Croydon Health Services NHS
NHS Trust

Guideline for the use of casirivimab and imdevimab (Ronapreve) for the management of COVID-19 infection (adults or children over 12 years) at CHS

Version:	2
Ratified by:	MAG
Date ratified:	9/11/21
Approving Committee/Group (Date)	
Date Approved by Medicines Management Committee: *(NB: All Procedural Documents which include details of drugs or their management must be approved by the Medicines Management Committee)*	Approved by Medical Advisory Group (MAG) on behalf of MMC on 09/11/2021
Name and Title of originator/author:	Ibrahim Hassan, Lead Pharmacist for Medicines Information and Formulary
Date issued:	9/11/21
Review due date:	9/11/24
Target audience:	All doctors, nurse, pharmacists involved with assessing patients with Covid-19, and prescribing, screening, supplying, preparing and administering casirivimab and imdevimab
Superseded documents	Version 1 of this guideline
Relevant Standards(e.g. NHSLA, CQC, HSE)	
Acknowledgements	
Key Words	Casirivimab, imdevimab, Ronapreve, nMAB, neutralising monoclonal antibody, Covid-19, coronavirus, SARS-CoV 2

EXECUTIVE SUMMARY

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.
It has been commissioned in England for treatment of patients in hospital who have confirmed infection with SARS-CoV-2 virus in the following groups:

Group 1: Patients hospitalised for acute COVID-19 illness: to be treated at the off-label dose of 2.4g

Group 2: Patients with hospital-onset COVID-19: to be treated at a dose of 1.2g, in line with the conditional marketing authorisation

This guideline summarises the inclusion and exclusion criteria for casirivimab and imdevimab for treatment of Covid-19, the testing required, and the processes for prescribing, screening, ordering, preparing and administering the therapy

CONTENTS

INTRODUCTION

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 casirivimab and imdevimab combination is licensed in Great Britain for use in prophylaxis and treatment of acute COVID-19 infection. The conditional marketing authorisation was based on the following evidence:

- Study 2067 (Weinrich et al, 2021): a Phase 3 randomised, double-blinded, placebo-controlled trial evaluating casirivimab and imdevimab for the treatment of non-hospitalised patients with at least one risk factor for severe COVID-19. This showed that the casirivimab and imdevimab combination led to a relative risk reduction for composite primary outcome of COVID-19-related hospitalisation or all-cause death through day 29 by 70% (p=0.0024). The study showed similar treatment effects across patients treated with 2.4g and 1.2g doses of the combination.

- Study 2069 (O'Brien et al, 2021): this was a Phase 3 randomised, double-blind, placebo-controlled trial studying casirivimab and imdevimab for prevention of COVID-19 in household contacts of individuals infected with SARS-CoV-2 (index case). The study population was stratified into two cohorts:
    - Cohort A comprised individuals with a negative SARS-CoV-2 PCR test result at baseline. Casirivimab and imdevimab led to a statistically significant 81% (p<0.0001) relative risk reduction in the development of symptomatic COVID-19 compared with placebo.

    - Cohort B comprised asymptomatic individuals with a positive SARS-CoV-2 PCR test result at baseline. Casirivimab and imdevimab led to a statistically significant 31% (p=0.038) relative risk reduction in the development of symptomatic COVID-19 compared with placebo.

On 16 June 2021 the RECOVERY trial announced findings that casirivimab and imdevimab reduced the relative risk of mortality by 20% (24% in the treatment group vs 30% in those who received standard care alone) in hospitalised patients with COVID-19 who had not mounted an antibody response of their own to the virus (were seronegative[1]) at the time of treatment. A national expert group was convened and considered available evidence, including risk of hospital admission and mortality from COVID-19 in both community and hospitalised patients as per QCOVID3®[2].

Therefore, the eligibility criteria for the use of casirivimab and imdevimab in hospitalised patients with COVID-19 has now been expanded to include the following two groups:

Group 1: Patients hospitalised for acute COVID-19 illness: to be treated at the off-label dose of 2.4g

Group 2: Patients with hospital-onset COVID-19: to be treated at a dose of 1.2g, in line with the conditional marketing authorisation

SCOPE

This guideline covers all inpatients admitted to Croydon Health Services NHS Trust, whether admitted for treatment of Covid-19 symptoms or where Covid-19 is diagnosed following admission. It covers all the indications and inclusion criteria where casirivimab + imdevimab can be prescribed within the Trust. It applies to all staff involved in prescribing, screening, supplying, preparing, and administering casirivamb + imdevimab

DEFINITIONS

CHS – Croydon Health Services NHS Trust

nMAB – neutralising monoclonal antibody – antibodies prepared through a monoclonal cell line for therapeutic use against infectious disease

SARS-CoV 2 – the virus causing Covid-19 infection

PCR test – polymerase chain reaction test, the gold standard nasal and throat swab test for detection of SARS-CoV 2 infection

Anti-S antibodies – antibodies to the spike protein present on the surface of SARS-CoV 2

Anti-N antibodies – antibodies to the nucleocapsid of SARS-CoV 2

IgG – Immunoglobulin G, a type of antibody which protects agains infection

ACCOUNTABILITIES AND RESPONSIBILITIES

Hospital consultants who will be initiating casirivimab and imdevimab are responsible for being alert to these guidelines and recommending treatment in line with them

Junior doctors are responsible for being aware of these guidelines and prescribing according to them, on the advice of a relevant consultant

Pharmacists are responsible for screening requests for casirivimab and imdevimab in line with these guidelines, and querying any discrepancies.

