Casirivimab and imdevimab prescribing guideline

Department of Health

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1. **Purpose**

This guideline has been developed by the Queensland Health COVID-19 Therapeutics Working Group to provide clinicians with information and guidance around the appropriate prescribing and safe administration of casirivimab and imdevimab (Ronapreve®) in patients diagnosed with COVID-19, and to ensure equity of access to new COVID-19 therapeutics. This guideline should be endorsed by local Drugs and Therapeutics Committees or equivalent prior to implementation.

2. **Background**

This guideline and procedure are based on the findings of the REGEN-COV and RECOVERY trials, the recommendations of the National COVID-19 Clinical Evidence Taskforce (NCCET), the NICE (UK) guidelines and NSW Clinical Excellence Commission guideline.

2.1 **Regulatory status**

Casirivimab and imdevimab has been granted provisional approval by the Therapeutic Goods Administration (TGA) for:

- Treatment of COVID-19 in adults and adolescents (age ≥12 years and weighing at least 40 kg); who do not require initiation of oxygen and who are at increased risk of progression to severe COVID-19.

- Prevention of COVID-19 in adults and adolescents (age ≥12 years and weighing at least 40 kg); who have been exposed to SARS-CoV-2 AND who either:
  - Have a medical condition making them unlikely to respond to or be protected by vaccination OR
  - Are not vaccinated against COVID-19

Approval has been made based on short-term efficacy and safety data. Continued approval depends on evidence from ongoing clinical trials and post-market assessment. The product is subject to additional monitoring in Australia.

2.2 **Mechanism of action**

Casirivimab and imdevimab is a recombinant human monoclonal antibody combination that simultaneously binds to two distinct sites on the spike protein of the SARS-CoV-2 virus, blocking its entry into the host cell. Clinicians should consider the SARS-CoV-2 variant being targeted and the possibility of reduced efficacy of casirivimab and imdevimab.
2.3 Efficacy

The data supporting casirivimab and imdevimab comes primarily from the REGEN-COV study which demonstrated efficacy of both 600 mg/600 mg and 1200 mg/1200 mg doses with an overall 2.2% absolute reduction and 70% relative risk reduction in COVID-19-related hospitalisations or all-cause deaths, and the RECOVERY trial which showed reduced mortality with high dose casirivimab and imdevimab in hospitalised patients with COVID-19 who were seronegative.[1, 2] In these patients, there was a significant reduction in mortality compared to standard of care (NNT approximately 20). There was no benefit demonstrated in seropositive patients.

NOTE: Current evidence suggests that casirivimab and imdevimab does not neutralise the Omicron strain of the SARS-CoV-2 virus. It should not be used unless genotyping confirms infection with an alternate strain.

3. Prescription and governance

Casirivimab and imdevimab has a restricted listing on the Queensland Health Medicines Formulary (List of Approved Medicines): on the advice of a specialist physician for the treatment of COVID-19 in accordance with recommendations in the National COVID-19 Clinical Evidence Taskforce Guidelines.

Individual governance of casirivimab and imdevimab prescribing should be managed by a lead clinician in each Hospital and Health Service.

3.1 Authorised prescribers

Prescribers are to complete a Casirivimab and imdevimab Request to Access Form (adult or paediatrics) for each patient, confirming patient suitability and consent to treatment.

For adult patients, patients should be assessed by their treating clinician, with suitable patients then discussed with the on-call adult Infectious Diseases physician or approved delegate for your service.

For paediatric patients, high risk children should be assessed initially by their treating paediatrician, with patient suitability confirmed on discussion with on-call paediatric Infectious Diseases for your service or at Children’s Health Queensland (CHQ).
3.2 Patient consent

There are no additional requirements for consent to administer casirivimab and imdevimab than is usual practice for any other TGA registered pharmaceutical. Clinicians should discuss the risks and benefits of treatment with the patient and/or their carer and document that this has been done in the patient record. A casirivimab and imdevimab Patient Information leaflet has been developed to assist with this and should be provided. Some clinicians may wish to obtain formal written consent and a consent form has been developed for this purpose. [Patient Information](#) and consent forms for [adults](#) and [children](#) are available online.

4. Access and supply

Access to casirivimab and imdevimab is regulated by the National Medical Stockpile and managed centrally in Queensland by Central Pharmacy. Supply of COVID-19 therapeutics including casirivimab and imdevimab is uncertain and vulnerable to constraints in the supply chain as demand fluctuates nationally and globally. To ensure equity of access and conserve this agent for those patients at the highest risk of disease progression, an expert group of lead clinicians from across the medical specialties was established to identify priority groups for treatment and develop a tiered access criteria. Access to casirivimab and imdevimab will move between Tier 1 (unlimited supply scenario) through increasing levels of restriction to Tier 3 in the event of critical shortages. Clinicians should liaise with their pharmacy to confirm the current tier of access. ([Refer appendix 1 – Tiered access criteria](#))

A small amount of stock will be made available to healthcare facilities that have the capacity to appropriately store and monitor casirivimab and imdevimab. Access will be closely monitored, and prescribers will be required to complete a Request to Access Casirivimab and imdevimab form for each patient, to be [available online here soon](#).

5. Model of care - outpatient setting

5.1 Overarching elements

1. Casirivimab and imdevimab may be delivered in a range of appropriate healthcare settings, depending on local requirements. Choice of setting should consider storage and transport of the drug in respect of the cold chain, preparation of the infusion and disposal.

