b. If 50 ml bag is used, then infusion rate is half of that listed above.

c. If local policies allow then the infusion can be administered as a fixed speed over 60 minutes.

9. Flush line at the same rate as the tocilizumab infusion with 10-20mL of sodium chloride 0.9%

10. Observe for hypersensitivity reaction during, and for 30 minutes after IV infusion.

If made at the bedside, administer infusion immediately after preparation and discard remaining vials. If made in an aseptic environment, the diluted solution may be stored at 2-8°C for up to 24 hours prior to administration.

1.1.7. Dose adjustment

For the purposes of this trial, no dose adjustment is made for impaired renal function or concomitant use of renal replacement therapy.

1.1.8. Potential drug interactions

Additional agents that are intended to modulate the immune response against influenza infection, other than those included in the REMAP-CAP platform, should not be administered.

1.1.9. Discontinuation

The treating clinician can discontinue the study drug at any time if doing so is regarded as being in the best interests of the patient.

Tocilizumab should be discontinued if there is development of a serious adverse event. Study drug can be discontinued at any time by the treating clinician if doing so is regarded as being in the best interests of the patient.

1.2. Baricitinib

1.2.1. Presentation

The following preparations are available:

- Baricitinib 4mg tablet (Olumiant®)
- Baricitinib 2mg tablet (Olumiant®)
- Baricitinib 1mg tablet (Olumiant®) [Only in some countries]

1.2.2. Storage

Store below 30°C. Store in the original package.

1.2.3. Warnings

Staff should wear a mask and gloves when dispersing Baricitinib. Do not prepare or disperse Baricitinib tablets if pregnant.

If a 2mg tablet must be split to create a 1mg dose (see below), this should be performed in a pharmacy in a suitable powder containment cabinet (e.g., laminar flow hood). In areas where all staff are in full PPE, and if local policies allow, the 2mg tablet may be cut in half using a tablet cutter with a blade.

1.2.4. Dosing

Baricitinib dose is dependent on age and renal function, based on the table below:

Table 1. Baricitinib dosing by age and renal function

Age	eGFR	Baricitinib dose
2 – 9 years	≥60 mL/min/1.73m^2	2mg daily
	≥30 and < 60 mL/min/1.73m^2	1mg daily
	<30 mL/min/1.73m^2	Withhold dose
	Receiving renal replacement therapy	Withhold dose
≥ 9 years	≥60 mL/min/1.73m^2	4mg daily
	≥30 and < 60 mL/min/1.73m^2	2mg daily
	≥15 and <30 mL/min/1.73m^2	1mg daily
	<15 mL/min/1.73m^2	Withhold dose

	Receiving renal replacement therapy	Withhold dose

If a 1mg dose is required, but 1mg tablets are not available, a 2mg tablet can be split to administer half a 2mg tablet once daily. Alternatively, 2mg of Baricitinib can be given every second day.

If you intend to split Baricitinib tablets, please note the warnings above.

1.2.5. Duration of therapy

Baricitinib will be administered for 10 doses or until hospital discharge, whichever occurs first.

1.2.6. Preparation and administration

1.2.6.1. *For patients who are able to swallow whole tablets*

Preferred method of administration is tablets swallowed whole.

1.2.6.2. *For patients with swallowing difficulties*

For patients who are unable to swallow whole tablets and have an enteral feeding tube in situ:

1. Place the tablet(s) in sterile water in an enteral syringe.
    a. Use 15mL of water for a gastrostomy tube, or 30mL of water for a nasogastric tube
2. Swirl gently until completely dispersed and an even suspension is formed. The tablet may take 5 minutes to completely disperse.
3. Administer the solution via the tube soon after preparation.
4. Rinse the enteral syringe with 15mL of water to ensure the entire dose is given

Note that this solution may block tubes that are smaller than size 12 French.

1.2.7. Dose adjustment

Baricitinib dose is adjusted for renal function (see Table 2). There is no adjustment for liver impairment.

1.2.8. Potential interactions

The dose of baricitinib may need to be reduced in patients taking strong Organic Anion Transporter 3 (OAT3) inhibitors, such as probenecid.