The pharmacy aseptic production unit are responsible for preparing any requests for casirivimab and imdevimab between 9am and 12noon Monday to Friday in a timely fashion

The pharmacy dispensary is responsible for dispensing any requests received between 12noon and 5.15pm Monday to Friday, and 9am to 5pm Saturday and Sunday, in a timely fashion

Outside of these hours the on call pharmacist is responsible for screening and attending to supply any requests for casirivimab and imdevimab

Nurses who will be preparing and administering, and the CCOT team, should be aware of these guidelines and have received training on how to prepare casirivimab and imdevimab, and prepare in line with these guidelines and associated risk assessment. Staff who have not received training should not prepare it

The Multidisciplinary Team is responsible for assessing any requests made for casirivimab and imdevimab in line with pathway 2 as described in this guideline, in a timely fashion, and responding to the MDT email group to state whether they approve of its use or not.

Pharmacy and the Practice Educator team are responsible for delivering necessary training to the ward and CCOT team regarding preparation and administration of casirivimab and imdevimab

PROCEDURE

Eligibility criteria

Patients must meet all of the eligibility criteria and none of the exclusion criteria under one of the following pathways[3, 4]:

Pathway ONE: Patients hospitalised with acute COVID-19:

- 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

- Hospitalised specifically for the management of acute symptoms of COVID-19[5]

AND

- Negative for baseline serum anti-spike (anti-S) antibodies against SARS-CoV-2[6] (see section on 'Serum antibody status' and 'Patients on replacement immunoglobulin' below)

If the above eligibility criteria are met and there are no exclusions, then the patient should be treated at the off-label dose of 2.4g

Pathway TWO: Patients with hospital-onset COVID-19

- 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

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

AND

- At high risk of progression to severe COVID-19 (see Appendix 1 for list of qualifying conditions)

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 [MDT] assessment)

AND

- A baseline serum antibody test (anti-S) against SARS-CoV-2 prior to treatment administration has been taken (for this pathway it is not necessary to wait until the antibody test is reported before commencing treatment)

If the above eligibility criteria are met and there are no exclusions, then the patient should be treated at the licensed dose of 1.2g

Patients that have been treated with casirivimab and imdevimab through pathway TWO, and who continue to deteriorate such that their acute COVID-19 illness requires hospital-based care are eligible for a second dose of casirivimab and imdevimab if they fulfil the criteria in pathway ONE.

MDT members can be reached via email: ch-tr.ronaprevemdt@nhs.net. – approval from a minimum of two MDT members is necessary for treatment. During out of hours, the first and second on-call pharmacists, along with the requesting consultant and an additional consultant (preferably an ITU or Respiratory consultant) should undertake the role of the MDT.

Exclusion criteria

- Children weighing less than 40kg
- Children aged under 12 years
- Known hypersensitivity reaction to the active substances or to any of the excipients of casirivimab and imdevimab listed in the Summary of Product Characteristics (SmPC) https://www.medicines.org.uk/emc/product/12863
- Previously received treatment in hospital with casirivimab and imdevimab at the 2.4g (combined) dose or higher

Serum antibody status

Patients may be tested for anti-S1 or anti-S2 antibodies using any validated quantitative or qualitative anti-S assay that measures either IgG or total antibody levels. Serostatus should be established in line with the pre-determined thresholds relevant to the assay being used by the testing laboratory. Quantitative assays with pre-specified thresholds for seropositivity should return clear binary (i.e. either 'negative' or 'positive') results based on these thresholds. For quantitative assays without a formal threshold for serostatus, clinical decision-making should guide treatment decisions. In immunocompromised groups, very low 'positive' levels of anti-S antibody on a quantitative assay (within the bottom 10% of the assay's positive range) should be interpreted in the context of clinical decision-making and laboratory advice and a decision to treat may still be made by the MDT on a case-by-case basis. Providers will be required to report anti-S antibody levels in treated patients, and the corresponding reference range of the local assay, for central monitoring.
If there are concerns or questions around laboratory sensitivity or cut-offs these should be discussed in the first instance with local laboratory leads who will have access to comparative and performance data from the EQA scheme participation.