2. It should be administered where the safety of patients, carers and providers can be maintained. This includes the requirements to observe the patient receiving for a
minimum of 60 minutes post-administration and having access to personnel and equipment to manage anaphylaxis or other adverse drug reactions.

3. As much as possible, it should avoid putting additional pressure on acute care services such as emergency departments.

5.2 Hospital in the home (HITH)

It is recommended that casirivimab and imdevimab is not delivered under HITH models of care. In addition to requiring monitoring during and after administration with readily available resuscitation facilities, the preparation and reconstitution of the multi-dose vial is complex and error prone and ideally performed in a sterile suite.

6. Clinical criteria for treatment

See also section 4. Access and Supply – note that the clinical criteria may be further restricted depending on stock availability. Refer to tiered access criteria in appendix 1.

6.1 Indications

NOTE: Current evidence suggests that casirivimab and imdevimab does not neutralise the Omicron strain of the SARS-CoV-2 virus. It should only be used if genotyping confirms infection with an alternate strain.

6.1.1 Post-exposure prophylaxis (PEP)

NOTE: There is currently limited availability of casirivimab and imdevimab for post-exposure prophylaxis, therefore PEP should primarily be reserved for close contacts exposed in high-risk settings such as hospitals or residential aged care facilities.

1. Adults aged ≥ 16 years and weighing at least 40 kg who are:
   - A contact of individual with confirmed SARS-CoV-2 AND
   - Asymptomatic with a negative PCR result AND
   - ≤ 4 days from exposure (day of first exposure = day 0) AND
   - Not vaccinated against COVID-19 (unvaccinated or partially vaccinated\(^*(\)) OR
   - Are immunosuppressed (regardless of their vaccination status) refer table 1.
AND (with the exception of immunosuppressed patients regardless of vaccination status) who have at least one of the following risk factors for severe disease:

- Diabetes mellitus (requiring medication)
- Obesity (BMI > 30 kg/m²)
- Chronic kidney disease (i.e. eGFR < 60 mL/min/1.73m²)
- Cardiovascular disease (including hypertension treated with medication)
- Chronic lung disease (including asthma treated with regular medication)
- Age ≥ 50

Repeat dosing can be administered after four weeks, however this should only be utilised in high risk settings.

^A fully vaccinated person is ≥ 14 days following receipt of the final dose of a primary course of a TGA approved COVID-19 vaccine. Dialysis dependent patients are considered fully vaccinated after receipt of a 3 dose primary course of COVID-19 vaccinations. Dialysis dependent patients are not considered immunosuppressed unless they are on concomitant immunosuppression or have another immunosuppressive syndrome (refer table 1)

Table 1: Criteria for immunosuppression

| Immunosuppressed patients | a) have a primary or acquired immunodeficiency such as haematological neoplasms, are post-transplant [solid organ (on immunosuppressive therapy) or haematopoietic stem cell transplant within 24 months], or have HIV/AIDS or other significant immunocompromising condition or
|                         | b) are on/ have been on recent immunosuppressive therapy such as chemotherapy, radiotherapy, high dose corticosteroids (equivalent to 20 mg or more of prednisone), biologics or disease-modifying anti-rheumatic drugs (DMARDs)

Response to COVID-19 vaccination among individuals from immunocompromised groups varies from no response or a sub-optimal response to an adequate response similar to that expected in the general population. Refer to the Tiered Access Criteria table at appendix 1 for risk stratification of immunocompromised groups.
2. Adolescents aged ≥12 years and weighing at least 40kg, who are:

- A contact of individual with confirmed SARS-CoV-2 **AND**
- Asymptomatic with a negative PCR result **AND**
- ≤ 4 days from exposure (day of first exposure = day 0) **AND**
- Have not been fully vaccinated (fully vaccinated patients are those who have received a second dose >2 weeks previously); **OR**
- Are immunosuppressed* (regardless of their vaccination status) – these patients are at highest risk if an additional risk factor also present as below but may also be eligible without an additional risk factor.

**AND** who are at high risk of deterioration

- Complex life limiting neurodisability with respiratory involvement
- Heart failure
- Respiratory conditions, e.g.: chronic lung disease requiring oxygen, severe cystic fibrosis, severe asthma
- Obesity (BMI ≥95th [CDC] / ≥97th [WHO] centile for age)
- **or**
- Two or more complex chronic conditions or comorbidities

* Guidance and detailed risk stratification available in the CHQ Paediatric Guideline.

Monoclonal antibody therapy is a limited resource and is currently reserved for those at the very highest risk of disease progression. Although established adult COVID-19 risks do extend into younger age groups (i.e. age, obesity, comorbidity) even these children remain at lower risk of severe disease than adults.

Fulfilling eligibility criteria does not automatically result in its prescription in children. Use in mild disease should be based on the patient’s individual risk of severe disease, including age, multiple risk factors, and COVID-19 vaccination status.

Approval to use casirivimab and imdevimab will be considered on a case-by-case basis after discussion with Paediatric Infectious Diseases.

**Repeat dosing** can be administered after four weeks, however this should only be utilised in high risk settings.
6.1.2 Treatment – mild/moderate disease in non-hospitalised patients (standard dose)

**Note:** Sotrovimab is the preferred monoclonal antibody therapy for non-hospitalised patients at risk of disease progression, due to drug availability, ease of administration and activity against the Omicron strain. Casirivimab and imdevimab may be considered for patients between day 5 – 7 of symptom onset.