1.2.9. Discontinuation

The treating clinician can discontinue the study drug at any time if doing so is regarded as being in the best interests of the patient.

Baricitinib should be discontinued if there is development of a SAE which, in the opinion of the treating clinician, could be related to participation in this domain. Study drug can be discontinued at any time by the treating clinician if doing so is regarded as being in the best interests of the patient.

2. INFLUENZA ANTIVIRAL DOMAIN

2.1. Baloxavir

2.1.1. Presentation

The following preparations will be provided by Roche:

- 20 mg white to light yellow, film-coated tablets
- White to light yellow granulate for oral suspension (2mg/ml, 20ml after reconstitution)

2.1.2. Storage

Tablets: Store between 15°C and 30°C. Store in the original package. Protect from light.

Oral solution (before and after reconstitution): Store below 30°C. Protect from light.

2.1.3. Warnings

None.

2.1.4. Dosing

Baloxavir dosing is based on weight, as shown in the table below:

Table 2. Baloxavir dosing by weight.

Weight	Baloxavir dose	Volume of oral suspension (2mg/ml)
< 20kg	2mg/kg on days 1 and 4	1ml/kg on days 1 and 4
20 – 80kg	40mg on days 1 and 4	20ml on days 1 and 4
> 80kg	80mg on days 1 and 4	40ml on days 1 and 4

2.1.5. Duration of therapy

The participant is to receive a dose of baloxavir on study day 1 and study day 4, while they remain admitted to hospital. A third dose may be administered on study day 7 if, in the opinion of the treating clinician, there has been insufficient clinical improvement.

2.1.6. Preparation and administration

2.1.6.1. *For patients unable to swallow whole tablets*

1. Place the tablet in at least 10 ml of water and gently swirl. In case multiple tablets are required, add 5-10 ml of water for each additional tablet. It may take up to 10 minutes for the tablet(s) to dissolve into a cloudy, light-pink suspension. Some sedimentation may occur.
2. After the tablet has dispersed, gently swirl the suspension again and immediately administer the entire suspension.
3. Administer orally, via NG tube or gastrostomy as appropriate and according to local policy.
4. Rinse the container with 5-10 ml of water and immediately administer the entire contents.

2.1.6.2. *Oral solution*

1. Gently tap the bottom of the bottle to loosen the granules.
2. Add a measured 20 mL of drinking water to the granules, using the included measuring cup.
3. Do not shake the bottle.
4. Gently swirl the suspension to ensure that the granules are evenly suspended.
5. Write the 'Discard after' time (10 hours from reconstitution time) on the bottle label.
6. Indicate the volume of oral suspension (2 mg/mL) to withdraw, based on body weight (see Table 3).

2.1.7. Dose adjustment

No dose adjustment is necessary for renal impairment, hepatic impairment, or extracorporeal membrane oxygenation.

2.1.8. Potential interactions

Baloxavir should not be taken within two hours of oral products that contain dairy, antacids, laxatives, calcium, iron, magnesium, selenium and zinc supplements as they significantly reduce absorption.

The tablets contain lactose as an excipient, so patients who are lactose intolerant should not be randomized to receive this medicine.

2.1.9. Discontinuation

The treating clinician can discontinue the study drug at any time if doing so is regarded as being in the best interests of the patient.

Baloxavir should be discontinued if an SAE develops that, in the treating clinician's opinion, could be possibly, probably or definitely related to participation in this domain.

3. ENDOTHELIAL DOMAIN

3.1. Imatinib

3.1.1. Presentation

The following preparations are available:

- Imatinib 100 mg capsule
- Imatinib 400 mg capsule
- Imatinib 100 mg tablet
- Imatinib 400 mg tablet
- Imatinib 600 mg tablet

3.1.2. Storage

Store in the original package, below 25°C. Protect from moisture.

3.1.3. Warnings

Occupational exposure may be harmful. Wear a mask, gloves and glasses if dispersing the tablet or opening the capsule. Do not disperse the tablet or open the capsule if you are pregnant.

3.1.4. Dosing

Imatinib will be administered enterally as an 800mg loading dose (Study Day 1), followed by 400mg administered once daily (Study Days 2-14) while the patient remains admitted to hospital.

