Liverpool Heart and Chest Hospital NHS
NHS Foundation Trust

**Reference Number:** FOI202425/311
**From:** Other

**Date:** 18 October 2024

**Subject:** Guidelines on the treatment of COVID-19

Q1 Does Liverpool Heart and Chest NHS Foundation Trust have any local treatment guidelines, pathways or protocols for treatment of COVID-19 infection?
Yes/No
If Yes, please provide a copy.

A1 Yes, please see attached document: Treatment of COVID-19 In Adults with Monoclonal Antibodies and Oral Antivirals v7.0

Please note, we follow both NICE and NHSE guidance for Trust guidelines for treatment of Covid.

# Treatment of COVID-19 In Adults with Monoclonal Antibodies and Oral Antivirals

## Policy

| For completion by Author | | | |
|---|---|---|---|
| Author(s) Name and Title: | Danny Forrest, Chief Pharmacist | | |
| Scope: | Trust Wide | Classification: | Clinical |
| Version Number: | 7.0 | Review Date: | 30/04/2026 |
| Replaces: | 6.1 | | |
| To be read in conjunction with the following documents: | COVID-19 rapid guideline: managing COVID-19 NICE guideline [NG191]<br>Nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 Technology appraisal guidance TA 878 29 March 2023<br>Remdesivir and tixagevimab plus cilgavimab for treating COVID-19 Technology appraisal guidance TA971 08 May 2024<br>NHSE Interim clinical commissioning policy: Remdesivir and molnupiravir for non-hospitalised patients with COVID-19 11th May 2023 | | |
| Document for public display: | No | | |
| Executive Lead | Dr Manoj Kudavalli, Medical Director | | |

| For completion by Approving Committee | | | |
|---|---|---|---|
| Equality Impact Analysis Completed: | | Yes | |
| Endorsement Completed: | Yes | Record of Changes | Yes |
| Authorised by: | Drug & Therapeutics | Authorisation date: | 15/05/2024 |

| For completion by Document Control | | | | | |
|---|---|---|---|---|---|
| Unique ID No: | T23DC139 | Issue Status: | Approved | Issue Date: | 30/05/2024 |
| After this document is withdrawn from use it must be kept in archive for the lifetime of the Trust, plus 6 years. | | | | | |
| Archive: | Document Control | | Date Added to Archive: | | |
| Officer responsible for Archive: | IG and Document Control Facilitator | | | | |

# Contents

# Document Statement

Antiviral medications inhibit viral replication and prevent progression of infection. Some nMABs are synthetic monoclonal antibodies that bind to the spike protein of SARS-CoV-2, preventing subsequent entry of the virus into the host cell and its replication. This effectively 'neutralises' the virus particle. Other nMABs bind to IL-6 receptors to produce an anti-inflammatory effect.

Evidence suggests that antivirals significantly improve clinical outcomes in patients with COVID-19 who are at high risk of progression to severe disease and/or death. The purpose of this document is to inform the safe prescribing, supply, preparation and administration of these medicines.

# 1. Roles and Responsibilities

All staff involved in the prescribing, supply, preparation or handling of these drugs must be familiar with this policy.

# 2. Controlled Document Standards

The above drugs will be used in the treatment of COVID-19 according to NICE TA 878[(1)]

# 3. Procedure

nMABs are synthetic monoclonal antibodies that bind to the spike protein of SARS-CoV-2, preventing subsequent entry of the virus into the host cell and its replication. This effectively 'neutralises' the virus particle. Antiviral medications inhibit viral replication and prevent progression of infection.

Evidence suggests that antivirals significantly improve clinical outcomes in patients with COVID-19 who are at high risk of progression to severe disease and/or death.

### 3.1 Recommendations

3.1.1 Nirmatrelvir plus ritonavir is recommended as an option for treating COVID-19 in adults, only if they:

- do not need supplemental oxygen for COVID-19 **and** have any of the following:

- have an increased risk for progression to severe COVID-19, as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab age 70 years and over
- a body mass index (BMI) of 35 kg/m2 or more
- diabetes
- heart failure.