1. **Adults who are:**
   - COVID-19 positive and day 6 or 7 of symptom onset; **AND**
   - Do not require oxygen for COVID-19; **AND**
   - Not fully vaccinated (a fully vaccinated person is ≥ 14 days following receipt of the final dose of a primary course of a TGA approved COVID-19 vaccine\(^\wedge\)); **OR**
   - Are immunosuppressed – (regardless of their vaccination status) refer [table 1](#).

   **AND** (with the exception of immunosuppressed patients regardless of vaccination status) who have at least one of the following risk factors for severe disease:
   - Diabetes mellitus (requiring medication)
   - Obesity (BMI > 30 kg/m\(^2\))
   - Chronic kidney disease (i.e. eGFR <60 mL/min/1.73m\(^2\))
   - Cardiovascular disease (including hypertension treated with medication)
   - Chronic lung disease (including asthma treated with regular medication)
   - Age ≥ 50

\(^\wedge\) Dialysis dependent patients are considered fully vaccinated after receipt of a 3 course primary dose of COVID-19 vaccinations. Dialysis dependent patients are not considered immunosuppressed unless they are on concomitant immunosuppression or have another immunosuppressive syndrome.
2. Adolescents aged ≥12 years and weighing at least 40kg, who are

- COVID-19 positive and day 6 or 7 of symptom onset; AND
- Do not require oxygen for COVID-19; AND
- Have not been fully vaccinated (fully vaccinated patients are those who have received a second dose ≥2 weeks previously); OR
- Are immunosuppressed† (regardless of their vaccination status) – these patients are at highest risk if an additional risk factor is also present as below but may also be eligible without an additional risk factor.

AND who are at high risk of deterioration

- Complex life limiting neurodisability with respiratory involvement
- Heart failure
- respiratory conditions, e.g.: chronic lung disease requiring oxygen, severe cystic fibrosis, severe asthma
- obesity (BMI ≥95th [CDC] / ≥97th [WHO] centile for age)
- or
- two or more complex chronic conditions or comorbidities

³ Guidance and detailed risk stratification available in the CHQ Paediatric Guideline.

Monoclonal antibody therapy is a limited resource and is currently reserved for those at the very highest risk of disease progression. Although established adult COVID-19 risks do extend into younger age groups (i.e. age, obesity, comorbidity) even these children remain at lower risk of severe disease than adults.

Fulfilling eligibility criteria does not automatically result in its prescription in children. Use in mild disease should be based on the patient’s individual risk of severe disease, including age, multiple risk factors, and COVID-19 vaccination status.

Approval to use casirivimab and imdevimab will be considered on a case-by-case basis after discussion with Paediatric Infectious Diseases.
6.1.3 Treatment – moderate/severe/critical in hospitalised disease in hospitalised patients (high dose)

**Note:** The use of casirivimab and imdevimab at high doses for severe or critically ill patients is off-label (i.e. not TGA approved for this indication or at this dose)

1. **Adults aged ≥ 16 years and weighing at least 40kg who are:**
   - Hospitalised with severe or critical COVID-19 infection **AND**
   - Seronegative for antibodies to SARS-CoV-2 (i.e. do not have an anti-COVID-19 IgG antibody detected within 24 hours of administration - request “urgent COVID-19 serology COVGQ” to Pathology Queensland)

Table 2: Severity criteria for adults

<table>
<thead>
<tr>
<th>Moderate disease</th>
<th>Patients with signs of pneumonia including SOB, tachypnoea, or cough without features of severe pneumonia (oxygen saturation ≥ 93% and &lt;95% on room air (RA))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Disease</td>
<td>Any of:</td>
</tr>
<tr>
<td></td>
<td>• Respiratory rate (RR) ≥ 30 breaths per minute</td>
</tr>
<tr>
<td></td>
<td>• Oxygen saturation ≤ 92% RA and/or requiring oxygen supplementation</td>
</tr>
<tr>
<td></td>
<td>• Lung infiltrates ≥ 50% on imaging</td>
</tr>
<tr>
<td>Critical Disease</td>
<td>Any of:</td>
</tr>
<tr>
<td></td>
<td>• Acute Respiratory Distress Syndrome (PaO₂/FiO₂ &lt; 200), includes patients deteriorating despite advanced forms or respiratory support (NIV, HFNO) or patients requiring mechanical ventilation.</td>
</tr>
<tr>
<td></td>
<td>• Bilateral opacities not explained by other aetiology</td>
</tr>
<tr>
<td></td>
<td>• Life-threatening organ dysfunction/failure</td>
</tr>
<tr>
<td></td>
<td>• Impairment of consciousness</td>
</tr>
<tr>
<td></td>
<td>• Septic Shock</td>
</tr>
<tr>
<td></td>
<td>o Sepsis with persistent hypotension despite volume resuscitation</td>
</tr>
</tbody>
</table>
2. Adolescents aged ≥12 years and weighing at least 40kg, who are:

Off label use of high dose casirivimab and imdevimab is on Paediatric Infectious Diseases specialist advice.

6.2 Contraindications

- Known hypersensitivity to casirivimab, imdevimab or any of the excipients (histidine, histidine monohydrochloride monohydrate, polysorbate 80, sucrrose)

6.3 Precautions

- Paediatric use: safety and efficacy have not been established in children < 12 years of age.
- Reduced sensitivity: Clinicians should consider the SARS-CoV-2 variant being targeted and the possibility of reduced sensitivity to casirivimab and imdevimab. Current evidence suggests casirivimab and imdevimab does not neutralise the Omicron strain. It should not be used unless genotyping confirms infection with an alternate strain.
- Pregnancy: casirivimab and imdevimab is classified as category B2 by the TGA. There are currently no data on the effects of casirivimab and imdevimab on a pregnant woman or baby. Casirivimab and imdevimab is a human immunoglobulin G (IgG) and may cross the placenta, the potential impact of this is not known. The National COVID-19 Clinical Evidence Taskforce has made a conditional recommendation that treatment should be considered if the benefit justifies the possible by unknown risks.
- Breastfeeding: There are no available data on the excretion of casirivimab or imdevimab in human milk and the potential risks and benefits to a breastfed baby are unknown. A decision whether to discontinue breastfeeding or abstain from casirivimab and imdevimab therapy should consider the benefit of breastfeeding in the baby and the benefit of therapy for the woman.

