CLINICAL GUIDELINE: TREATMENT OF COVID-19 (ADULTS AND CHILDREN)

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Intended audience	All Manx Care clinical staff	
Superseded documents	Clinical Guideline: Treatment of Patients Hospitalised Due to COVID-19 (adults and children), December 2012 Clinical Guideline: Treatment of Patients with Symptomatic Hospital-Onset COVID-19 (adults and children), December 2012 Guidance on the Management of Non-Hospitalised Patients with COVID-19 Infection and Eligible for Treatment (adults and children)	
Stakeholders consulted prior to ratification	CAG	
Ratified by	IMOG	Date 19 July 2023
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Changes made during latest review	n/a	

Contents

1. INTRODUCTION

The management of COVID-19 was reviewed by NICE in April 2023. This changed the recommended treatment pathways for COVID-19.

The existing Manx Care guidance documents have been updated and incorporated into this combined document. The treatment pathway is no longer clearly divided into the original three categories of patient (Infected Vulnerable Patients in Primary Care; Patients Hospitalised due to Covid-19; Patients who develop Covid as an Inpatient), so this document brings together the previous guidance documents and updates them in line with NICE Guidance.

1.1 Purpose

This document aims to aid clinicians in offering best care and advice in treating patients, supported by national policy. Clinical judgement in the initiation, review, escalation and de-escalation of patients should be supported where possible by multidisciplinary team assessment.

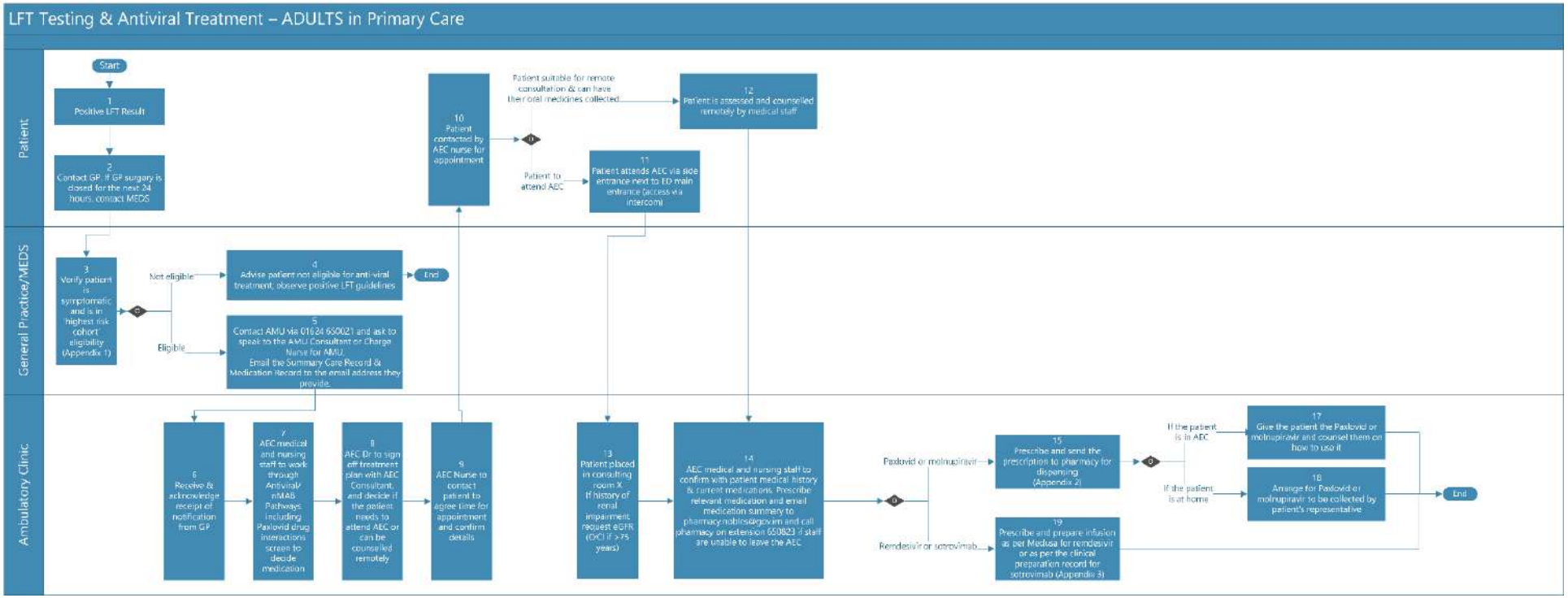
This guideline outlines the criteria for use of Paxlovid (nirmatrelvir/ritonavir), remdesivir, molnupiravir, sotrovimab, tocilizumab and baricitinib in patients who have a confirmed COVID-19 infection.

2. RELATED GUIDANCE

More detail on the management of Covid patients can be found in the full NICE Guidance document, available at https://www.nice.org.uk/guidance/ng191/resources/fully-accessible-version-of-the-guideline-pdf-pdf-51035553326 .

