Ensuring the safe and appropriate use of casirivimab and imdevimab

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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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:

<table>
<thead>
<tr>
<th>Product initially supplied to Australia</th>
<th>As approved in ARTG documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Labelling</strong></td>
<td>'Casirivimab and Imdevimab 120 mg/mL Concentrate for Solution for Infusion'</td>
</tr>
<tr>
<td><strong>Shelf-life</strong></td>
<td>Labelled with a 24-month shelf-life</td>
</tr>
<tr>
<td><strong>Route of administration</strong></td>
<td>Carton, labels and package insert only list intravenous infusion</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td>Package insert only includes information regarding the use for the treatment of COVID-19</td>
</tr>
</tbody>
</table>

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.