6.4 Drug interactions

No formal drug-drug interaction studies have been conducted. Casirivimab and imdevimab are not renally excreted or metabolised by the CYP450 enzymes, therefore interactions with concomitant renally cleared medications or substrates, inducers or inhibitors of cytochrome P450 enzymes are unlikely.
7. Prescribing and administration

7.1 Clinical setting

Casirivimab and imdevimab should be administered in an appropriate site by staff with experience in monitoring infusion reactions and managing adverse events (including anaphylaxis).

In determining choice of setting, consider:

- Personnel and equipment to manage anaphylaxis must be present during the minimum 30-minute infusion and for at least 60 minutes of observation following administration by either intravenous infusion or subcutaneous injection.

- Availability of an adequate dedicated area for the reconstitution and preparation of the infusion or subcutaneous injections. Ideally casirivimab and imdevimab is given immediately after preparation. However, if this is not possible, the syringes for subcutaneous injection and the diluted solution for infusion may be prepared in advance in an appropriate place elsewhere and stored in a refrigerator for up to 24 hours (include infusion time).

7.2 Baseline tests

Treatment of mild-moderate asymptomatic patients and post-exposure prophylaxis:

Immediately prior to commencing the infusion, where feasible it is recommended that patients have blood taken for COVID serology (request COVGQ). Do not delay infusion pending result.

Treatment of severe or critically ill patients:

Baseline COVID-19 serology is essential to confirm negative serostatus prior to commencing treatment. (request “urgent COVID-19 serology COVGQ” to Pathology Queensland)

7.3 Dose

The dose of casirivimab and imdevimab depends on the indication (table below).

- There is no adjustment for age, weight, renal or hepatic impairment.

- Orders should state the indication

- Co-prescribe adrenaline IM as a single dose as per local guidelines for the emergency management of anaphylaxis.
**ieMR ordering:** to prescribe casirivimab and imdevimab select “Add order” and search for drug name “casirivimab-imdevimab

- **For adults:** Choose order set “casirivimab-imdevimab in sodium chloride 0.9% IV (single bag) adult” and complete prescription

- **For children ≥ 12 years and >40 kg:** Choose order set “casirivimab-imdevimab in sodium chloride 0.9% IV (single bag) paediatric ≥12 yrs and ≥= 40 kg” and complete prescription

(See Appendix 1 for ieMR screenshots).

**Non ieMR ordering:** casirivimab and imdevimab should be prescribed as a single STAT order on the front of the National Inpatient Medication Chart: “casirivimab xx mg/ imdevimab xx mg in 100 mL sodium chloride 0.9% infused over 30 minutes”

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**TREATMENT**

**Asymptomatic, mild – moderate: STANDARD DOSE**

*Intravenous infusion*

a single combined dose of **600mg casirivimab and 600mg imdevimab** by intravenous infusion over 30 minutes.

*Subcutaneous injection*

Single doses of **600mg of casirivimab and 600mg of imdevimab** administered consecutively by separate subcutaneous injections.

NB: Intravenous infusion is strongly recommended; however subcutaneous injection is an alternative route when intravenous infusion is not feasible or would lead to a delay in treatment

**Severe or critical (seronegative patients): HIGH DOSE***

a single combined dose of **1200mg casirivimab and 1200mg imdevimab** by intravenous infusion over 30 minutes.

* The RECOVERY trial investigated a single dose of 8000 mg (4000 mg casirivimab plus 4000 mg imdevimab). The lower dose recommended here aligns with the recommendations in the NICE (UK) guidelines which are based on pharmacokinetic data indicating a flat dose-response curve. The current vials supplied by Roche do not allow for administration of 8000 mg dosing.
**POST EXPOSURE PROPHYLAXIS (PEP)**

**Initial dose**

*Intravenous infusion*

A single combined dose of 600mg casirivimab and 600mg imdevimab by intravenous infusion over 30 minutes.

*Subcutaneous injection*

Single doses of 600mg of casirivimab and 600mg of imdevimab administered consecutively by separate subcutaneous injection.

**Repeat dose for ongoing prophylaxis***

After an initial loading dose, subsequent doses are given once every 4 weeks. Commence 4 weeks after initial PEP dose.

*Intravenous infusion*

A single combined dose of 300mg casirivimab and 300mg imdevimab by intravenous infusion over 30 minutes.

*Subcutaneous injection*

Single doses of 300mg of casirivimab and 300mg of imdevimab administered consecutively by separate subcutaneous injection.

*Note – there is no data on repeat dosing beyond 24 weeks (6 doses)*

---

**7.4 Presentation**

There are TWO multidose vials in the product.