3 GENERAL GUIDANCE

3.1 Decision Algorithm for Primary Care - ADULTS

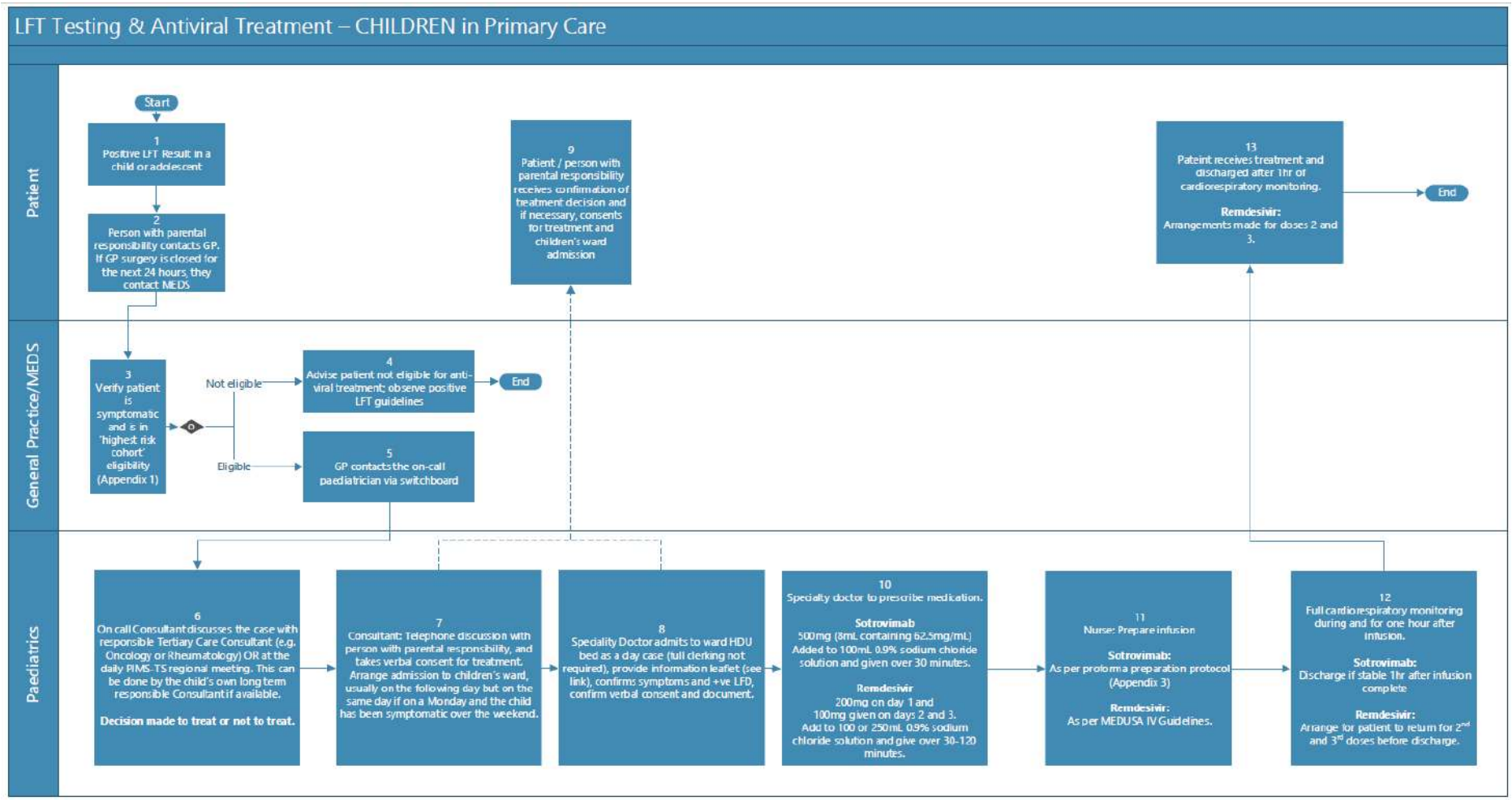


Full documents embedded here:

23-05 Childrens algorithm.pdf

23-08 Adult decision algorithm v

3.2 Decision Algorithm for Primary Care - CHILDREN



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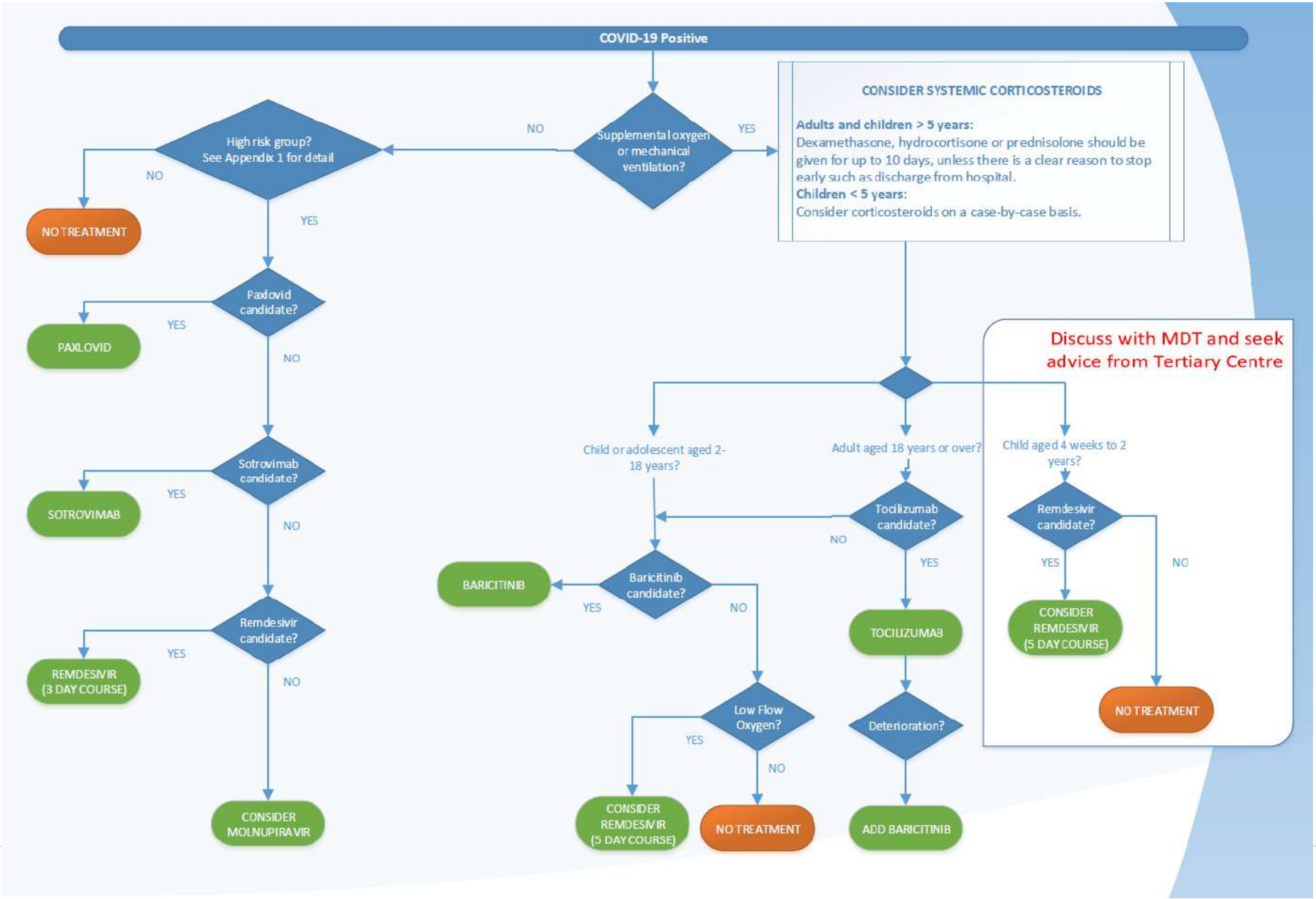
3.3 Treatment Flowchart



4 MEDICATION-SPECIFIC GUIDANCE

4.1 Nirmatrelvir / Ritonavir (Paxlovid)

Eligibility criteria for nirmatrelvir/ritonavir (Paxlovid)

- Adults within 5 days of symptom onset. By exception, a decision may be made to initiate treatment within 5-7 days of treatment onset (off-label).
- Patient must be symptomatic and showing no signs of clinical recovery.
- eGFR of at least 30mL/min. A dosage adjustment is needed for those with eGFR 30-60mL/min.

Do not initiate nirmatrelvir/ritonavir (Paxlovid) treatment in:

- Patients whose symptoms began more than 7 days ago.
- Patients who need supplementary oxygen for the management of their COVID-19 symptoms.
- Patients with a history of advanced or decompensated liver cirrhosis.
- Patients with stage 4 or 5 CKD (eGFR less than 30mL/min).
- Anyone who is pregnant, or may become pregnant.
- Children less than 18 years of age.
- Patients who need to take medication which interacts with nirmatrelvir/ritonavir and the effects cannot be mitigated or avoided.

Drug Interactions with nirmatrelvir/ritonavir (Paxlovid)

Nirmatrelvir/ritonavir (Paxlovid) has the potential to increase exposure to many medicines. Often, this can be managed by temporarily withholding the interacting drug, or reducing the dose of the interacting drug. In addition, many medicines will affect exposure to nirmatrelvir and ritonavir.
Due to the wide range and severity of potential interactions, it is vital that a detailed interaction screen is carried out in all patients prescribed nirmatrelvir/ritonavir (Paxlovid).

The University of Liverpool COVID-19 website is used to carry out an interaction screen. Go to www.covid19-druginteractions.org . Select the interaction checker to run a check on your patients' medication. See also 'prescribing resources' on the same site.
Further information is available from the SPC (www.medicines.org.uk/emc/product/13145).
Contact Pharmacy for further advice.