3.1.2 Remdesivir is recommended as an option for treating COVID-19 in hospitals in:

- adults, only if they have a high risk of serious illness (risk factors as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab).

  Remdesivir is only recommended if the company provides it according to the commercial arrangement.

  This recommendation is from NICE's technology appraisal guidance on remdesivir and tixagevimab plus cilgavimab for treating COVID-19 :TA971

3.1.3 Molnupiravir

Consider a 5-day course of molnupiravir for adults with COVID-19 who:

• do not need supplemental oxygen for COVID-19 **and**

- are within 5 days of symptom onset **and**
- are thought to be at high risk of progression to severe COVID-19. (NHS England's Interim Clinical Commissioning Policy on remdesivir and molnupiravir provides a list of people prioritised for treatment with antivirals.)

3.1.4 Sotrovimab is recommended as an option for treating COVID-19 in adults and young people aged 12 years and over and weighing at least 40 kg, only if:

- they do not need supplemental oxygen for COVID-19

**and**

- they have an increased risk for progression to severe COVID-19, as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab **and**
- nirmatrelvir plus ritonavir is contraindicated or unsuitable.

Sotrovimab is only recommended if the company provides it according to the commercial arrangement.

3.1.5 Tocilizumab is recommended, within its marketing authorisation, as an option for treating COVID-19 in adults who:

- are having systemic corticosteroids

**and**

- need supplemental oxygen or mechanical ventilation.

Tocilizumab is only recommended if the company provides it according to the commercial arrangement.

The summary of product characteristics for tocilizumab specifies that it should only be offered when there is no evidence of a bacterial or viral infection (other than SARS-CoV-2) that might be worsened by tocilizumab. It also states that the efficacy of tocilizumab has not been established in the treatment of COVID-19 in people who do not have elevated C-reactive protein levels. [

3.1.6 Baricitinib

Consider baricitinib for people 2 years and over in hospital with COVID-19 who:

• need supplemental oxygen for COVID-19 **and**

• are having or have completed a course of corticosteroids such as dexamethasone, unless they cannot have corticosteroids **and**

• have no evidence of infection (other than SARS-CoV-2) that might be worsened by baricitinib.

In March 2023, this was an off-label use of baricitinib.

Baricitinib may be considered in people who meet the above criteria, and who cannot have tocilizumab. When there is clinical deterioration despite treatment with tocilizumab, it may be appropriate to add baricitinib.

### 3.2 Dosage

Refer to relevant data sheets;

*Nirmatrelvir/ritonavir SPC https://www.medicines.org.uk/emc/product/13145*
*Remdesivir SPC https://www.medicines.org.uk/emc/product/11597*
*Molnupiravir SPC https://www.medicines.org.uk/emc/product/13044*
*Sotrovimab SPC www.medicines.org.uk/emc/product/13097*
*Tocilizumab SPC https://www.medicines.org.uk/emc/product/6673/smpc*
*Baricitinib SPC https://www.medicines.org.uk/emc/product/7486/smpc*

### 3.3 Contraindications and cautions

COVID-19 vaccines nMABs are not intended to be used as a substitute for vaccination against COVID-19. Concomitant administration of an nMAB with COVID-19 vaccines has not been studied. Refer to local/national guidelines for vaccine administration and guidance on the risks associated with administration of a SARS-CoV-2 vaccine.

Visit https://www.medicines.org.uk/emc/ for full information on specific drugs.

*Nirmatrelvir/ritonavir SPC https://www.medicines.org.uk/emc/product/13145*

Nirmatrelvir/ritonavir has a risk of serious adverse reactions due to interactions with other medicinal products (see Appendix 1 for a list of these products)

Initiation of Nirmatrelvir/ritonavir, a CYP3A inhibitor, in patients receiving medicinal products metabolised by CYP3A or initiation of medicinal products metabolised by CYP3A in patients already receiving Nirmatrelvir/ritonavir, may increase plasma concentrations of medicinal products metabolised by CYP3A. Initiation of medicinal products that inhibit or induce CYP3A may increase or decrease concentrations of Nirmatrelvir/ritonavir, respectively.

