



Safety Notice 024/21



Health

Ensuring the safe and appropriate use of casirivimab and imdevimab

7 December 2021

Distributed to:

- Chief Executives
- Directors of Clinical Governance
- Director, Regulation and Compliance Unit

Action required by:

- Chief Executives
- Directors of Clinical Governance

We recommend you also inform:

- Drug and Therapeutics Committees
- Directors of Medical Services
- Directors of Pharmacy
- Directors and Managers of Intensive Care Units
- Directors and Managers of Respiratory Services
- Directors and Managers of Infectious Diseases
- Directors and Managers of Ambulatory Care/HITH

Expert Reference Group

Content reviewed by:

- Chief Pharmacist Unit
- Clinical Leads of ICU, ID and Respiratory Communities of Practice
- HealthShare NSW
- State Preparedness and Response Branch

Clinical Excellence Commission

Tel: 02 9269 5500

[Email](#)

[Internet Website](#)

[Intranet Website](#)

Review date

June 2022

Casirivimab and imdevimab (Ronapreve®) injection is [provisionally registered](#) by the Therapeutic Goods Administration (TGA) for use in Australia for the treatment of COVID-19 and post-exposure prophylaxis against COVID-19.

Restricted indications in NSW

Considering the safety risks outlined in this Safety Notice, use of casirivimab and imdevimab in NSW is restricted to the following indications –

- 1) For treatment of confirmed COVID-19 per the CEC [Use of casirivimab and imdevimab injection for COVID-19](#) Drug Guideline when:
 - a. sotrovimab is not appropriate **OR**
 - b. sotrovimab is not available **OR**
 - c. administration via subcutaneous route is required due to intravenous access not being feasible/possible.
- 2) For post-exposure prophylaxis (to be given as soon as possible following exposure to SARS-CoV-2) in patients that: are unvaccinated **OR** partially vaccinated **OR** may have a suboptimal response to a primary course of COVID-19 vaccination (e.g. severe immunosuppression from a medical condition or medication) **OR** are likely to have low immunity to SARS-CoV-2 due to waning immunity (e.g. completion of a primary schedule of COVID-19 vaccination > 6 months ago).

AND

meet at least one of the below –

- have at least one risk factor for progression to severe COVID-19 as outlined in the CEC [Use of casirivimab and imdevimab injection for COVID-19](#) Drug Guideline
- were exposed to SARS-CoV-2 in a setting with a high-risk of transmission including, but not limited to: residential aged care facility, disability group home, healthcare facility or correctional facility.

Safety risks

Casirivimab and imdevimab supplied to Australia will be in co-packaged cartons containing ONE vial of casirivimab and ONE vial of imdevimab which **must be administered together** (in the same intravenous bag or via concurrent subcutaneous injections). The preparation and administration of casirivimab and imdevimab is complex and involves multiple steps increasing the likelihood of error.

The TGA has provisionally registered both single-use and multi-dose vials for listing on the Australian Register of Therapeutic Goods:

- Multidose vials (only presentation currently available in Australia) contain 11.1 mL of casirivimab or imdevimab however the cartons are labelled as 20 mL (see Figure 1) which refers to the vial capacity.
- Single-use vials (not currently available in Australia) contain 2.5 mL of the casirivimab or imdevimab however the cartons are labelled as 6 mL which refers to the vial capacity.



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Figure 1. Image of casirivimab and imdevimab vials and carton which will be supplied to Australia initially (co-packaged multidose vials).



Other risks with product initially supplied to Australia

The TGA has [permitted supply](#) of certain batches of product with carton and vial label artwork, batch expiry dates and a package insert differing to the registered Australian product on the ARTG (see Figure 1 above). The differences are summarised below:

	Product initially supplied to Australia	As approved in ARTG documentation
Labelling	'Casirivimab and Imdevimab 120 mg/mL Concentrate for Solution for Infusion'	'Ronapreve® 120 mg/mL Solution for Injection or Infusion'
Shelf-life	Labelled with a 24-month shelf-life	12-month shelf-life has been approved by the TGA
Route of administration	Carton, labels and package insert only list intravenous infusion	TGA approved route of administration is via intravenous infusion or subcutaneous injection
Indication	Package insert only includes information regarding the use for the treatment of COVID-19	Provisional TGA registration the treatment of COVID-19 as well as for post-exposure prophylaxis

Suggested actions for the Local Health Districts/Networks

1. Distribute this Safety Notice to all relevant clinicians/committees.
2. Local Drug and Therapeutics Committee are to ensure that:
 - a. Casirivimab and imdevimab use is according to the:
 - i. CEC [Use of casirivimab and imdevimab injection for COVID-19](#) Drug Guideline and the restricted indications outlined in this Safety Notice
 - ii. Quick Guide – Preparation of casirivimab and imdevimab injection for administration via intravenous infusion
 - iii. Quick Guide – Preparation of casirivimab and imdevimab injection for administration via subcutaneous injection
 - b. Given the complexity of casirivimab and imdevimab preparation and administration, guidance from Pharmacy should be sought (where possible) including advice on storage and handling of multi-dose vials.
 - c. Casirivimab and imdevimab:
 - i. is prescribed as a **single** order which includes the dose of each monoclonal antibody. For example, 600 mg casirivimab/600 mg imdevimab.
 - ii. orders state the indication for use (e.g. treatment, post-exposure prophylaxis (initial or repeat dosing)).Liaison with local eMeds teams may be required to ensure appropriate order sentences are built.
 - d. Clinicians are educated that casirivimab and imdevimab **must be administered together** (in the same intravenous bag or via concurrent subcutaneous injections). Consider the use of ancillary labels on product packaging and paper-based medication charts and alerts on Electronic Medication Management systems stating this information.
 - e. Cartons labelled 'Casirivimab and Imdevimab 120 mg/mL Concentrate for Solution for Infusion' are used within the shelf-life approved by the TGA (i.e. reduce expiry by 12 months) – **overlabelling may be required**.
 - f. The package insert included with the initial supply should be **discarded** prior to dispensing or distribution to clinical areas to minimise confusion.
3. Ensure a system is in place to document actions taken in response to this Safety Notice.
4. Confirm receipt of this notice to CEC-MedicationSafety@health.nsw.gov.au within 48 hours.