Dosage of nirmatrelvir/ritonavir (Paxlovid)

Nirmatrelvir/ritonavir has a complex dosage schedule. Great care is required when prescribing and administering this medication.

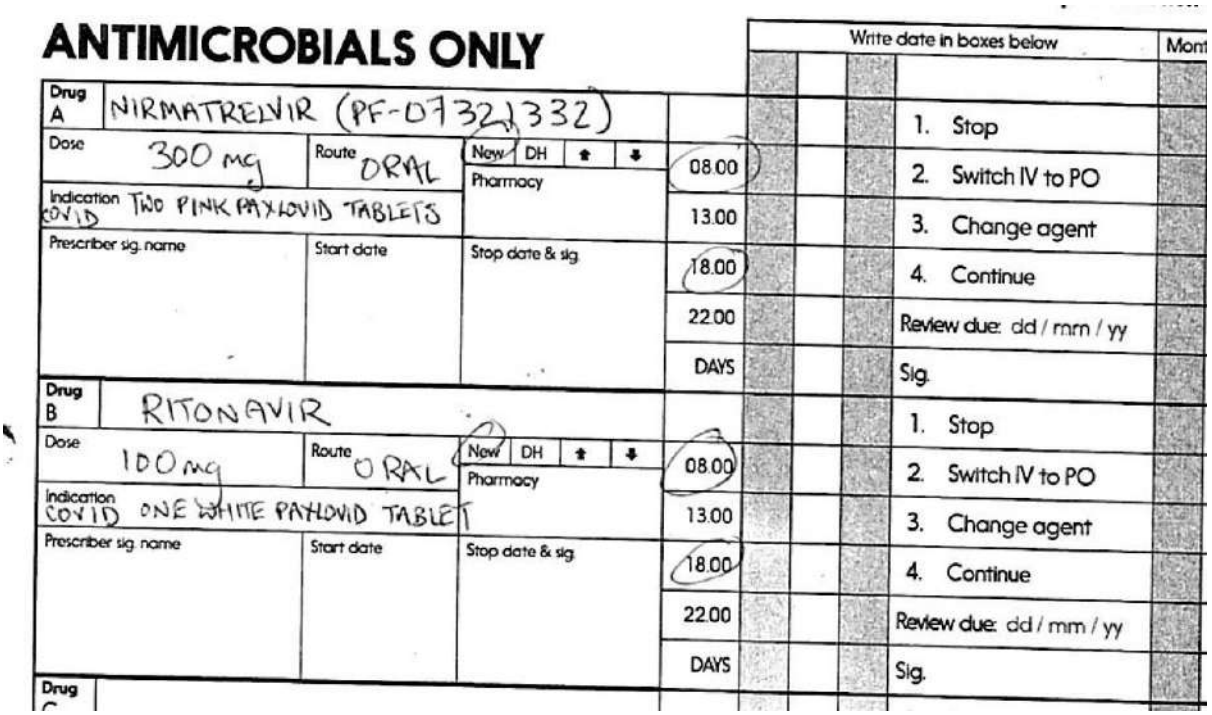
The pack consists of the following:
20 Pink tablets containing 150mg of nirmatrelvir.
10 White tablets containing 100mg of ritonavir.

The standard dose is 300mg nirmatrelvir (two pink tablets) and 100mg ritonavir (one white tablet) twice a day for 5 days.
In moderate renal impairment (eGFR 30-60mL/min), the dose is 150mg nirmatrelvir (one pink tablet) and 100mg ritonavir (one white tablet) twice a day for 5 days.

For patients prescribed this from the Ambulatory Clinic, pre-printed prescription is used for antivirals including nirmatrelvir/ritonavir (Paxlovid) [Appendix 2]

For inpatients, the safest way to prescribe nirmatrelvir/ritonavir is as follows:

Standard Dose:



ANTIMICROBIALS ONLY

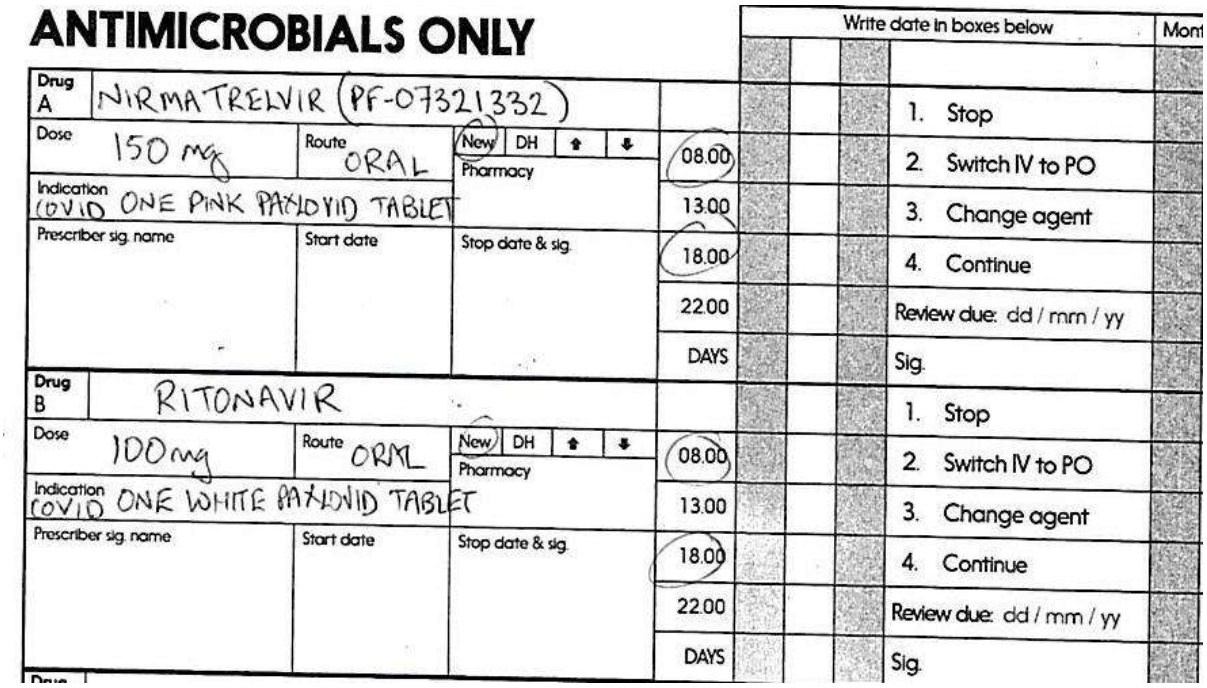
Write date in boxes below

Drug A: NIRMATRELVIR (PF-07321332)
Dose: 300 mg | Route: ORAL | New | DH | Pharmacy
Indication: COVID TWO PINK PAXLOVID TABLETS
Prescriber sig. name | Start date | Stop date & sig.
08.00 / 13.00 / 18.00 / 22.00 / DAYS

Drug B: RITONAVIR
Dose: 100 mg | Route: ORAL | New | DH | Pharmacy
Indication: COVID ONE WHITE PAXLOVID TABLET
Prescriber sig. name | Start date | Stop date & sig.
08.00 / 13.00 / 18.00 / 22.00 / DAYS

1. Stop
2. Switch IV to PO
3. Change agent
4. Continue
Review due: dd / mm / yy
Sig.

Reduced dose in Renal Failure:



ANTIMICROBIALS ONLY

Write date in boxes below

Drug A: NIRMATRELVIR (PF-07321332)
Dose: 150 mg | Route: ORAL | New | DH | Pharmacy
Indication: COVID ONE PINK PAXLOVID TABLET
Prescriber sig. name | Start date | Stop date & sig.
08.00 / 13.00 / 18.00 / 22.00 / DAYS

Drug B: RITONAVIR
Dose: 100 mg | Route: ORAL | New | DH | Pharmacy
Indication: COVID ONE WHITE PAXLOVID TABLET
Prescriber sig. name | Start date | Stop date & sig.
08.00 / 13.00 / 18.00 / 22.00 / DAYS

1. Stop
2. Switch IV to PO
3. Change agent
4. Continue
Review due: dd / mm / yy
Sig.

Adverse Effects with nirmatrelvir/ritonavir (Paxlovid)

Elevated hepatic transaminases, clinical hepatitis and jaundice have occurred with ritonavir. Nirmatrelvir/ritonavir (Paxlovid) can cause diarrhoea and nausea and vomiting. Anti-emetics should be considered where appropriate, but this would not usually necessitate stopping therapy.
For inpatients, renal and hepatic function should be monitored carefully during treatment with nirmatrelvir/ritonavir (Paxlovid). U+E's and LFT's should be checked daily.
Discontinue treatment where there is evidence of severe hepatic impairment or if the patient's eGFR falls to below 30mL/min.
Reduce the dose of nirmatrelvir if the patient's eGFR falls to below 60mL/min.

Pregnancy and breastfeeding

Nirmatrelvir/ritonavir (Paxlovid) should not be used during pregnancy or where the patient is at risk of becoming pregnant.

Note that nirmatrelvir/ritonavir (Paxlovid) may reduce the efficacy of combined oral contraceptives. Patients should use an effective alternative contraceptive method or an additional barrier method during treatment and until after one complete menstrual cycle after stopping nirmatrelvir/ritonavir (Paxlovid).

There is no data on breastfeeding while taking nirmatrelvir/ritonavir (Paxlovid). Breastfeeding should be discontinued during treatment and for at least 7 days after the last dose of nirmatrelvir/ritonavir (Paxlovid).

4.2 Remdesivir

Eligibility criteria for remdesivir

Remdesivir is indicated in:

- **Adults and children (at least 4 weeks of age and weighing at least 3kg) who have COVID-19 pneumonia and require supplemental oxygen or mechanical ventilation.**
    - Remdesivir should only be considered after tocilizumab (adults) and baricitinib (adults and children aged 2 or more) have been considered and considered to be contraindicated or not possible.
    - Remdesivir should only be considered in patients receiving low flow oxygen. This is oxygen delivered via a simple face mask or nasal cannula with a flow rate up to 15 litre/min.
    - Treatment must commence within 10 days of symptom onset, unless the patient is significantly immunocompromised, in which case this window does not apply.
    - These patients are eligible for a **five day course** of remdesivir.
- **Adults and children weighing at least 40kg who are at increased risk of progressing to severe COVID-19 but do not currently require supplemental oxygen.**
    - Treatment must commence within 7 days of symptom onset.
    - The patient must still be symptomatic and showing no signs of clinical recovery.
    - Nirmatrelvir/ritonavir (Paxlovid) and sotrovimab should be considered before remdesivir in this patient group. Only use remdesivir if these options are contraindicated or not possible.
    - These patients are eligible for a **three day course** of remdesivir.

Do not initiate remdesivir treatment in:

- Patients who require high-flow supplementary oxygen, continuous positive airway pressure, non-invasive mechanical ventilation or invasive mechanical ventilation.
- Patients who are asymptomatic or who are showing signs of recovery from COVID-19.
- Patients with eGFR <30mL/min, unless the patient is on haemodialysis.
- Patients with ALT >5 times the upper limit of normal.

Dosage of Remdesivir

	Adults and children >40kg	Children at least 4 weeks old and weighing between 3kg and 40kg
Day 1 (Loading Dose)	200mg	5 mg/kg
Days 2 onwards (Daily Maintenance Dose)	100mg	2.5 mg/kg

Treatment should usually last a maximum of 5 days (3 days in those not requiring supplemental oxygen).
Duration of treatment may be extended to 10 days in patients who require low flow oxygen and are significantly immunocompromised.

Ongoing need for treatment should be assessed daily.

Method of Administration of Remdesivir

Remdesivir should be given as an IV infusion after reconstitution and further dilution. It is an acidic solution, and likely to cause tissue damage in the event of extravasation. A central line or a large peripheral vein should be used. It should be given over 30 to 120 minutes.

100mg and 200mg doses may be given in a 100mL or 250mL bag of 0.9% sodium chloride. Doses less than 100mg may be given in 50mL or 100mL of 0.9% sodium chloride.

Information on preparation and administration can be found on the Medusa Injectable Medicines Guide. For access, visit the Pharmacy SharePoint site (http://edrmgi/sites/hospital/Pages/pharmacy.aspx) and select 'Injectable Medicines Guide (MEDUSA)'.

Pregnancy and breastfeeding

Remdesivir should not be used during pregnancy unless the clinical condition of the women requires treatment with it.

Excretion of remdesivir and/or metabolites into breast milk can be assumed based on animal studies, therefore a decision must be made whether to discontinue breastfeeding or to discontinue remdesivir therapy based on risk benefit analysis.

Monitoring of remdesivir

Renal and hepatic function should be monitored carefully during treatment. U+E's and LFT's should be checked daily and treatment should be stopped if ALT ≥5 times the upper limit of baseline or eGFR <30mL/min/1.73m^2.

Adverse drug effects of remdesivir

Reported adverse effects include increased transaminase elevations, nausea, headache and drug sensitivity reactions, ranging from rash to anaphylaxis.

Drug Interactions with remdesivir

- No significant interaction has been found between remdesivir and other treatments used for COVID-19, including corticosteroids.
- Further information can be found on the university of Liverpool COVID-19 Drug interactions website: https://www.covid19-druginteractions.org

4.3 Molnupiravir

Eligibility criteria for molnupiravir

- Within 5 days of symptom onset. By exception, a decision may be made to initiate treatment within 5-7 days of treatment onset (off-label).
- Patient must be symptomatic and showing no signs of clinical recovery.
- Treatment with nirmatrelvir/ritonavir (Paxlovid) and remdesivir are either contraindicated or impossible.
- eGFR of at least 30mL/min.

Do not initiate molnupiravir treatment in:

- Patients whose symptoms began more than 7 days ago.
- Patients who require supplementary oxygen for the management of their COVID-19 symptoms.
- Patients with stage 4 or 5 CKD (eGFR less than 30mL/min), unless they are on haemodialysis.
- Anyone who is pregnant, or may become pregnant.
- Children less than 18 years of age.

Dosage of molnupiravir

The recommended dose is 800mg (four 200mg capsules) taken orally every 12 hours for 5 days.

A pre-printed prescription is used for antivirals including molnupiravir within AEC [Appendix 2].

Adverse Effects with molnupiravir

The most common adverse effects are diarrhoea, nausea, dizziness and headache, all of which were described as mild or moderate.
More rarely, rash and urticaria have been reported.

Pregnancy and breastfeeding

Human data are lacking, but animal studies have demonstrated reproductive toxicity with molnupiravir. Molnupiravir should be avoided in women who are pregnant or could be pregnant. The effects of infant exposure via milk are unknown. Mothers should avoid breastfeeding during treatment and for 4 days after the last dose of molnupiravir.