- One vial containing 11.1 mL solution of 1 332 mg of casirivimab (120 mg/mL)
- One vial containing 11.1 mL solution of 1 332 mg of imdevimab (120 mg/mL)

The solutions for injection or infusion are clear to slightly opalescent and colourless to pale yellow. The vials are labelled 20 mL; this refers to their capacity - they contain 11.1 mL of solution.
7.5 Storage and stability

**Undiluted vials:** Refrigerate at 2-8°C in original package. Do not freeze. Do not shake. Protect from light.

**Punctured multi-dose vials:** If not used immediately after initial puncture, the product can be stored for 16 hours at room temperature up to 25°C or refrigerated between (2-8°C) for up to 48 hours. **Due to the potential risk of microbial contamination, it is recommended that punctured vials are discarded after 24 hours if prepared “on the bench”**.

**Infusion solution:** The diluted solution of casirivimab and imdevimab is intended for immediate use. If immediate administration is not possible, the diluted solution may be stored for up to 12 hours at room temperature (up to 25°C) or if prepared by pharmacy under aseptic conditions, refrigerated (2-8°C) for up to 48 hours.

**Syringes for subcutaneous injection:** Prepared syringes should be administered immediately. If not used immediately, the prepared syringe can be stored for 6 hours at room temperature (up to 25°C) or refrigerated (2-8°C) for up to 24 hours.

7.6 Preparation and administration

The preparation of casirivimab and imdevimab for infusion or subcutaneous injection is complex and sites with access to sterile production suites may wish to prepare it in the sterile suite.

It is acknowledged that this is not always possible and so where doses of casirivimab and imdevimab are prepared “on the bench” it is recommended that prepared doses are used immediately, and any remaining product in the punctured multidose vials is refrigerated and discarded if not used within 24 hours.

**CAUTION:** The occupational hazard of intermittent low dose exposure to casirivimab and imdevimab is not known. Therefore, additional precautions are advised when preparing and administering casirivimab and imdevimab:

- **Wear a P2/N95 mask, disposable gloves, protective eyewear, and a disposable apron.**
- The infusion bag may be prepared using standard aseptic technique
- Reconstitution or preparation should occur in a dedicated preparation area away from patients and carers

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- Do not shake vials when reconstituting as this can damage the protein and form a froth.

**ALERT**: Emergency resuscitation personnel, equipment and medications must be available for immediate use in the event of a hypersensitivity or anaphylactic reaction to casirivimab and imdevimab. Refer to local HHS policies for the management of anaphylaxis.

### 7.6.1 For intravenous infusion

#### Preparation Steps

1. Remove the casirivimab and imdevimab vials from refrigerator approximately 20 minutes prior to preparation of the infusion and allow to come to room temperature. Do not expose to direct heat and do not shake the vials.

2. Visually inspect the vials to ensure they are free from particulate matter and that there is not damage to the vial or discoloration present. The solution should be clear to slightly opalescent and colourless to pale yellow. If the vials are identified to be unusable, contact Pharmacy. Do not discard the vials – quarantine in a separate clearly marked section of the refrigerator.

3. Clearly label the multi-dose vials with the date and time of initial puncture.

4. Withdraw the appropriate volume of casirivimab and imdevimab from each respective vial. (refer to table 3 below)

5. Inject into a 100 mL sodium chloride 0.9% infusion bag.


#### Table 3: Dosing volumes for intravenous administration using MULTIDOSE vials

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Volume to be withdrawn from each vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment and post-exposure prophylaxis (initial dose)</td>
<td>600 mg casirivimab plus</td>
<td>Withdraw 5 mL (= 600 mg) of casirivimab and 5 mL (= 600 mg) imdevimab from each respective vial</td>
</tr>
<tr>
<td></td>
<td>600 mg imdevimab</td>
<td>Inject total volume of 10 mL into infusion bag</td>
</tr>
</tbody>
</table>
High Dose – for critically ill

<table>
<thead>
<tr>
<th>Dosage</th>
<th>1 200 mg casirivimab plus 1 200 mg imdevimab</th>
<th>Withdraw 10 mL (= 1 200 mg) of casirivimab and 10 mL (= 1 200 mg) imdevimab from each respective vial</th>
<th>Inject total volume of 20 mL into infusion bag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-exposure prophylaxis (ongoing dose)</td>
<td>300 mg casirivimab plus 300 mg imdevimab</td>
<td>Withdraw 2.5 mL (= 300 mg) of casirivimab and 2.5 mL (= 300 mg) imdevimab from each respective vial</td>
<td>Inject total volume of 5 mL into infusion bag</td>
</tr>
</tbody>
</table>

**Administration Steps**

1. If refrigerated, allow the IV infusion bag to equilibrate to room temperature for approximately 30 minutes prior to administration.
2. Do not use the same IV line to administer other medications at the same time.
3. Attach an infusion set to the infusion bag using standard bore tubing. Administer using a 0.2 micron in-line filter attached to the patient end of the IV giving set.
4. Prime the infusion set with the casirivimab and imdevimab infusion and then infuse intravenously over 30 minutes (until the bag is finished) via a central or peripheral line.
5. After the casirivimab and imdevimab infusion is complete, flush the giving set with at least 20 mL of sodium chloride 0.9% (at the same rate as the casirivimab and imdevimab infusion).
6. **Observe the patient during the infusion and for 60 minutes after infusion cessation** in case of hypersensitivity reactions or anaphylaxis.

**7.6.2 For subcutaneous injection**

**Preparation Steps**

1. Remove the casirivimab and imdevimab vials from refrigerator and allow to come to room temperature for approximately 20 minutes before preparation. Do not expose to direct heat and do not shake the vials.
2. Obtain 3 mL syringes with luer connection, 21-gauge transfer needles and 25-gauge needles for subcutaneous injection.