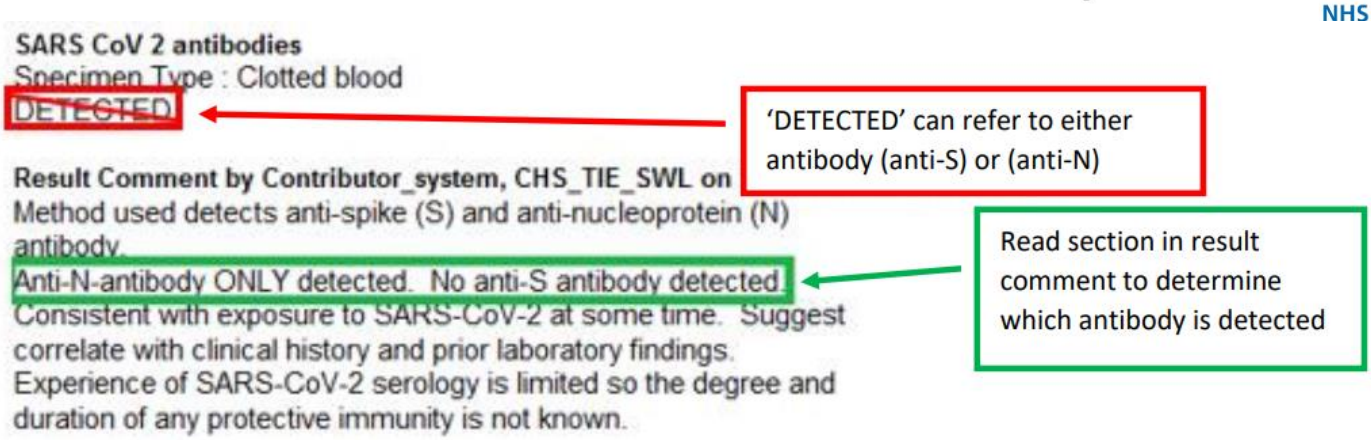
Patients on replacement immunoglobulin

In immunodeficient patients on replacement immunoglobulin (intravenous or subcutaneous), the positive detection of anti-S antibodies should be regarded as a 'positive of unknown significance'. Patients on replacement immunoglobulin testing positive only for anti-S (and negative for anti-N antibodies) should therefore be considered to be seronegative for SARS-CoV-2, and MDT assessment should judge their eligibility for nMAB treatment. Should evidence for passive transmission of anti-N antibodies through replacement immunoglobulin emerge in the future, the detection of anti-N antibodies should also be regarded as a 'positive of unknown significance'.

SARS CoV 2 antibody reporting status at Croydon Health Services

In order to be eligible for treatment with casirivimab and imdevimab via pathway 1, it is a requirement for the patient to be anti-S antibody negative only. There are some instances where an individual may be anti-S antibody negative but anti-N antibody positive; these patients would be eligible for treatment provided all other criteria were met.

Care should be taken interpreting the antibody results; patients who are anti-N positive but anti-S negative may still have "Detected" displayed in the blood result header. It is important to review the whole document to establish specifically whether anti-S antibodies have been detected or not detected. See figure below:



Cautions

- COVID-19 Vaccines
  - Casirivimab and imdevimab is not intended to be used as a substitute for vaccination against COVID-19.
  - Refer to current vaccination guidelines with respect to timing of vaccination post treatment with casirivimab and imdevimab anti-SARSCoV-2 monoclonal antibodies.
- Refer to the **Summary of Product Characteristics for full list of cautions** https://www.medicines.org.uk/emc/product/12863
- Reported cautions included:
  - Hypersensitivity Reactions including Anaphylaxis
    If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur,

    immediately discontinue administration and initiate appropriate medications and/or supportive care

  - Infusion-related reactions (IRR)
    - Typically observed during or within 24 hours of infusion. Examples of IRR (but not limited to) are nausea, chills, dizziness (or syncope), rash, urticaria and flushing.
    - If an IRR occurs, consider interrupting, slowing or stopping the infusion and administer appropriate medications and/or supportive care.

Pregnancy

- There are no or limited amount of data from the use of casirivimab and imdevimab in pregnant women.
- Casirivimab and imdevimab should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the foetus considering all associated health factors.
- If a woman becomes pregnant while taking this medicine, the individual should be informed that any potential risk to the foetus is unknown.

Breast-feeding

- It is unknown whether casirivimab and imdevimab are excreted in human milk.
- A clinical decision must be made whether to discontinue breastfeeding or to discontinue/abstain from casirivimab and imdevimab therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Dosing and administration

- For patients hospitalised with COVID-19 (pathway one); then a **single dose only** of 2.4g [1.2g (10ml of 120mg/ml) of casirivimab and 1.2g (10ml of 120mg/ml) of imdevimab] can be prescribed
- For patients with hospital-onset COVID-19 (pathway two); then a dose of 1.2g [600mg (5ml of 120mg/ml) of casirivimab and 600mg (5ml of 120mg/ml) of imdevimab] can be prescribed. Patients may also be eligible for a 2.4g repeat dose if they continue to deteriorate such that their acute COVID-19 illness requires hospital-based, providing they fulfil the eligibility criteria in pathway 1) above.
- The required dose [2.4g (20ml) or 1.2g (10ml)] need to be added to 250ml of sodium chloride 0.9% and administered via intravenous infusion over 30 minutes via a 0.2 to 5micron low-protein binding filter (polyethersulfone (Supor®), polysulfone or polyamide)
- Prescribe using **CRS Millennium: Casirivimab + imdevimab (Ronapreve)**
- The following when required medications (for allergic reactions) should also be prescribed on CRS Millennium:
  - Paracetamol IV 6hrly PRN – see order sentences **(Note: check if patient is prescribed regular paracetamol)**
  - Chlorphenamine 10mg IV Once only PRN
  - Hydrocortisone 100mg IV Once only PRN
  - Adrenaline 500microgram IM Once only PRN
- **For further administration information, refer to the Medusa IV Guide available at:** https://stginet.unily.com/sites/iv-drug-administration/SitePageModern/44779/iv-drug-administration
- Casirivimab and imdevimab should not be infused concomitantly in the same intravenous line with other medication

Drug interactions

For further information, refer to the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

Safety reporting

Any suspected adverse drug reactions (ADRs) for patients receiving casirivimab and imdevimab should be reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/

Co-administration

Corticosteroids

Administration of systemic dexamethasone or hydrocortisone is recommended in the management of patients with severe or critical COVID-19. Corticosteroids are not suggested in non-severe COVID-19 disease. Updated WHO guidance on the use of systemic corticosteroids in the management of COVID-19 can be found here. Casirivimab and imdevimab should not be regarded as an alternative to corticosteroids.