4.4 Sotrovimab

Eligibility criteria for sotrovimab

- Patients aged 12 years or older.
- Within 5 days of symptom onset. By exception, a decision may be made to initiate treatment within 5-7 days of treatment onset (off-label).
- Patient must be symptomatic and showing no signs of clinical recovery.
- Treatment with nirmatrelvir/ritonavir (Paxlovid), remdesivir and molnupiravir are contraindicated or impossible.
- Treatment has been endorsed by a relevant MDT.

Do not initiate sotrovimab treatment in:

- Patients whose symptoms began more than 7 days ago.
- Patients who are asymptomatic or who are showing signs of recovery from COVID-19.
- Patients who require supplementary oxygen for the management of their COVID-19 symptoms.
- Children aged less than 12 years.
- Adolescents (aged 12-17 years) who weigh less than 40kg.

Dosage of sotrovimab

The recommended dose of sotrovimab is 500mg as a single intravenous infusion over 30 minutes.
Treatment should be initiated as soon as possible after COVID-19 diagnosis, and within 7 days of the onset of symptoms. For full preparation instructions, see [Appendix 3]

Further information on preparation and administration can be found on the Medusa Injectable Medicines Guide. For access, visit the Pharmacy SharePoint site (http://edrmgi/sites/hospital/Pages/pharmacy.aspx) and select 'Injectable Medicines Guide (MEDUSA)'.
Sotrovimab is a monoclonal antibody. As such, handling should be kept to a minimum and personal protective equipment must be worn.
Monoclonal antibodies can target a variety of different molecules. The specific target of sotrovimab is the spike protein on the outside of the COVID-19 virus. It does not target tissues or physiological processes in individuals.

Adverse drug reactions of sotrovimab

The most commonly reported adverse effects are hypersensitivity reactions, including rash, dermatitis and other skin reactions, infusion-related reactions and bronchospasm. Hypersensitivity has a reported incidence of 1-10%. Rarely, sotrovimab may cause anaphylaxis. Emergency measures for the management of anaphylaxis must be available when sotrovimab is used.

Mild or moderate hypersensitivity reactions may be managed by slowing or stopping the infusion along with appropriate supportive care.

Pregnancy and breastfeeding

Sotrovimab binds specifically to a protein found on the COVID-19 virus. However, the drug would be expected to pass from the mother to the developing fetus.
It may only be used in pregnant women when the expected benefit to the mother justifies the risk.

The excretion of sotrovimab in milk has not been studied. The decision on whether to continue/ discontinue breastfeeding or treatment should be made based on the benefit of breastfeeding and the benefit of patient.

4.5 Tocilizumab

Eligibility criteria for tocilizumab

- Adult patients only (18 years or older).
- Patient has been admitted to hospital due to COVID-19 infection which is either confirmed by microbiological testing or staff are confident that COVID-19 is the most likely diagnosis based on clinical and radiological features.
- Patient has severe pneumonia requiring respiratory support, such as high-flow nasal oxygen, non-invasive ventilation, or invasive mechanical ventilation.
- Patient is receiving corticosteroids unless contraindicated.

EITHER:

- Hypoxaemia with evidence of inflammation but not yet critically ill requiring respiratory support, and within the following parameters:
    - C-reactive protein level of at least 75 mg/L AND
    - Oxygen saturation of <92% on room air OR a requirement for supplemental oxygen.

OR:

- Patient is in the early stages of critical illness regardless of their C-reactive protein level. Patient is within 48 hours of starting respiratory support (high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation).

If the patient has severe COVID-19 or is critically ill, consider adding baricitinib to their tocilizumab.

Exclusion criteria for tocilizumab

- Hypersensitivity to tocilizumab.
- Previously treated with tocilizumab or other IL-6 inhibitors, such as sarilumab within the current admission.
- Baseline alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than 10 times the upper limit of normal (ULN)
- Absolute neutrophil count (ANC) below 1 x 10^9/L
- Platelet count below 50 x 10^9/L

Cautions

- Pre-existing condition or treatment resulting in ongoing immunosuppression
- Co-existing infection that might be worsened by tocilizumab
- Patients with a history of recurring or chronic infections or with underlying conditions (e.g. diverticulitis, diabetes and interstitial lung disease) which may predispose patients to infections.
- Viral activation (e.g. Hepatitis B) has been reported with biologic therapies
- Live and live attenuated vaccines should not be given concurrently with tocilizumab as clinical safety has not been established
- Physicians should be vigilant for symptoms potentially indicative of new-onset central demyelinating disorders. The potential for central demyelination with tocilizumab is currently unknown.

A full list of cautions can be found on the SPC, available at
https://www.medicines.org.uk/emc/product/6673

Dose and method of administration of tocilizumab

The recommended dose of tocilizumab is 8 mg/kg body weight (up to a maximum dose of 800mg) for a single dose. A second dose should not be considered.
The following dose bandings may be used :

Weight	Dose
<41kg	8mg/kg (round to nearest 20mg)
41-45kg	360mg
46-55kg	400mg
56-65kg	480mg
66-80kg	600mg
81-90kg	680mg
>91kg	800mg

Tocilizumab is given as an intravenous infusion over 60 minutes in a 100mL sodium chloride 0.9% infusion bag. Remove an equivalent volume from the bag before adding tocilizumab. Tocilizumab should not be infused concomitantly in the same IV line with other medications. Information on preparation and administration can be found on the Medusa Injectable Medicines Guide. For access, visit the Pharmacy SharePoint site (http://edrmgi/sites/hospital/Pages/pharmacy.aspx) and select 'Injectable Medicines Guide (MEDUSA)'.

Tocilizumab is a monoclonal antibody and so reduce direct handling to a minimum and wear appropriate personal protective equipment. Patients can develop hypersensitivity reactions, therefore monitor for anaphylaxis signs such as flushing, fever, chills, rash, pruritus, urticaria, headache and hypertension. The patient's pulse, blood pressure, temperature & respiration rate should be measured after 15 minutes, then every 30 minutes until 1-hour post infusion.

Adverse drug effects of tocilizumab

The most commonly reported ADRs were upper respiratory tract infections, nasopharyngitis, headache, hypertension and increased ALT. The most serious ADRs were serious infections, complications of diverticulitis, and hypersensitivity reactions. Any suspected ADRs for patients receiving tocilizumab should be reported directly to the MHRA via the new dedicated COVID-19 yellow card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/

Pregnancy and breastfeeding

Women of childbearing potential must use effective contraception during and up to 3 months after treatment. A study in animals has shown an increased risk of spontaneous abortion/embryo-foetal death at a high dose, the potential risk for humans is unknown so the use of tocilizumab should not be used during pregnancy unless clearly necessary.
The excretion of tocilizumab in milk has not been studied in animals. The decision on whether to continue/ discontinue breastfeeding or treatment should be made based on the benefit of breastfeeding and the benefit of patient.

Co-administration

There is no interaction of tocilizumab with dexamethasone/ hydrocortisone, baricitinib or remdesivir.
If the patient deteriorates despite treatment with tocilizumab, consider adding baricitinib to their therapy.