3. Visually inspect the vials to ensure they are free from particulate matter and that there is no damage to the vial or discolouration present. The solution should be clear to slightly opalescent and colourless to pale yellow. If the vials are identified to be unusable, contact Pharmacy. Do not discard the vials – quarantine in a separate clearly marked section of the refrigerator.

4. Clearly label the vial with the date and time of initial puncture.

5. Gather the appropriate number of syringes (see table 2, below).

6. Withdraw the appropriate volume of casirivimab and imdevimab from each respective vial into each syringe (see table 4) to prepare the number of syringes required for each dose.

7. Replace the 21-gauge transfer needle with a 25-gauge needle for subcutaneous injection.

8. The prepared syringes should be administered immediately. If immediate administration is not possible, store the prepared syringes at room temperature up to 25°C for no more than 6 hours, or refrigerated at 2°C to 8°C for no more than 24 hours.

Table 4: preparation of syringes for subcutaneous injection using MULTIDOSE vials

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Volume to prepare syringes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment and post-exposure prophylaxis (initial dose)</td>
<td>600 mg casirivimab plus 600 mg imdevimab</td>
<td>Casirivimab – Prepare TWO syringes each containing 2.5 mL (= 300 mg) casirivimab. Total volume 5 mL (= 600 mg) of solution from vial of casirivimab (120 mg/mL) Imdevimab – Prepare TWO syringes each containing 2.5 mL (= 300 mg) imdevimab. Total volume 5 mL (= 600 mg) of solution from vial of imdevimab (120 mg/mL) Total for one dose = 4 syringes each containing 2.5 mL</td>
</tr>
</tbody>
</table>

Casirivimab and imdevimab prescribing guideline – Department of Health
Post-exposure prophylaxis (ongoing dose) | 300 mg casirivimab plus 300 mg imdevimab
---|---
| **Casirivimab** – withdraw 2.5 mL (= 300 mg) of solution from the vial to prepare ONE syringe containing 2.5 mL (= 300mg) casirivimab
| **Imdevimab** - withdraw 2.5 mL (= 300 mg) of solution from the vial to prepare ONE syringe containing 2.5 mL (= 300mg) imdevimab
| **Total for one dose** = 2 syringes each containing 2.5 mL

**Administration Steps**

1. For the administration of casirivimab and imdevimab 1 200 mg dose (600 mg casirivimab and 600 mg imdevimab) – FOUR syringes are required (see table 4)
2. For the administration of casirivimab and imdevimab 600 mg dose (300 mg casirivimab and 300 mg imdevimab) – TWO syringes are required (see table 4)
3. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 10 – 15 minutes prior to injection
4. Administer the prepared subcutaneous injections consecutively. Space the injections apart, administering each at a different site – into the upper thigh, the upper outer arms or abdomen - except for 5 cm around the navel. The waistline should also be avoided. DO NOT inject into skin that is tender, damaged, bruised or scarred.
5. **Observe the patient for 60 minutes after administration of the injections** in case of hypersensitivity reactions or anaphylaxis.

**7.7 Observation and monitoring**

Hypersensitivity reactions, including anaphylaxis, have been reported with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

**INTRAVENOUS INFUSION**

Patients must be observed **during and for at least 60 minutes** after the end of the infusion.
• Infusion reactions include nausea, chills, dizziness (or syncope), dyspnoea, pruritis and rash, urticaria and flushing

• For mild-moderate infusion reactions, consider interrupting, slowing or stopping the infusion and administering appropriate medications and/or supportive care.

• If signs and symptoms of a significant hypersensitivity/anaphylaxis occur – STOP the infusion immediately and commence supportive care.

SUBCUTANEOUS INJECTION

Patients must be observed for at least 60 minutes after the administration of subcutaneous injections.

• Injection site reactions have been reported with subcutaneous administration of casirivimab and imdevimab. Commonly reported signs and symptoms for these reactions included erythema, pruritis, ecchymosis, oedema, pain/tenderness and urticaria.

7.8 Adverse effects and reporting

The most frequently reported adverse drug reactions are hypersensitivity reactions which include infusion related reactions (IRR) and injection site reactions (ISR).

Adverse effects – subcutaneous injection

• Common (>1%): injection site reactions 4.2%
• Uncommon (<1%): lymphadenopathy 0.5%, dizziness 0.4%
• Rare (<0.1%): pruritis <0.1%

Adverse effects – intravenous infusion

• Uncommon (<1%): dizziness (0.2%), nausea (0.4%), rash (0.1%), chills (0.1%), IRR (0.1%)
• Rare (<0.1%): anaphylaxis (0.02%), flushing (<0.1%), urticaria (<0.1%)

It may be difficult to distinguish between adverse effects of casirivimab and imdevimab and signs and symptoms of COVID-19. However, because casirivimab and imdevimab is a provisionally approved product with no post-marketing data, all possible and confirmed adverse events must be reported. These should be notified to the TGA Reporting adverse events | Therapeutic Goods Administration (TGA) and reported via Riskman.
7.9 Monitoring of treatment outcomes

The use of casirivimab and imdevimab requires reporting of clinical outcomes to the National Medical Stockpile Taskforce. Prescribers agree to these terms when completing a request to access form. Data required includes eligibility, confirmation of full dose delivery and outcome: recovery, progression to hospitalisation, oxygen requirement, ICU or death.

8. Vaccination post casirivimab and imdevimab

The US Centers for Disease Control and Prevention advises delaying COVID-19 vaccination until 90 days after administration of monoclonal antibodies as part of COVID-19 treatment, to avoid potential interference with the immune response to the COVID-19 vaccination. This advice applies to those who have not received any vaccine dose as well as those who have received the first dose but not the second dose.