There is no interaction of casirivimab and imdevimab with either dexamethasone or hydrocortisone expected.

Remdesivir

The Clinical Commissioning Policy for the use of remdesivir in hospitalised patients with COVID-19 can be found here. There is no interaction of casirivimab and imdevimab with remdesivir expected.

IL-6 inhibitors

The Clinical Commissioning Policy for the use of IL-6 inhibitors (tocilizumab or sarilumab) in hospitalised patients with COVID-19 who require supplemental oxygen can be found here. There is no interaction of IL-6 inhibitors with casirivimab and imdevimab expected.

Baricitinib

There is no interaction of casirivimab and imdevimab with baricitinib expected.

TRAINING

Nurses will requires specific training in order to be able to prepare and check the preparation of casirivimab and imdevimab. This training includes need for appropriate PPE, risks associated with preparation of nMABs, and a step by step understanding of the process of preparing an infusion of casirivimab and imdevimab

MONITORING COMPLIANCE TRAINING

Element to be monitored	Lead	Tool	Frequency	Reporting arrangements	Acting on recommendations and Lead(s)	Change in practice and lessons to be shared
Appropriateness of prescribing	Lead Pharmacist Formulary and MI	Blue Teq	Each request	MMC / MAG	Medical Director	Trust comms, consultant meetings
Dispensing and preparation workload	Dispensary lead and ward area leads		Monthly	Ad-hoc to principal pharmacist medicines safety and governance	Chief pharmacist, Heads of Nursing, CCOT lead	Trust comms

REFERENCES

Rapid Policy Statement: Interim Clinical Commissioning Policy: Casirivimab and imdevimab in the treatment of COVID-19 in hospitalised patients. Department of Health & Social Care. 04/11/2021

Summary of Product Characteristics for Ronapreve. Available at https://www.medicines.org.uk/emc/product/12863. [Accessed on 4/11/2021]

ASSOCIATED DOCUMENTATION

Trust risk assessment for preparation and administration of casirivimab and imdevimab at ward level

Specialist Pharmacy Services resource webpage for use of casirivimab and imdevimab in hospital settings

VERSION HISTORY TABLE

Version	Date	Author	Ratified by	Comment/Reason for change
1		Ibrahim Hassan	MAG	New guideline
2	9/11/21	Ibrahim Hassan	MAG	Updates to pathways and eligibility based on changed to commissioned indications from NHS England

APPENDIX A – CONSULTATION TEMPLATE

1.	Procedural Document's Name:	Treatment guideline for casirivimab and imdevimab (Ronapreve) for inpatients with Covid-19 at Croydon Health Services (adults or children over 12 years) version 2
2.	Procedural Document Author:	Ibrahim Hassan

3.	**Group/Committee Consulted**	**Date**
	MAG	9/11/21

4	**Name and Title of Key Individuals Consulted**	**Date**
	Matthew Huntley, Principal Pharmacist Medicines Safety and Governance	5/11/21
	Louise Coughlan, Chief Pharmacist	5/11/21

5	Comments received Minor changes to formatting, change to make section on immunoglobulins a separate section, clarification RE need for only 2 members of MDT to approve, addition of clarifying section on how to read result of antibody test including picture.

APPENDIX B – COHORTS WITH IMPAIRED IMMUNE FUNCTION

The following patient cohorts are considered to have impaired immune function, be at significant risk of an adverse COVID-19 outcome, and have a high clinical capacity to benefit from treatment with nMABs. This list of conditions below, generated through consensus of clinical experts, is not exhaustive and other causes of impaired immune function may be deemed apt for treatment with nMABs by MDT assessment.

1. Primary immunodeficiency

    • Common variable immunodeficiency (CVID)
    • Undefined primary antibody deficiency on intravenous immunoglobulin (IVIg) (or eligible for IVIg treatment) • Hyper-IgM syndromes
    • Good's syndrome (thymoma plus B-cell deficiency)
    • Severe Combined Immunodeficiency (SCID)
    • Autoimmune polyglandular syndromes/Autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
    • Primary immunodeficiency associated with impaired type I interferon signalling
    • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)

2. Secondary Immunodeficiency

    • Any secondary immunodeficiency patient requiring immunoglobulin replacement therapy
    • Haematological malignancies
        o Chronic lymphocytic leukaemia (CLL)
        o B-cell lymphoma o Follicular lymphoma
        o Waldenstrom's macroglobulinaemia
    • Multiple myeloma
    • Post-CAR-T cell therapy for B-acute lymphoblastic leukaemia and B-cell lymphoma
    • Recipients of rituximab or other CD20 depleting monoclonal antibodies (such as ofatumumab and ocrelizumab)
    • Patients on conventional immunosuppressive therapy across rheumatology, neurology, dermatology, nephrology and gastroenterology
    • Patients on other biologics such as abatacept and small molecule JAK-inhibitors (such as and tofacitinib, baricitinib)
    • Patients receiving chronic high-dose corticosteroid therapy: >20mg (0.5mg/kg) prednisolone (or equivalent) per day for more than four weeks
    • Recipients of solid organ, bone marrow or stem cell transplants (irrespective of time since transplant or use of immunosuppressive medications)