These interactions may lead to:

• Clinically significant adverse reactions, potentially leading to severe, life-threatening or fatal events from greater exposures of concomitant medicinal products.

• Clinically significant adverse reactions from greater exposures of Nirmatrelvir/ritonavir.

• Loss of therapeutic effect of Nirmatrelvir/ritonavir and possible development of viral resistance.

Hepatic transaminase elevations, clinical hepatitis and jaundice have occurred in patients receiving ritonavir. Therefore, caution should be exercised when administering Nirmatrelvir/ritonavir to patients with pre-existing liver diseases, liver enzyme abnormalities or hepatitis.

Remdesivir SPC https://www.medicines.org.uk/emc/product/11597

Hypersensitivity reactions including infusion-related and anaphylactic reactions have been observed during and following administration of remdesivir. Signs and symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnoea, wheezing, angioedema, rash, nausea, vomiting, diaphoresis, and shivering. Slower infusion rates, with a maximum infusion time of up to 120 minutes, can be considered to potentially prevent these signs and symptoms. Monitor patients for hypersensitivity reactions during and following administration of remdesivir as clinically appropriate. Patients receiving remdesivir in an outpatient setting should be monitored after administration according to local medical practice. If signs and symptoms of a clinically significant hypersensitivity reaction occur, immediately discontinue administration of remdesivir and initiate appropriate treatment.

*Sotrovimab SPC* Xevudy 500 mg concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

Hypersensitivity reactions, including serious and/or life-threatening reactions such as anaphylaxis, have been reported following infusion of sotrovimab. Hypersensitivity reactions typically occur within 24 hours of infusion. Signs and symptoms of these reactions may include nausea, chills, dizziness (or syncope), rash, urticaria and flushing. If signs and symptoms of severe hypersensitivity reactions occur, administration should be discontinued immediately and appropriate treatment and/or supportive care should be initiated.

If mild to moderate hypersensitivity reactions occur, slowing or stopping the infusion along with appropriate supportive care should be considered.

Tocilizumab SPC RoActemra 20mg/ml Concentrate for Solution for Infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

Serious hypersensitivity reactions have been reported in association with infusion of Tocilizumab. Such reactions may be more severe, and potentially fatal in patients who have experienced hypersensitivity reactions during previous infusions even if they have received premedication with steroids and antihistamines. Appropriate treatment should be available for immediate use in the event of an anaphylactic reaction during treatment. If an anaphylactic reaction or other serious hypersensitivity / serious infusion related reaction occurs, administration of Tocilizumab should be stopped immediately and should be permanently discontinued.

**Information for nurses**

**3.4 Administration:**

**Sotrovimab**

*In normal working hours:*

Sotrovimab will be supplied ready-made from the pharmacy aseptic unit in a 50mL bag of sodium chloride 0.9% containing 500mg sotrovimab. The bags must not be shaken. Infuse via a 0.2µm filter as a single IV infusion for 30 minutes.

*Out of hours and weekends:*
500mg vials of sotrovimab will be available in the Pharmacy Emergency Drugs Cupboard fridge.

The infusion required is 500mg (8mL) of sotrovimab 62.5mg/mL added to a 50mL bag of sodium chloride 0.9% (without removing any fluid from the bag). If the diluent bag used is at room temperature, there is no need to allow the vial to warm first. If the infusion is prepared in a clinical area it should be used immediately.

**Nirmatrelvir/ritonavir**

A missed dose should be taken as soon as possible and within 8 hours of the scheduled time, and the normal dosing schedule should be resumed. If more than 8 hours has elapsed, the missed dose should not be taken and the treatment should resume according to the normal dosing schedule.

If a patient requires hospital-based care due to severe or critical COVID-19 after starting treatment with Nirmatrelvir/ritonavir, the patient should complete the full 5-day treatment course at the discretion of his/her healthcare provider.

Remdesivir

Take the vials out of the fridge and allow remdesivir solution to come to room temperature (20°C to 25°C) before dilution.

200mg of remdesivir (day 1 loading dose) and 100mg of remdesivir maintenance doses should be diluted in either a 250ml or 100ml pre-filled bag of 0.9% sodium chloride solution and infused over a minimum of 30 minutes.