Patients should be provided with a letter documenting the date and location of their dose. Templates will be available here soon.

9. Compliance and evaluation

Regular prescribing reports will be provided through interrogation of iPharmacy, ieMR and CHARM programs. Reports will be made available to Medication and Pharmacy Planning Response Group (MPPRG).

10. References


# Appendix 1 – Tiered access criteria

<table>
<thead>
<tr>
<th>Tier 1 (includes all Tiers 2 &amp; 3 criteria)</th>
<th>Tier 2 (includes all Tier 3 criteria)</th>
<th>Tier 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unvaccinated or partially vaccinated</strong></td>
<td><strong>Diabetes mellitus treated with medication (Type 1 or 2)</strong></td>
<td><strong>&gt;50 yrs</strong> with an additional COVID risk factor (obesity, diabetes (non-diet controlled), CKD with GFR &lt;60, heart failure) OR significant underlying bronchiectasis</td>
</tr>
<tr>
<td></td>
<td><strong>Obesity (BMI &gt;30kg/m^2)</strong></td>
<td><strong>Age ≥ 50 years</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Chronic kidney disease with eGFR &lt;60ml/min/1.73m^2</strong></td>
<td><strong>Chronic liver disease</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Cardiovascular disease (including hypertension treated with medication)</strong></td>
<td><strong>Age ≥ 50 yrs</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Chronic lung disease (including asthma treated with regular medication)</strong></td>
<td><strong>Chronic liver disease</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Age ≥ 50 years</strong></td>
<td><strong>Age ≥ 50 yrs</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Chronic liver disease</strong></td>
<td><strong>&gt;50 yrs</strong> with an additional COVID risk factor (obesity, diabetes (non-diet controlled), CKD with GFR &lt;60, heart failure) OR significant underlying bronchiectasis</td>
</tr>
<tr>
<td><strong>Immunosuppressive therapy:</strong></td>
<td><strong>Rituximab / obintuzumab / BITE antibodies &gt;12 months</strong></td>
<td><strong>Rituximab / obintuzumab / BITE antibodies within 6-12 months</strong></td>
</tr>
<tr>
<td>Biologic agents / TKIs / cellular therapies (irrespective of vaccination status)</td>
<td><strong>CAR-T &gt;24mths</strong></td>
<td><strong>CAR-T within 12-24mths</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Alemtuzumab &gt;6mths</strong></td>
<td><strong>Ibrutinib, acalabrutinib, venetoclax within 6mths</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Bortezomib / Carfilzomib</strong></td>
<td><strong>Daratumumab within 6 months</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Lenalidomide / Pomalidomide</strong></td>
<td><strong>Ruxolitinib within 6 months</strong></td>
</tr>
<tr>
<td></td>
<td><strong>TKIs and other targeted therapies (dasatinib, nilotinib, imatinib, osimertinib, erlotinib, Crizotinib, alectinib, Lorlatinib, etc)</strong></td>
<td><strong>Alemtuzumab within 3-6mths</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Checkpoint inhibitors (pembrolizumab, nivolumab, durvalumab, atezolizumab)</strong></td>
<td><strong>JAK inhibitors: baricitinib, tofacitinib, upadacitinib</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Complement inhibitors (eculizumab)</strong></td>
<td><strong>Checkpoint inhibitors (pembrolizumab, nivolumab, durvalumab, atezolizumab)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Anti-IL-17 (secukinumab, ixekizumab); Anti-IL-4 (dupilumab); Anti-IgE (omalizumab); Anti-IL-5 (mepolizumab, benralizumab); Anti-IL-23 (ustekinumab); Anti- (integrins: natalizumab, vedolizumab); Anti-IL-6 (tocilizumab); Anti-TNF (infliximab, adalimumab, etanercept, golimumab, certolizumab)</strong></td>
<td><strong>JAK inhibitors: baricitinib, tofacitinib, upadacitinib</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Rituximab / obintuzumab / BITE antibodies within 6 months</strong></td>
<td><strong>Rituximab / obintuzumab / BITE antibodies within 6 months</strong></td>
</tr>
<tr>
<td></td>
<td><strong>CAR-T within 12mths</strong></td>
<td><strong>CAR-T within 12mths</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Alemtuzumab within 3mths</strong></td>
<td><strong>Alemtuzumab within 3mths</strong></td>
</tr>
<tr>
<td>TIER 1 (includes all Tiers 2 &amp; 3 criteria)</td>
<td>TIER 2 (includes all Tier 3 criteria)</td>
<td>TIER 3</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>--------------------------------------</td>
<td>--------</td>
</tr>
</tbody>
</table>
| Immunosuppressive therapy: Corticosteroids / DMARDs (irrespective of vaccination status) | • Azathioprine \( \leq 1 \text{mg/kg/day} \)  
• Mercaptopurine \( \leq 0.5 \text{mg/kg/day} \)  
• Methotrexate \( \leq 10 \text{mg/week} \)  
• Prednisone \( \leq 10 \text{mg/day} \)  
• Dapsone  
• Hydroxychloroquine  
• mTOR inhibitors (sirolimus; everolimus) | • Mycophenolate  
• Calcineurin inhibitors (cyclosporin or tacrolimus)  
• Azathioprine \( > 1 \text{mg/kg/day} \)  
• Mercaptopurine \( > 0.5 \text{mg/kg/day} \)  
• Methotrexate \( > 10 \text{mg/week} \)  
• Sulfasalazine  
• Leflunomide dose \( \geq 10 \text{mg/day} \)  
• Prednisone 10-20mg per day (or equivalent) for > 4 weeks | • Prednisone >20mg day (or equivalent) for > 4 weeks  
• Combination therapy with corticosteroids and x2 DMARDs, |
| Transplantation (irrespective of vaccination status) | • Autologous stem cell transplantation >12mths | • Allogeneic stem cell transplantation >2 years and / or off immune suppression  
• Autologous stem cell transplantation 6-12 mths | • Solid organ transplantation on immunosuppression  
• Allogeneic stem cell transplant on immunosuppression / chronic GVHD  
• Autologous stem cell transplantation within 6mths |
| Chemotherapy / malignancy (irrespective of vaccination status) | • Acute myeloid leukaemia induction / consolidation >6mths  
• Acute lymphoblastic leukaemia induction / consolidation / maintenance >12mths  
• Lung cancer on active chemotherapy +/- immunotherapy >6mths  
• Other malignancies (both haematological and solid cancer): moderate intensity chemotherapy >2weeks | • Acute myeloid leukaemia induction / consolidation within 3-6mths  
• Acute lymphoblastic leukaemia induction / consolidation / maintenance within 6-12mths  
• Lung cancer on active chemotherapy +/- immunotherapy within 3-6mths | • Acute myeloid leukaemia induction / consolidation within 3mths  
• Acute lymphoblastic leukaemia induction / consolidation / maintenance within 6mths  
• Lung cancer on active chemotherapy +/- immunotherapy within 3mths  
• Other malignancies (both haematological and solid cancer): moderate intensity chemotherapy within 2weeks (as defined by high risk of severe neutropenia (neutrophils <0.5) for 3-5 days duration post-chemotherapy)  
• High dose cyclophosphamide (>1gm/m2) within 2 weeks |
| Immunodeficiency disorders | • Secondary hypogammaglobulinemia requiring immunoglobulin replacement – risk related to underlying therapy / disease resulting in 2nd hypogammaglobulinaemia | • Primary antibody deficiency syndromes (CVID, XLA) without additional COVID risk factors | • Major antibody deficiency (i.e CVID or XLA) with an additional COVID risk factor (age >55, obesity, diabetes (non-diет controlled), CKD, heart failure) OR significant underlying |
Casirivimab and imdevimab prescribing guideline – Department of Health