3. Patients with any of the following diagnoses:
        o Down's syndrome
        o Sickle cell disease
        o Chronic kidney disease (stage 5)
        o HIV/AIDS (irrespective of viral load or CD4 count)
        o Liver cirrhosis
        o Rare neurological conditions such as motor neurone disease, multiple sclerosis, myasthenia gravis or Huntington's chorea
4. Patients who have received radiotherapy in the last 6 months
5. Patients currently on or have received the following chemotherapy regimens (Groups B and C in the table below) in the last 12 months and are considered to be at higher risk of Grade 3/4 febrile neutropenia or lymphopenia

Group B	Group C
10-50% risk of grade 3/4 febrile neutropenia or lymphopenia	>50% risk of grade 3/4 febrile neutropenia or lymphopenia
• Etoposide based regimens • CMF • Irinotecan and Oxaliplatin based regimens • Cabazitaxel • Gemcitabine • Chlorambucil • Temozolomide • Daratumumab • Rituximab • Obinutuzumab • Pentostatin • Proteosome inhibitors • IMIDs • PI3Kinase inhibitors • BTK inhibitors • JAK inhibitors • Venetoclax • Trastuzumab-emtansine • Anthracycline-based regimens • Fluorouracil, epirubicin and cyclophosphamide (FEC) • Methotrexate, vinblastine, adriamycin/doxorubicin, cisplatin (MVAC) • Adriamycin/doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD) • Cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) • All acute myeloid leukaemia/acute lymphocytic regimens • Bleomycin, etoposide and platinum • Highly immunosuppressive chemotherapy (e.g. FluDAP, high dose Methotrexate & Cytarabine) • Trifluradine/ Tipiracil • KTE-X19 • Gilteritinib 10 • Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisolone (BEACOPP) • Liposomal doxorubicin • Taxane – 3-weekly • Nab-paclitaxel • Carboplatin-based regimens • Ifosphamide-based regimens • Bendamustine • Cladrabine • Topotecan • Cyclophosphamide/Fludarabine combinations • Ifosphamide, carboplatin, etoposide (ICE) • Gemcitabine, dexamethasone, cisplatin (GDP) • Isatuximab • Polatuzumab • Acalabrutinib • Dexamethasone, cytarabine, cisplatin (DHAP) • Etoposide, methylprednisolone, cytarabine, cisplatin (ESHAP) • Cyclophosphamide, vincristine, doxorubicin, dexamethasone (CVAD) • Dacarbazine-based regimens • Lomustine • Magalizumab • Brentuximab vedotin • Asparaginase-based regimens	• All acute myeloid leukaemia/acute lymphocytic regimens • Bleomycin, etoposide and platinum • Highly immunosuppressive chemotherapy (e.g. FluDAP, high dose Methotrexate & Cytarabine) • Trifluradine/ Tipiracil • KTE-X19 • Gilteritinib

APPENDIX C – CASIRIVIMAB AND IMDEVIMAB MDT MEMBERS

Subhro Banerjee
Rizwan Rajak
Reza Motazed
Srikanth Akunuri
Theo Fenton
Soonie Patel
Yogini Raste
Mary Twagira
Imran Qureshi
Steven Vidgeon
Fathi Al-Jehani
Sanjay Gupta
Anna Brockman
Jackie Green
Louise Coughlan
Oluseyi Alabi
David Smith
Matthew Huntley
Ibrahim Hassan

APPENDIX D – PHARMACY PROCEDURE FOR SUPPLY OF CASIRIVIMAB AND IMDEVIMAB AT CHS

Procurement

The amount of product received by Trusts is based upon allocations from London Procurement Partnership (LPP). The product is available to order from Roche Products Limited via a standard Powergate order or via email: uk.cc@roche.com. Blueteq code: 9106843 should be added to the order for processing and reimbursement reasons.

Receiving stock and quarantine

- Quarantine in clearly marked section of vaccine fridge, until the quarantine fridge is received
- Stock must be quarantined until the new expiry date can be added (300mg cartons) and DHCP documents removed.

Amending expiry date and removal DHPC document

- Over label 300mg cartons with the new expiry date in the pharmacy department, under the supervision of a pharmacist.
- Expiry dates should be amended by batch number as below using the pre-prepared label and worksheet available.
- The DHPC document must be removed and discarded as this is not relevant to the use described in the Commissioning Policy.
- Once, this has been completed, move the stock out of quarantine to the LBS fridge in Pharmacy.