3.1.5. Duration of therapy

Enteral imatinib is to be commenced as soon as possible after allocation status is revealed. Imatinib is to be administered for a total of 14 days or until hospital discharge, whichever occurs first.

3.1.6. Preparation and administration

3.1.6.1. *For patients unable to swallow whole tablets or capsules*

1. Disperse the tablet in 200mL of water. If necessary, tablets will disperse in 20-50mL of water in 30 minutes.
    a. Note that using a lesser volume of water than 200mL may increase the risk of gastrointestinal side effects.
2. Administer orally, via NG tube or gastrostomy as appropriate and as per local policy.

3.1.7. Dose adjustment

No dose adjustment is required for renal or hepatic impairment.

3.1.8. Potential interactions

Imatinib may increase the concentration of fentanyl. If fentanyl is co-administered with imatinib, patients should be monitored at frequent intervals and fentanyl dose adjusted until stable drug effects are achieved. Additional agents, other than those specified in the platform, that are intended to modulate endothelial function are not permitted.

3.1.9. Discontinuation

The treating clinician can discontinue the study drug at any time if doing so is regarded as being in the best interests of the patient.

Imatinib should be discontinued if an SAE develops that, in the treating clinician's opinion, could be possibly, probably or definitely related to participation in this domain. Imatinib therapy should be discontinued immediately and not restarted.

It is recommended that full blood count (to monitor for cytopenia) and liver function tests (bilirubin, ALT +/- AST) should be performed, as part of usual care, at least twice per week whilst the patient is receiving enteral imatinib.

The development of the following in a participant allocated to enteral imatinib should prompt discontinuation of imatinib therapy:

- Neutropenia (neutrophil count $<1.0 \times 10^9$/L) and/or thrombocytopenia (platelet count $<50 \times 10^9$/L)
- Elevation of bilirubin 3 times the upper limit of normal, or ALT/AST 5 times the upper limit of normal

APPENDIX 1. SUMMARY OF CHANGES FROM VERSION 1 TO VERSION 2

- Removal of Hydroxychloroquine. This agent has been removed from the COVID-19 Antiviral Domain of REMAP-CAP on the basis of results from the RECOVERY and WHO SOLIDARITY trials.
- Addition of Vitamin C and Simvastatin to reflect the addition of these domains to the platform.
- Clarification for duration of lopinavir/ritonavir, interferon, anakinra, and tocilizumab interventions to reflect the extension of these therapies to the Moderate Illness Severity State (i.e., patients not requiring organ support in ICU).
- Clarification of warnings regarding preparation for interferon, anakinra, and sarilumab.
- Clarification of preparation of infusions of interferon, anakinra, and sarilumab, particularly with reference to the use of Baxter Viaflex bags.
- Addition of a tocilizumab dose banding table, to be used at the discretion of sites to reduce wastage.

APPENDIX 2. SUMMARY OF CHANGES FROM VERSION 2 TO VERSION 2.1

- Updated advice about the preparation of IFN-β1a, anakinra, tocilizumab, and sarilumab by people who are pregnant or trying to conceive.

APPENDIX 3. SUMMARY OF CHANGES FROM VERSION 2.1 TO VERSION 3

- Removal of COVID-19 Immune Modulation Domain agents (anakinra, interferon-beta-1a, tocilizumab, and sarilumab). This domain has been closed.
- Removal of lopinavir/ritonavir from the COVID-19 Antiviral Domain, and addition of ivermectin to this domain.
- Addition of Cysteamine.

APPENDIX 4. SUMMARY OF CHANGES FROM VERSION 3 TO VERSION 4

- Removal of interventions specified in the COVID-19 Antiviral Domain (ivermectin), Simvastatin Domain (simvastatin), and Vitamin C Domain (vitamin C). These domains are now closed.
- Addition of interventions specified in the Influenza Immune Modulation Domain (tocilizumab and Baricitinib).

APPENDIX 5. SUMMARY OF CHANGES FROM VERSION 4 TO VERSION 5

- Removal of interventions specified in the Cysteamine Domain (cysteamine). This domain is now closed.
- Addition of interventions specified in the Endothelial Domain (imatinib) and Influenza Antiviral Domain (baloxavir).