<table>
<thead>
<tr>
<th>TIER 1 (includes all Tiers 2 &amp; 3 criteria)</th>
<th>TIER 2 (includes all Tier 3 criteria)</th>
<th>TIER 3</th>
</tr>
</thead>
</table>
| (irrespective of vaccination status)     | • Primary immunodeficiency syndromes where immunoglobulin replacement is required (excluding specific antibody deficiency)  
• HIV with CD4 >250 | bronchiectasis OR on immunosuppressive therapy.  
• Combined immunodeficiency syndromes including transplanted SCID where immunoglobulin replacement is required.  
• HIV with CD4 <250  
• Aplastic anaemia on active therapy |

| Chronic kidney disease (irrespective of vaccination status) |  
• Dialysis with additional COVID risk factor (age >55, obesity, diabetes (non-diet controlled), heart failure) OR significant underlying bronchiectasis etc |  |

Immunosuppressant biologics where sotrovimab is NOT likely to be of benefit

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-integrins</td>
<td>natalizumab, vedolizumab</td>
</tr>
<tr>
<td>Anti-TNF-α antibodies</td>
<td>infliximab, adalimumab, etanercept, golimumab, certolizumab</td>
</tr>
<tr>
<td>Anti-IL1 antibodies</td>
<td>anakinra</td>
</tr>
<tr>
<td>Anti-IL6 antibodies</td>
<td>Tocilizumab</td>
</tr>
<tr>
<td>Anti-IL17 antibodies</td>
<td>secukinumab, ixekizumab</td>
</tr>
<tr>
<td>Anti-IL4 antibodies</td>
<td>dupilumab</td>
</tr>
<tr>
<td>Anti-IL23 antibodies</td>
<td>ustekinumab</td>
</tr>
<tr>
<td>Immune checkpoint inhibitors</td>
<td>nivolumab, pembrolizumab, ipilimumab, atezolizumab</td>
</tr>
</tbody>
</table>
Appendix 2 – ieMR screenshots
# 11. Version control

<table>
<thead>
<tr>
<th>Version</th>
<th>Amendments</th>
<th>Author/s</th>
<th>Approved</th>
</tr>
</thead>
</table>
| **v 1-0** | New document | Tina Patterson  
Andrew Henderson | 23/12/2021 |
| **v 1-2** | Review and feedback incorporated | COVID-19 Therapeutics Working Group (CTWG) | 11/01/2022 |
| **v 1-2** | Endorsed | Medications and Pharmacy Planning and Response Group (MPPRG) | 14/01/2022 |
| **v 1-3** | s4.0 Access & Supply – insertion of advice regarding tiered levels of access to respond to fluctuations in the supply chain.  
s6.0 Clinical criteria for treatment – addition of a statement that criteria may be restricted depending on current stock levels.  
p9 – addition of a statement regarding variable response to COVID-19 vaccination added to Table 1: Criteria for immunosuppression  
Addition of Appendix 1 – Tiered access criteria table | Approved: Andrew Henderson  
Chair, COVID-19 Therapeutics Working Group (CTWG)  
Endorsed: Keith McNeil  
A/Deputy Director-General, CMO and CCIO Prevention Division | 1/02/2022 |