Small volume vials 300mg		
Batch number	Expiry date on carton	New in-use expiry
N7561B01	31/12/2022	31/12/2021
N7578B01	31/5/2023	31/5/2022

Completion of Blueteq

All Trusts are required to complete a Blueteq form for each patient eligible for treatment with casirivimab and imdevimab. Blueteq forms will be completed by the pharmacy High Cost Drug team following completion of the below *form:

Interim form for the use of Casirivimab and imdevimab (Ronapreve) in adult patients with COVID-19 pneumonia

Patient NHS No:		**GP Postcode:**	
Patient Hospital No:		**Consultant Name:**	
Patient's Initials and DoB:		**Consultant Contact Details:**	
Treatment Start Date:			
Responses to all of the criteria in either pathway must be "Yes" in order for the patient to be eligible for treatment with Ronapreve			
Pathway ONE: Patients hospitalised with acute COVID-19		**Pathway TWO: Patients with hospital-onset COVID-19**	
1. I confirm that the patient is hospitalised with SARS-CoV-2 infection* * In the absence of a confirmed virological diagnosis, casirivimab and imdevimab should only be used when a multidisciplinary team have a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis	Yes ☐ No ☐	1. I confirm that the patient is in hospital with SARS-CoV-2 infection which has been confirmed by a 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	Yes ☐ No ☐
2. I confirm that one of the following apply(please select): ☐ The patient had a negative test for baseline serum anti-spike (anti-S) antibodies against SARS-CoV-2 ☐ The patient had a positive/marginal test (within the bottom 10% of the assay's positive range) for baseline serum anti-spike (anti-S) antibodies against SARS-CoV-2 with a MDT determined treatment decision** ☐ The patient is immunodeficient and on replacement human immunoglobulin therapy** **Refer to the interim clinical commissioning policy with respect to antibody testing and to use in patients on human immunoglobulin treatment	Yes ☐ No ☐	2. I confirm one of the following apply (please select): ☐ The patient is at high risk of progression to severe COVID-19 ☐ 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 [MDT] assessment)	Yes ☐ No ☐

<table>
<tr><td>3. I confirm the patient has been hospitalised specifically for the management of acute symptoms of COVID-19</td><td>Yes ☐
No ☐</td><td>3. I confirm the patient was hospitalised for indications other than for the management of acute symptoms of COVID-19</td><td>Yes ☐
No ☐</td></tr>
<tr><td rowspan="2">4. I confirm the patient does not meet any of the following exclusion criteria
• Children weighing less than 40kg
• Children aged under 12 years
• Known hypersensitivity reaction to the active substances or to any of the excipients of casirivimab and imdevimab listed in the Summary of Product Characteristics (SmPC) https://www.medicines.org.uk/emc/product/12863
• Previously received treatment in hospital with casirivimab and imdevimab at the 2.4g (combined) dose or higher</td><td rowspan="2">Yes ☐
No ☐</td><td>4. I confirm a baseline serum antibody test (anti-S) against SARS-CoV-2 has been taken prior to treatment administration*

* All patients being considered for treatment with casirivimab and imdevimab for COVID-19 during their hospital stay should have their baseline serum antibody (anti-S) status measured prior to treatment, with appropriate patient consent, to support service evaluation and surveillance.</td><td>Yes ☐
No ☐</td></tr>
<tr><td>5. I confirm the patient does not meet any of the following exclusion criteria
• Children weighing less than 40kg
• Children aged under 12 years
• Known hypersensitivity reaction to the active substances or to any of the excipients of casirivimab and imdevimab listed in the Summary of Product Characteristics (SmPC) https://www.medicines.org.uk/emc/product/12863
• Previously received treatment in hospital with casirivimab and imdevimab at the 2.4g (combined) dose or higher</td><td>Yes ☐
No ☐</td></tr>
</table>

*form will be completed by hand until it becomes available on CRS Millennium, after which it should be completed electronically on the patient's record

Name and Signature of HCP completing the form: **Date:**

Supply of product

The product (casirivimab and imdevimab) is currently only stocked in Pharmacy.

1. Monday to Friday 9.00am-12pm

Pharmacy technical service team will prepare Casirivimab and imdevimab for requests received between 9.00am-12pm Monday to Friday.

Pharmacists to liaise with the Technical Services team, and order the medicines using a standard medicine request sheet.

2. Monday to Friday 12pm-5:15pm and Saturdays & Sundays 9am to 5pm

Requests for casirivimab and imdevimab received by pharmacy from 12pm to 5:15pm during Weekdays and 9am to 5pm during Weekends will need to be prepared at ward level by the nursing staff. This is provided that the nursing staff, have undertaken the appropriate training to prepare the medicine.

Pharmacists to supply Casirivimab and imdevimab per dispensing process below.

6. Outside of Pharmacy working hours

Supply for casirivimab and imdevimab can be obtained from pharmacy through contacting the on-call Pharmacist via switchboard. This supply will also need to be prepared at ward level by the nursing staff. This is provided that the nursing staff, have undertaken the appropriate training to prepare the medicine.

Pharmacists to supply Casirivimab and imdevimab per dispensing process below.

Dispensing and supply

- Casirivimab and imdevimab is located in LBS fridge in the dispensary.
- Casirivimab and imdevimab **MUST** be booked out from JAC
- Each original pack contains co-packaged 6ml single use vials of casirivimab and imdevimab:
    - 1 x 6ml vial containing 300mg/2.5ml casirivimab
    - 1 x 6ml vial containing 300mg/2.5ml of imdevimab

Although the nominal volume of each vial is 2.5mL, the actual fill volume for each of the vials is expected to be greater.