For further information on interactions, please visit the university of Liverpool covid-19 drug interactions website: https://www.covid19-druginteractions.org/

Ongoing Monitoring

Patients who have been treated with tocilizumab should be given an information leaflet and advised to report any signs of infection. The infection risk remains for approximately 3 months after the last dose. The Information leaflet is available at https://www.sps.nhs.uk/wp-content/uploads/2021/03/COVID-19-Patient-Discharge-Information-Leaflet-Tocilizumab-Sarilumab.pdf
This information should also be shared with the patient's GP, who should be made aware of the infection risk and escalate if appropriate.

4.6 Baricitinib

Baricitinib is indicated in:

- Adults and children (at least 2years of age) who are hospitalised due to COVID-19 pneumonia and require supplemental oxygen or another form of respiratory support.

Eligibility criteria for baricitinib

- Patient must be hospitalised specifically for the management of confirmed COVID-19.
- Patient must have viral pneumonia syndrome.
- Patient must be receiving dexamethasone or an equivalent corticosteroid unless contraindicated.
- Estimated glomerular filtration rate (eGFR) must be at least 30mL/min. If the patient is 9 years old or older, an eGFR of 15 mL/min is acceptable for treatment.

Do not initiate baricitinib treatment in:

- Patients who are less than 2 years of age.
- Patients with an eGFR less than 15 mL/min or receiving renal replacement therapy.
- Patients with a neutrophil count less than $0.5x10^9$ cells/L.
- Patients with active tuberculosis.
- Patients who are pregnant or breastfeeding.

Dosage and administration of baricitinib

Age	Renal function (eGFR)	Dose
9 years or older	≥ 60 mL/min	4mg daily for 10 days (or until discharge if sooner)
	30-60 mL/min	2mg daily for 10 days (or until discharge if sooner)
	15-30 mL/min	2mg every 2nd day for 10 days (or until discharge if sooner)
2-8 years	≥ 60 mL/min	2mg daily for 10 days (or until discharge if sooner)
	30-60 mL/min	2mg every 2nd day for 10 days (or until discharge if sooner)

NB: The baricitinib dose may need to be reduced if the patient also takes a strong OAT3 inhibitor such as probenecid. For advice, go to www.covid19-druginteractions.org/checker , speak to your pharmacist, or contact Medicines Information on 650818 or medinfo@gov.im.

For patients with swallowing difficulties, baricitinib tablets may be dispersed in water immediately prior to administration. This is off-label. Add the tablet to approximately 10mL of water in a container, and swirl to allow it to disperse (approximately 5 minutes). A small amount of juice may be added to improve the taste.
Rinse the cup with a little water and administer this to the patient to ensure they get a full dose.

For patients with feeding tubes, disperse the tablet as above, but use 30mL to disperse the tablet and 15mL to rinse the container. This is also off-label.

Pregnancy and breastfeeding

Baricitinib must not be used during pregnancy. Women of childbearing potential must use effective contraception during treatment and for at least 1 week after stopping treatment.

Baricitinib and its metabolites are likely to be present in breast milk, and the consequences of infant exposure are unknown. Baricitinib should not be used during breast-feeding.

Monitoring of baricitinib

Renal function and neutrophil counts should be monitored carefully during treatment, and treatment discontinued if the patient satisfies one of the exclusion criteria.

Liver function should be monitored and treatment with baricitinib reviewed if liver injury is suspected.

Adverse drug effects of baricitinib

Baricitinib carries a risk of venous thromboembolism, and VTE prophylaxis should be considered.
There is a risk of reactivation of viruses such as herpes zoster or herpes simplex.

Drug Interactions

- No significant interaction has been found between baricitinib and other treatments used for COVID-19, including corticosteroids.
- Further information can be found on the university of Liverpool COVID-19 Drug interactions website: https://www.covid19-druginteractions.org

5 References

General resources

National Institute for Health and Care Excellence, 29th March 2023. **COVID-19 rapid guideline: Managing COVID-19.** Available at https://www.nice.org.uk/guidance/ng191

National Institute for Health and Care Excellence, 29 March 2023. NICE Guideline TA878. **Casirivimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19.** Available at: https://www.nice.org.uk/guidance/ta878

NHS England, 11 May 2023. **Rapid Policy Statement. Interim Clinical Commissioning Policy: remdesivir and molnupiravir for non-hospitalised patients with COVID-19.** Available at https://www.england.nhs.uk/publication/interim-clinical-commissioning-policy-remdesivir-and-molnupiravir-for-non-hospitalised-patients-with-covid-19/

British National Formulary via Formulary Complete. Available from: https://www.formularycomplete.com/

Nirmatrelvir/ritonavir

Summary of Product Characteristics, Paxlovid 150 mg/100 mg film-coated tablets, Pfizer, Oct 2022. Available at: https://www.medicines.org.uk/emc/product/13145

Remdesivir

Medusa Injectable Medicines Guide. Remdesivir Powder For Reconstitution For Infusion. [online]. Monograph published 5 Nov 2020. Injmed.wales.nhs.uk.

Summary of Product Characteristics, Veklury 100 mg Powder For Concentrate For Solution For Infusion, Gilead, Jan 2023. Available at: https://www.medicines.org.uk/emc/product/11597

Molnupiravir

Summary of Product Characteristics. Lagevrio 200mg ad capsules, MSD, Apr 2023. Available at: https://www.medicines.org.uk/emc/product/13044

Sotrovimab

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Tocilizumab
Medusa Injectable Medicines Guide. Tocilizumab concentrate for infusion. [online]. Monograph published 20 Apr 2023. Injmed.wales.nhs.uk.

Summary of Product Characteristics. RoActemra 20mg/ml Concentrate for Solution for Infusion, Roche, Nov 2022. Available at: https://www.medicines.org.uk/emc/product/6673

Baricitinib
Summary of Product Characteristics. Olumiant 2mg film-coated tablets, Eli Lilly, Mar 2023. Available at: https://www.medicines.org.uk/emc/product/2434

Legacy Documents (superseded)

Interim Clinical Commissioning Policy: Remdesivir For Patients Hospitalised With COVID-19 28th November 2022 [online] Available at: https://www.england.nhs.uk/coronavirus/documents/interim-clinical-commissioning-policy-remdesivir-for-patients-hospitalised-due-to-covid-19-adults-and-adolescents-12-years-and-older/

COVID-19 therapeutic Alert. Remdesevir for Patients Hospitalised Due to Covid-19. Department of Health and Social Care, UK. 28 November 2022. Available at https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment_id=104099

DHSC COVID-19 Therapeutic Alert: Interleukin-6 inhibitors (tocilizumab or sarilumab) for adult patients hospitalised due to COVID-19 , 29 Nov 2022. Available from: https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment_id=104111

Interim Clinical Commissioning Policy: Interleukin-6 inhibitors (tocilizumab or sarilumab) for hospitalised patients with COVID-19 (adults). 28 November 2022. Available at https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment_id=104107

Appendix 1A: Highest Risk Clinical Subgroups in Primary Care

See the full UK guidance here.

Down's syndrome and other genetic disorders
All individuals with Down's Syndrome or other chromosomal disorders known to affect immune competence.