**Molnupiravir**

If the patient misses a dose of Lagevrio within 10 hours of the time it is usually taken, the patient should take as soon as possible and resume the normal dosing schedule. If a patient misses a dose by more than 10 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time. The patient should not double the dose to make up for a missed dose.

Tocilizumab

Calculate the volume of tocilizumab concentrate required for the prescribed dose.
Remove the equivalent volume from a 100mL sodium chloride 0.9% infusion bag and discard.
Withdraw the dose from the vial(s) and add to the infusion bag.
Mix by gently inverting the infusion bag to avoid foaming.
Give over 60 minutes via an infusion pump

### 3.5 Supply:

Infusions of sotrovimab will be made by the Pharmacy Aseptic Unit on receipt of a prescription. Orders should be sent to the Pharmacy Aseptic Unit as early as possible, by 1pm at the latest to ensure that the infusion will be available for administration on the same day (Monday to Friday only).

Any orders after 1PM will be made the next morning, unless the clinician wishes to start treatment earlier, in which case the infusion will need to made at ward level (after 1pm on Friday will need to made at ward level)

Tocilizumab vials, baricitinib tablets, remdesevir vials and Paxlovid capsules will be dispensed from Pharmacy during normal working hours against a prescription. They are available from Pharmacy in the Pharmacy Emergency Drugs Cupboard out of hours.

### 3.6 Storage

The infusion should not be shaken and must be protected from light during storage and transportation.

On arrival on the ward:

Option 1:
sotrovimab should be started as soon as possible after it is received on to the ward. Allow the bag to equilibrate to room temperature for approximately 30 minutes prior to administration.

Option 2 (only if unavoidable reason for delay):
The infusion bag should be stored in the fridge at 2-8ºC until ready for use (24 hour expiry). Allow the bag to equilibrate to room temperature for approximately 30 minutes prior to administration.

### 3.7 Documentation

The following process should be followed for any patient prescribed an nMAB or antiviral within this policy:

- An entry made within EPR
- Completion of the eligibility criteria screening document on EPR.
- Prescribing of the nMAB/Antiviral on EPR and subsequent notification of pharmacy either during normal hours or out of hours.
- Blueteq form required – the chief pharmacist must be emailed of any patient being treated.
- Clinical outcome and safety reporting (see reporting section.)
- Inclusion of sotrovimab, molnupiravir, baricitinib, remdesivir, tocilizumab or paxlovid treatment and the date administered must be within the discharge letter to ensure the GP is informed.

### 3.8 Adverse Effects further information: https://www.medicines.org.uk/emc/

### 3.9 Monitoring and review

Patients should be monitored for signs of hypersensitivity reactions, including anaphylaxis (for 1 hour post infusion), and infusion-related reactions (IRRs).

- Hypersensitivity reactions: if there are signs or symptoms of clinically significant hypersensitivity reaction or anaphylaxis, immediately discontinue the infusion and manage the patient using the Trust's Anaphylaxis pathway.
- Infusion-related reactions: if an IRR occurs during administration, consider interrupting, reducing the rate by 50% or stopping the infusion. Patients should be monitored for signs and symptoms of IRRs for 24 hours after administration. If an IRR occurs administer appropriate medications and/or supportive care.

### 3.10 Pregnancy and women of childbearing potential

Clinicians should refer to the SmPCs above for the relevant products for further information on use in pregnancy and women of childbearing potential. All healthcare professionals are asked to ensure that any patients who receive a COVID-19 antiviral while pregnant are reported to the UK COVID-19 antivirals in pregnancy registry on 0344 892 0909 so that they can be followed up. For more information go to http://www.uktis.org/.

### 3.11 Co-administration

Corticosteroids

The UK CAS Alert on the use of corticosteroids in patients with COVID-19 can be found here. 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. Please refer to the recommendation on the use of corticosteroids in the National Institute for Health and Care Excellence (NICE) Rapid Guideline on Managing COVID-19. nMABs and antivirals should not be regarded as an alternative to corticosteroids.