- Each patient will require either **2 or 4 x original packs** to make up the required dose of casirivimab and imdevimab.
- Overlabelled batch numbers and expiry dates should be recorded on JAC during dispensing.
- “Kit for Ward Preparation” must be booked out of JAC and supplied with casirivimab and imdevimab packs. These are kept on top of the LBS fridge.
- “Clinical Area Preparation Record” Sheet must also be supplied- see appendix E and F. These are also kept on top of LBS fridge
- The casirivimab and imdevimab packs, “Kit for Ward Preparation” and “Clinical Area Preparation Record” Sheet must all be placed in one bag and ready for collection by a member of ward staff. Collection needs to be signed for on the PbR register.

APPENDIX E – CLINICAL AREA PREPARATION RECORD TO MAKE UP 2.4G DOSE [CASIRIVIMAB 1200MG AND IMDEVIMAB 1200MG IN 250ML SODIUM CHLORIDE 0.9% INFUSION BAG (TOTAL VOLUME = 270ML)] PREPARED USING CASIRIVIMAB AND IMDEVIMAB 300MG IN 2.5ML VIALS

Set up
Step 1 Check that the dose prescribed matches the kits and preparation record selected e.g. Casirivimab 1200mg and Imdevimab 1200mg
Step 2 Casirivimab and Imdevimab infusion preparation method is complex and requires 2 persons to prepare safely: • The ***preparer*** who will prepare the product. • The ***checker*** who will ensure the method is followed accurately and perform documented independent checks at key points in the preparation process.
Step 3 Remove from the refrigerator a Casirivimab 1200mg and Imdevimab 1200mg 2.5mL vial size kit for ward preparation containing: • 4 cartons of Casirivimab and Imdevimab 120mg/mL Concentrate for Solution for Infusion Each carton contains • 1 x Casirivimab 300mg in 2.5mL (120mg/mL) vial • 1 x Imdevimab 300mg in 2.5mL (120mg/mL) vial Select a Casirivimab 1200mg and Imdevimab 1200mg room temperature consumable kit for ward preparation containing: • 1 x Sodium Chloride 0.9% 250mL Infusion Bag • Syringes, needles, and administration filter
Step 4 Visually inspect both the Casirivimab and Imdevimab vials. • The solution for each vial should be clear to slightly opalescent, colourless to pale yellow. Should particulate matter and discoloration be observed, the vial must be discarded and replaced with a new vial.
Step 5 Place to the left side of the preparation area: • 4 x Casirivimab 300mg in 2.5mL (120mg/mL) vials • 4 x Imdevimab 300mg in 2.5mL (120mg/mL) vials • 1 x Sodium Chloride 0.9% 250ml Infusion Bag
Step 6 Prepare an infusion additive label with the following details: • Casirivimab 1200mg and Imdevimab 1200mg in Sodium Chloride 0.9% (Total volume = 270mL) • Date and time prepared • [Additional details as required by local label format]

Preparation of Infusion Bag					
Step 1 Bring 1 x Sodium Chloride 0.9% 250mL Infusion Bag from the left side of the preparation area into the middle, swab the bung with a sterile 70% alcohol wipe and allow to dry.					
Step 2 Bring 4 x Casirivimab 300mg in 2.5mL (120mg/mL) vials from the left side of the preparation area into the middle, swab the bung with sterile 70% alcohol wipe and allow to dry.					
Step 3 Attach a needle to a 10mL luer lock syringe and draw up **1 x 10mL** of Casirivimab 300mg in 2.5mL (120mg/mL) from the 4 vials ***NB: Each vial contains excess volume and therefore some liquid may remain after the required volume has been withdrawn.***					
Drug name, strength and volume withdrawn checked by *checker (initial)*					
Step 4 Add **10mL** of Casirivimab 120mg/mL to the Infusion Bag. Discard the syringe and needle into a yellow lidded sharps bin					
Addition of Casirivimab to Infusion Bag checked by *checker (initial)*					
Step 5 Place the used Casirivimab vials to the right side of the preparation area.					
Step 6 Bring 4 x Imdevimab 300mg in 2.5mL (120mg/mL) vials from the left side of the preparation area into the middle, swab the bung sterile 70% alcohol wipe and allow to dry.					
Step 7 Attach a needle to a 10mL luer lock syringe and draw up **1 x 10mL** of Imdevimab 300mg in 2.5mL (120mg/mL) from the 4 vials ***NB: Each vial contains excess volume and therefore some liquid may remain after the required volume has been withdrawn.***					
Drug name, strength and volume checked by *checker (initial)*					
Step 8 Add **10mL** of Imdevimab 120mg/mL to the same Infusion Bag. Discard the syringe and needle into a yellow lidded sharps bin					
Addition of Imdevimab to Infusion Bag checked by *checker (initial)*					
Step 9 Place the used Imdevimab vials to the right side of the preparation area					
Step 10 Gently mix the filled infusion bag by slowly inverting 10 times. **Do not shake**					
Step 11 Attach the pre-prepared label to the bag					
Step 12 Ensure the product is administered using an [Insert local in-line or add-on 0.2µm to 5µm polyethersulfone, polysulfone, or polyamide end filter used]					
Step 13 Record details of the patient who will receive the bag below, and file the completed *Clinical Area Preparation Record* in accordance with local guidance					
Patient Name		Hospital No		Date of Birth	