Solid cancer
metastatic or locally advanced inoperable cancer
lung cancer (at any stage)
people receiving any chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months
people who have had cancer resected within 3 months and who received no adjuvant chemotherapy or radiotherapy
people who have had cancer resected within 3 to 12 months and receiving no adjuvant chemotherapy or radiotherapy are expected to be at less risk (and thus less priority) but still at increased risk compared with the non-cancer populations

Haematological diseases and recipients of haematological stem cell transplant (HSCT)
allogeneic HSCT recipients in the last 12 months or active graft versus host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases)
autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
individuals with haematological malignancies who have received CAR-T cell therapy in the last 24 months, or until the lymphocyte count is within the normal range
individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months, or radiotherapy in the last 12 months
all people who do not fit the criteria above, and are diagnosed with:
myeloma (excluding monoclonal gammopathy of undetermined significance (MGUS))
AL amyloidosis
chronic B-cell lymphoproliferative disorders (chronic lymphocytic leukaemia, follicular lymphoma)
myelodysplastic syndrome (MDS)
chronic myelomonocytic leukaemia (CMML)
myelofibrosis
any mature T-cell malignancy
all people with sickle cell disease
people with thalassaemia or rare inherited anaemia with any of the following:
severe cardiac iron overload (T2 * less than 10ms)
severe to moderate iron overload (T2 * greater than or equal to 10ms) plus an additional co-morbidity of concern (for example, diabetes, chronic liver disease or severe hepatic iron load on MRI)
individuals with non-malignant haematological disorders (for example, aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (for example, anti-CD20, anti-thymocyte globulin (ATG) and alemtuzumab) within the last 12 months

Renal disease
renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who have:
received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)
an additional substantial risk factor which would in isolation make them eligible for monoclonals or oral antivirals
non-transplant renal patients who have received a comparable level of immunosuppression[footnote 3]
patients with chronic kidney stage (CKD) 4 or 5 (an estimated glomerular filtration rate (eGFR) less than 30ml per min per 1.73m2) without immunosuppression

Liver diseases
people with cirrhosis Child-Pugh (CP) class A,B and C, whether receiving immune suppressive therapy or not. Those with decompensated liver disease (CP B and C) are at greatest risk
people with a liver transplant
people with liver disease on immune suppressive therapy (including people with and without cirrhosis)

Solid organ transplant recipients
Solid organ transplant recipients not in any of the above categories.

(continued on next page)

Immune mediated inflammatory disorders[footnote 4]
people who have received a B-cell depleting therapy (anti-CD20 drug for example, rituximab, ocrelizumab, ofatumab, obinutuzumab) in the last 12 months.
people who have been treated with cyclophosphamide (IV or oral) in the 6 months prior to positive PCR or relevant COVID test
people who are on corticosteroids (equivalent to greater than 10mg per day of prednisolone) for at least the 28 days prior to positive PCR
people who are on current treatment with mycophenolate mofetil, oral tacrolimus, azathioprine, mercaptopurine (for major organ involvement such as kidney, gastro-intestinal tract, liver and/or interstitial lung disease), methotrexate (for interstitial lung disease or asthma[footnote 5] only) and/or ciclosporin. No minimum dose threshold is suggested[footnote 6]
people who exhibit at least one of: (a) uncontrolled or clinically active disease (that is, required recent increase in dose or initiation of new immunosuppressive drug or IM steroid injection or course of oral steroids within the 3 months prior to positive PCR); and/or (b) other high risk comorbidities (for example, body mass index (BMI) greater than 30, diabetes mellitus, hypertension, major organ involvement such as significant kidney, liver or lung inflammation or significantly impaired renal, liver and/or lung function)

Respiratory[footnote 7]
asthma in people on oral corticosteroids (defined above)[footnote 8]. Any asthma patient taking immunosuppressants for their asthma including but not exclusively methotrexate, ciclosporin
COPD on long term home non-invasive ventilation (NIV). Patients on long term oxygen therapy. People with moderate or severe disease (FEV1 greater than or equal to 50% predicted) who have required 4 or more courses of prednisolone 30mg for 5 days or greater in last 12 months
interstitial lung disease (ILD) - all patients with idiopathic pulmonary fibrosis
sub-types of ILD - for example, connective tissue disease related, sarcoidosis, hypersensitivity pneumonitis, NSIP (non specific interstitial pneumonia) who have received a B-cell depleting therapy in last 12 months, or IV or oral cyclophosphamide in the 6 months prior to testing positive for COVID-19. Any ILD patient on current treatment with corticosteroids, mycophenolate mofetil, azathioprine, tacrolimus, cyclosporin or methotrexate. No minimum dose criteria
any people with any type of ILD who may not be on treatment due to intolerance but has severe disease with an FVC predicted less than 60%
NIV - all patients requiring this type of support regardless of the underlying disorder (which might include COPD, obesity hypoventilation syndrome, scoliosis, bronchiectasis, genetic muscular diseases refer to neurology section)[footnote 9]
lung cancer patients, refer to 'Solid cancer' section above
lung transplant patients (refer to solid organ transplant section)
pulmonary hypertension (PH): groups 1 and 4 from PH classification[footnote 10]

Immune deficiencies
common variable immunodeficiency (CVID)
undefined primary antibody deficiency on immunoglobulin (or eligible for Ig)
hyper-IgM syndromes
Good's syndrome (thymoma plus B-cell deficiency)
severe combined immunodeficiency (SCID)
autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
primary immunodeficiency associated with impaired type I interferon signalling
x-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
any person with secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy

HIV/AIDS
people with high levels of immune suppression, have uncontrolled or untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis
people on treatment for HIV with CD4 less than 350 cells per mm3 and stable on HIV treatment or CD4 greater than 350 cells per mm3 and additional risk factors (for example, age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, alcoholic dependency)[footnote 11]

Neurological disorders
Conditions associated with neuromuscular respiratory failure requiring chronic ventilatory support:
motor neurone disease
Duchenne muscular dystrophy
Conditions that require use of specific immunotherapies:[footnote 12]
multiple sclerosis (MS)
myasthenia gravis (MG)
other immune mediated disorders
Dementia and neurodegenerative disorders when associated with severe frailty:[footnote 13]
Alzheimer's disease, vascular disease, Lewy body disease, or frontotemporal atrophy
Parkinson's Disease
Huntington's disease
progressive supranuclear palsy and multiple system atrophy

Appendix 1B: Children and Young People (CYP) aged 12-18 who may be considered greater risk

See the full UK guidance here.

Non-hospitalised individuals in the older than 12 and younger than 18 years age range considered at high risk from COVID-19 and to be prioritised for consideration of treatment with neutralising monoclonal antibodies when symptomatic and SARS-CoV-2 PCR positive. Concerned clinicians should refer for regional MDT case discussion through local established pathways, who will confirm eligibility and consider risk benefit and whether to proceed with offer of treatment.

Children and young people (CYP) at substantial risk
Complex life-limiting neurodisability with recurrent respiratory infections or compromise.