**3.12 Patient Counselling**

Concomitant administration of an nMAB with COVID-19 vaccines has not been studied. Refer to local/national guidelines for vaccine administration and guidance on the risks associated with administration of a SARS-CoV-2 vaccine.

Further information on the timing of COVID-19 vaccination following administration of nMABs is available at the following sites:

- Liverpool COVID-19 Interactions (covid19-druginteractions.org) https://www.covid19-druginteractions.org/checker
- Interactions information for COVID-19 vaccines – SPS – Specialist Pharmacy Services https://www.sps.nhs.uk/articles/interactions-information-for-covid-19-vaccines/

**3.13 Reporting:**

Blueteq forms will be required for each patient. These forms will be completed by pharmacy for each patient.

**Safety Reporting**

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

# 4. Policy Implementation Plan

The policy will be available on the Trust internet and also sent via corporate communication and direct to consultants, pharmacy staff and ward managers for further dissemination.

In addition to this policy, SOPs will be used to support safe supply and use of the drug.

# 5. Monitoring of Compliance

Via completion of blueteq.

# 6. References

1. Summary of Product Characteristics: Sotrovimab Xevudy 500 mg concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed 13/05/24

2. Summary of Product Characteristics: Tocilizumab RoActemra 20mg/ml Concentrate for Solution for Infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
   Accessed 13/05/24Summary of Product Characteristics: Paxlovid
   Paxlovid 150 mg/100 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
   Accessed 13/05/24
3. Nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 Technology appraisal guidance TA 878 29 March 2023
4. COVID-19 rapid guideline: managing COVID-19 NICE guideline [NG191] 23 March 2021
5. Remdesivir and tixagevimab plus cilgavimab for treating COVID-19 Technology appraisal guidance TA971 08 May 2024
6. Summary of Product Characteristics: Remdesivir
   https://www.medicines.org.uk/emc/product/11597 Accessed 13/05/24
7. Summary of Product Characteristics: Molnupiravir
   https://www.medicines.org.uk/emc/product/13044 Accessed 13/05/24
8. Summary of Product Characteristics: Baricitinib
   *https://www.medicines.org.uk/emc/product/7486/smpc* Accessed 13/05/24

# 7. Appendices

**Appendix 1**

**University of Liverpool Covid 19 drug interaction checker**

**https://www.covid19-druginteractions.org/checker**

## 8. Endorsed By:

| Name of Lead Clinician / Manager or Committee Chair | Position of Endorser or Name of Endorsing Committee | Date |
|---|---|---|
| Dr Wat | Drug & Therapeutics | 15/05/24 |

## 9. Record of Changes

| Section No | Version No | Date of Change | Description of Amendment | Description of Deletion | Description of Addition | Reason |
|---|---|---|---|---|---|---|
| 3 and 3.1 | 6 | 17/5/23 | | Deleted covid treatments no longer indicated by NICE | Added new priority order of covid treatments and indications | NICE TA and CG |
| 3.2,3.3 ,3.4 | 6 | 17/5/23 | | | Added tocilizumab information | NICE TA |
| 3 | 6.1 | 11/10/23 | | Baricitinib Time period to start paxlovid | | NICE TA |
| 7 | 6.1 | 11/10/23 | Updated risk factors | | | NICE TA |
| 3 | 7.0 | 15/05/24 | Recommendations | | | NICE TA |
| 3.2 | 7.0 | 15/05/24 | | Removed dosages | Hyperlinks to SPCs added | streamline |
| 3.3 | 7.0 | 15/05/24 | | | Remdesivir | NICE TA |
| 3.4 | 7.0 | 15/05/24 | | | Remdesivir and Molnupiravir | NICE TA |
| | 7.0 | 15/05/24 | | | | NICE TA |
| 3.10 | 7.0 | 15/05/24 | | Removed pregnancy info | Hyperlinks to SPCs | streamline |
| 6 | 7.0 | 15/05/24 | Updated references | | | NICE TA |
| 7 | 7.0 | 15/05/24 | | Removed risk factor list | Inserted hyperlinks instead | streamline |