Document	SPSCI04a - Clinical Area Preparation Record - ~~casirivimab~~ 1200mg and ~~imdevimab~~ 1200mg in 250mL NaCl 0.9% (2.5mL vials)	Version Number	1.2	Date Issued	05/11/2021	Issued By	NWPQA
		Site Name:		Review Date	01/11/2023	Approved by	

APPENDIX F – CLINICAL AREA PREPARATION RECORD TO MAKE UP 1.2G DOSE [CASIRIVIMAB 600MG AND IMDEVIMAB 600MG IN 250ML SODIUM CHLORIDE 0.9% INFUSION BAG (TOTAL VOLUME = 260ML)] PREPARED USING CASIRIVIMAB AND IMDEVIMAB 300MG IN 2.5ML VIALS

Set up
Step 1 Check that the dose prescribed matches the kits and preparation record selected e.g. Casirivimab 600mg and Imdevimab 600mg
Step 2 Casirivimab and Imdevimab infusion preparation method is complex and requires 2 persons to prepare safely: • The ***preparer*** who will prepare the product. • The ***checker*** who will ensure the method is followed accurately and perform documented independent checks at key points in the preparation process.
Step 3 Remove from the refrigerator a Casirivimab 600mg and Imdevimab 600mg 2.5mL vial size kit for ward preparation containing: • 2 cartons of Casirivimab and Imdevimab 120mg/mL Concentrate for Solution for Infusion Each carton contains • 1 x Casirivimab 300mg in 2.5mL (120mg/mL) vial • 1 x Imdevimab 300mg in 2.5mL (120mg/mL) vial Select a Casirivimab 600mg and Imdevimab 600mg 2.5mL vial size room temperature consumable kit for ward preparation containing: • 1 x Sodium Chloride 0.9% 250mL Infusion Bag • Syringes, needles, and administration filter
Step 4 Visually inspect both the Casirivimab and Imdevimab vials. • The solution for each vial should be clear to slightly opalescent, colourless to pale yellow. Should particulate matter and discoloration be observed, the vial must be discarded and replaced with a new vial.
Step 5 Place to the left side of the preparation area: • 2 x Casirivimab 300mg in 2.5mL (120mg/mL) vials • 2 x Imdevimab 300mg in 2.5mL (120mg/mL) vials • 1 x Sodium Chloride 0.9% 250ml Infusion Bag
Step 6 Prepare an infusion additive label with the following details: • Casirivimab 600mg and Imdevimab 600mg in Sodium Chloride 0.9% (Total volume = 260mL) • Date and time prepared • [Additional details as required by local label format]

Preparation of Infusion Bag					
Step 1 Bring 1 x Sodium Chloride 0.9% 250mL Infusion Bag from the left side of the preparation area into the middle, swab the bung with a sterile 70% alcohol wipe and allow to dry.					
Step 2 Bring 2 x Casirivimab 300mg in 2.5mL (120mg/mL) vials from the left side of the preparation area into the middle, swab the bung with sterile 70% alcohol wipe and allow to dry.					
Step 3 Attach a needle to a 5mL luer lock syringe and draw up **1 x 5mL** of Casirivimab 300mg in 2.5mL (120mg/mL) from the 2 vials ***NB: Each vial contains excess volume and therefore some liquid may remain after the required volume has been withdrawn.***					
Drug name, strength and volume withdrawn checked by *checker (initial)*					
Step 4 Add **5mL** of Casirivimab 120mg/mL to the Infusion Bag. Discard the syringe and needle into a yellow lidded sharps bin					
Addition of Casirivimab to Infusion Bag checked by *checker (initial)*					
Step 5 Place the used Casirivimab vials to the right side of the preparation area.					
Step 6 Bring 2 x Imdevimab 300mg in 2.5mL (120mg/mL) vials from the left side of the preparation area into the middle, swab the bung sterile 70% alcohol wipe and allow to dry.					
Step 7 Attach a needle to a 5mL luer lock syringe and draw up **1 x 5mL** of Imdevimab 300mg in 2.5mL (120mg/mL) from the 2 vials ***NB: Each vial contains excess volume and therefore some liquid may remain after the required volume has been withdrawn.***					
Drug name, strength and volume checked by *checker (initial)*					
Step 8 Add **5mL** of Imdevimab 120mg/mL to the same Infusion Bag. Discard the syringe and needle into a yellow lidded sharps bin					
Addition of Imdevimab to Infusion Bag checked by *checker (initial)*					
Step 9 Place the used Imdevimab vials to the right side of the preparation area					
Step 10 Gently mix the filled infusion bag by slowly inverting 10 times. **Do not shake**					
Step 11 Attach the pre-prepared label to the bag					
Step 12 Ensure the product is administered using an [Insert local in-line or add-on 0.2µm to 5µm polyethersulfone, polysulfone, or polyamide end filter used]					
Step 13 Record details of the patient who will receive the bag below, and file the completed *Clinical Area Preparation Record* in accordance with local guidance					
Patient Name		Hospital No		Date of Birth	

Document	SPSCI04c - Clinical Area Preparation Record – casirivimab 600mg and imdevimab 600mg in 250mL NaCl 0.9% (2.5mL vials)	Version Number	1	Date Issued	05/11/2021	Issued By	NWPQA
		Site Name:		Review Date	01/11/2023	Approved by	