Standard Operating Procedure
for the use of Casirivimab and Imdevimab
in Manx Care Inpatients with COVID-19

1. Introduction & Scope

Casirivimab and imdevimab is a neutralising monoclonal antibody (nMAB) combination that binds specifically to two different sites on the spike protein of the SARS-CoV-2 virus particle, blocking its entry into the host cell and therefore inhibiting its replication.

The RECOVERY trial has demonstrated that the casirivimab and imdevimab combination reduced the relative risk of mortality by 20%, and the absolute risk of mortality by 6%, in hospitalised patients with COVID-19 who had not mounted an antibody response of their own to the virus, i.e. were seronegative, at the time of treatment.

The casirivimab and imdevimab combination is licensed in Great Britain for use in the prophylaxis and treatment of acute COVID-19 infection. **The use of casirivimab and imdevimab in patients hospitalised with COVID-19 (cohort 1) at the dose proposed in the current national specification and repeated in this SOP is off-label. The use in patients with hospital-onset COVID-19 (cohort 2) is within the licence.**

This standard operating procedure (SOP) describes the relevant criteria required for the prescribing and administration of casirivimab and imdevimab for patients hospitalised due to COVID-19.

2. Responsibilities

2.1 Staff performing any stage of the consenting, prescribing, dispensing or administration of casirivimab and imdevimab should be aware of this procedure.

2.2 Any deviations from the content of this procedure should be brought to the attention of authorising consultant, consultant virologist or ward pharmacist.

3. Eligibility Criteria

Patients must meet <u>all</u> of the eligibility criteria and none of the exclusion criteria

Cohort 1 – Patients Hospitalised Due to Active COVID-19 (total dose of 2.4g.)

Patients hospitalised due to COVID-19 are eligible for casirivimab and imdevimab if **all three** of the following criteria are met:

1. SARS-CoV-2 infection is confirmed by polymerase chain reaction (PCR) test or where a multidisciplinary team (MDT) has a high level of confidence that the clinical and/or radiological features suggest that COVID-19 is the most likely diagnosis

AND

2. Hospitalised specifically for the management of acute symptoms of COVID-19

AND

3. Negative for baseline serum anti-spike (anti-S) antibodies against SARS-CoV-2

Patients who have been treated with a combined dose of 1.2g of casirivimab and imdevimab (cohort 2) but continue to deteriorate such that their illness requires hospital-based care may be eligible for a 2.4g repeat dose if they fulfil the above criteria.

Cohort 2 – Patients With Hospital-Onset COVID-19 (total dose of 1.2g.)

Patients with hospital-onset COVID-19 are eligible for casirivimab and imdevimab if **all four** of the following criteria are met:

1. SARS-CoV-2 infection is confirmed by polymerase chain reaction (PCR) test **within the preceding 72 hours** or where a multidisciplinary team (MDT) has a high level of confidence that the clinical and/or radiological features suggest that COVID-19 is the most likely diagnosis

AND

2. Hospitalised for indications other than for the management of acute symptoms of COVID-19

AND

3. At high risk of progression to severe COVID-19, OR COVID-19 infection presents a material risk of destabilising a pre-existing condition or illness or compromising recovery from surgery or other hospital procedure (as determined by multidisciplinary team assessment)

AND

4. A baseline serum anti-spike (anti-S) test against SARS-CoV-2 has been taken prior to treatment (NB: The result does not need to be awaited prior to treatment as it does not affect eligibility in this cohort).

4. Exclusion Criteria

4.1 The following patients are **not** eligible for treatment:

4.1.1 Individuals weighing less than 40kg
4.1.2 Children aged under 12 year
4.1.3 Known hypersensitivity reaction to the active substances or to any of the excipients of casirivimab and imdevimab
4.1.4 Previous treatment with a 2400mg combined dose of casirivimab and imdevimab during the current course of infection

5. Special warning and precautions for use

5.1 Referral should be made to the Summary of Product Characteristics (SmPC) [2] for casirivimab and imdevimab for special warnings and precautions for use.

5.2 There are no confirmed clinically significant drug-drug interactions between casirivimab and imdevimab and other medicines however for up to date information please refer to Liverpool COVID-19 interactions website[3].

6. Prescribing

6.1 The decision to prescribe casirivimab and imdevimab must only be made by a Consultant.

6.2 The authorising Consultants name and the decision-making discussion should be documented in the patient's clinical notes.

6.3 The recommended dose of casirivimab and imdevimab is 2.4g, (1.2g each of casirivimab and imdevimab) to be administered as a combined single intravenous infusion.

6.4 During pharmacy opening hours, the ward Pharmacist must be contacted once the prescription is completed for casirivimab and imdevimab.

7. Screening and Supply from Pharmacy

7.1 Supply of casirivimab and imdevimab is available from 9am to 5pm Monday-Friday, and 9am to 12pm on Saturdays. Out of hours, requests can be made via the on-call pharmacist via switchboard who will ensure details are passed over to the relevant ward pharmacist on the next working day or supplied as appropriate.

8. Administration

8.1 Casirivimab and imdevimab is to be administered by intravenous infusion over a minimum of 30mins.

8.2 The preparation and administration of casirivimab and imdevimab must be performed by two registered nurses using aseptic technique at a ward level.

8.3 The nMABs will be delivered to the ward as a pre-prepared kit. All the necessary consumables required for dilution and administration will be supplied by the ward area.

8.4 The preparation of casirivimab and imdevimab at a ward level must be undertaken in accordance with the worksheet enclosed with the kits.[5]

8.5 Casirivimab and imdevimab is a fridge product and will need to be brought to room temperature for approx. 20-30mins prior to reconstitution.

8.6 1.2g (10ml of 120mg/ml) of casirivimab and 1.2g (10ml of 120mg/ml) of imdevimab should be diluted in a 250mL bag of 0.9% sodium chloride and infused over a minimum of 30 minutes.

8.7 Casirivimab and imdevimab should not be infused concomitantly in the same intravenous line with other medication.

8.8 Administration should be under conditions where management of severe hypersensitivity reactions, such as anaphylaxis, is possible.

8.9 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.

8.10 The rate of infusion may be slowed, interrupted or discontinued if the patient develops any signs of infusion-associated events or other adverse events.

9. Follow Up

9.1 PCR testing should be undertaken at least weekly during the patient's time in hospital, and again in any subsequent follow up visits.

9.2 Discharge letters must explicitly record that casirivimab + imdevimab has been given, together with the dose and date of administration.

9.2 Report all adverse effects on the Yellow card System (https://coronavirus-yellowcard.mhra.gov.uk/)

10. References

1. Interim Clinical Commissioning Policy https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment_id=103846 – Accessed on 24/09/2021

2. Summary of Product Characteristics – Ronapreve 120mg/mL solution for injection or infusrion. Accessed via Ronapreve 120 mg/mL solution for injection or infusion - Patient Information Leaflet (PIL) - (emc) (medicines.org.uk) on 24/09/2021

3. Liverpool COVID-19 Drug Interactions Checker via www.covid19-druginetractions.org/checker

11. Appendices

Worksheets for ward area

Casirivimab and Imdevimab ward preparation worksheet – HIGH DOSE (Cohort 1)

3-1 HIGH DOSE-Clinical-Area-Pr

Casirivimab and Imdevimab ward preparation worksheet – LOW DOSE (Cohort 2)

3-2 LOW DOSE-Clinical-Area-Pr