CYP at significant risk if 2 or more of these risk factors are present

Primary immunodeficiency:
common variable immunodeficiency (CVID)
primary antibody deficiency on immunoglobulin (or eligible for immunoglobulin replacement)
hyper-IgM syndromes
Good's syndrome (thymoma plus B-cell deficiency)
severe combined immunodeficiency (SCID)
autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
primary immunodeficiency associated with impaired type I interferon signalling
x-linked agammaglobulinaemia (and other primary agammaglobulinaemias)

Secondary immunodeficiency:
HIV CD4 count less than 200 cells per mm^3
solid organ transplant
HSCT within 12 months, or with GVHD
CAR-T therapy in last 24 months
induction chemotherapy for acute lymphoblastic leukaemia (ALL), non-Hodgkin's lymphoma, chemotherapy for acute myeloid leukaemia (AML), relapsed and/or refractory leukaemia or lymphoma

Immunosuppressive treatment:
chemotherapy within the last 3 months
cyclophosphamide within the last 3 months
corticosteroids greater than 2mg per kg per day for 28 days in last 4 weeks
B cell depleting treatment in the last 12 months

Other conditions:
high BMI (greater than 95th Centile)
severe respiratory disease (for example, cystic fibrosis or bronchiectasis with FEV1 less than 60%)
tracheostomy or long-term ventilation
severe asthma (PICU admission in 12 months)
neurodisability and/or neurodevelopmental disorders
severe cardiac disease
severe chronic kidney disease
severe liver disease
sickle cell disease or other severe haemoglobinopathy
trisomy 21
complex or chromosomal genetic or metabolic conditions associated with significant comorbidity
multiple congenital anomalies associated with significant comorbidity
bronchopulmonary dysplasia - decisions should be made taking in to account degree of prematurity at birth and chronological age
infants less than 1 year with congenital heart disease (CHD):[footnote 14]
cyanotic congenital heart disease
haemodynamically significant acyanotic CHD and history of prematurity
those due for corrective surgery, to avoid complications or delay due to SARS-CoV-2 infectio

Appendix 2: Outpatient Prescription

manx care

Nobles' Hospital COVID-19 Antiviral/nMab Adult Outpatient Prescription Form (for non-hospitalised patients)

Doctor/Nurse checklist (Use alongside SOP/Pathway for full guidance)

Weight: _____ kg
Allergies:

Affix Patient Label

Eligibility Criteria:	Date	Result	Doctor / Nurse (Print Name & Sign)
LFD test		Positive / Negative (please circle)	
eGFR		_____ mL/min	
List OTC medications			
Interactions checked for intended antiviral - see www.covid19-druginteractions.org/checker		Covid Drugs and all Co-medications selected. ❒ 'Personalised Report' downloaded and printed ❒ Either there are no interactions or the interactions are manageable	
Is patient high risk as per Appendix 1 of pathway/SOP? Yes / No		State condition that deems patient high risk _____	
Contraindications checked		Yes / No (please circle)	
Date of onset of symptoms		[redacted]	

Pharmacy checklist:

Eligibility Criteria:	Date	Result	Pharmacist (Name, Signature and Date)
Drug history checked for current medications		No significant interactions **OR** See recommendations below:	

manx care
Keeirl Vannin

Prescription

Choose ONLY ONE appropriate prescription below - **CROSS THROUGH ALL REMAINING PRESCRIPTIONS**

Renal Function	Drug	Dose	Directions	Pharmacy	Checked by / Given by
eGFR ≥60 mL/min Calculate CrCl if >75 years)	**(PAXLOVID) Nirmatrelvir (PF-07321332) 150mg / Ritonavir 100mg tablets**	**2** x 150mg Nirmatrelvir + 1 x 100mg Ritonavir	PO TWICE daily for 5 days		[redacted]
Renal Impairment eGFR <60 mL/min Calculate CrCl if >75 years)	**(PAXLOVID) Nirmatrelvir (PF-07321332) 150mg / Ritonavir 100mg tablets**	**1** x 150mg Nirmatrelvir + 1 x 100mg Ritonavir	PO TWICE daily for 5 days. Discard the remaining 150mg tablet in each blister.		
[redacted]	**MOLNUPIRAVIR**	**4 x 200mg capsules**	PO TWICE daily for 5 days		
	SOTROVIMAB	**500mg**	ONE SINGLE DOSE IV (Give in 100mL sodium chloride 0.9% over 30 minutes)		BN: EXP: Given by: Checked by:
eGFR ≥30 mL/min (except if on haemodialysis) + ALT < 5 x ULN (ULN is 50U/L)	**REMDESIVIR**	Day 1 **200mg** date	ONCE A DAY IV (Give in 100mL sodium chloride 0.9% over 30 minutes) for THREE days		**Day 1** Date: BN: EXP: Given by: Checked by:
		Day 2 **100mg** date			**Day 2** Date: BN: EXP: Given by: Checked by:
		Day 3 **100mg** date			**Day 3** Date: BN: EXP: Given by: Checked by:
Supportive Medication					

Additional PIL given to patient ☐ Scanned to Mediviewer ☐ Scanned to GP ☐

Pharmacy Cost Code: N1A. CALL AEC ON 650922 WHEN READY

Prescriber Name	PRINT NAME	**Pharmacist Name (Clinical Screen)**	PRINT NAME
Signature		**Signature**	
Date	dd/mm/yy	**Date**	dd/mm/yy

Appendix 3: Sotrovimab preparation

Specialist Pharmacy Service

Clinical Area Preparation Record – Sotrovimab 500mg in 100mL Sodium Chloride 0.9% Infusion Bag (Total volume = 108mL)

Set up
Step 1 Remove from the refrigerator: • 1 x Sotrovimab 500mg (62.5mg/mL) Concentrate for Solution for Infusion vial. Select: • 1 x Sodium Chloride 0.9% 100mL Infusion Bag • 1 x 10mL luer lock syringe • 1 x drawing up needle • 1 x 0.2 micron administration filter
Step 2 Visually inspect the Sotrovimab vial • The solution should be clear, colourless or yellow to brown and free from visible particles Should particulate matter or discoloration be observed, the vial must be discarded and replaced with a new vial.
Step 3 Place to the left side of the preparation area: • 1 x Sotrovimab 500mg vial • 1 x Sodium Chloride 0.9% 100ml Infusion Bag
Step 4 Prepare an infusion additive label with the following details: • Sotrovimab 500mg in Sodium Chloride 0.9% (Total volume = 108mL) • Date and time prepared

Report ALL adverse effects on the Yellow Card System:

https://coronavirus-yellowcard.mhra.gov.uk/

Preparation of Infusion Bag
Step 1 Bring the Sodium Chloride 0.9% 100mL 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 the Sotrovimab 500mg vial 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 Gently swirl the vial several times before use without creating air bubbles. **Do not shake or vigorously agitate the vial.**
Step 4 Attach a drawing up needle to a 10mL luer lock syringe and draw up **1 x 8mL** of Sotrovimab 500mg (62.5mg/mL) from the vial
Step 5 Add **8mL** of Sotrovimab (62.5mg/mL) to the Sodium Chloride 0.9% 100mL Infusion Bag. Discard the syringe and needle into a yellow lidded sharps bin
Step 6 Gently rock the infusion bag back and forth 3 to 5 times. ***NB: Do not invert the infusion bag. Avoid forming air bubbles. Do not shake***
Step 7 Attach the pre-prepared label to the bag
Step 8 Ensure the product is administered using a 0.2µm filter as a single IV infusion for 30 minutes using an infusion pump. **Monitor for signs of hypersensitivity.** Discontinue the infusion immediately in the event of a severe reaction. Mild or moderate reactions may be managed by slowing or stopping the infusion.
Step 9 Flush the line with a sufficient volume of sodium chloride 0.9% to ensure the complete dose is given.
Step 10 Record details of the patient who will receive the bag below, and file this completed form in the patient's notes. Ensure the brand, batch number and expiry date are also recorded in the medical notes or drug chart.

Patient Name		Hospital No		Date of Birth	

Document	SPSS02 - Clinical Area Preparation Record - Sotrovimab 500mg in 100mL NaCl 0.9% Infusion Bag	Version Number	1	Date Issued	14/12/2021	Issued By	NWPQA / C Rore
		Site Name:	Nobles Hospital	Review Date	14/12/2023	Approved by	