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**IMMEDIATE MESSAGE TO:**

1. Directors of Pharmacy
2. Medical Directors NHS Boards

28 November 2022

Dear Healthcare Professional

**CAS DRUG ALERT – No. 15 – Immediate Effect - Treatment Of Hospital-Onset Covid-19 In Adults And Children**

Please see attached CMO letter about the updated UK-wide policy (with Immediate Effect) to provide access to antiviral treatment options for Hospital-Onset COVID-19 In Adults and Children.

The published UK-wide policy has been updated, effective with immediate effect, following consideration of the updated COVID therapeutic guideline from the World Health Organization (WHO), a review of the latest available evidence (including pharmacokinetic and pharmacodynamic data) and the extension to the marketing authorisation for remdesivir to cover adults and children (of all ages) weighing 40kg and above who do not require supplemental oxygen and who are at risk of progressing to severe COVID-19.

The updated policy revises the available treatment choices for eligible adults and children (weighing 40kg and above) admitted to hospital for a non-COVID reason, but who nonetheless test positive for COVID during their hospital stay. Treatment choices are now nirmatrelvir/ritonavir (Paxlovid) (first line), or remdesivir (second line). Exceptionally, sotrovimab may be considered where the available antiviral treatments are deemed to be unsuitable and its use is supported following multi-disciplinary team (MDT) assessment.

Could Medical Directors and Directors of Pharmacy please forward this alert to relevant healthcare professional colleagues, including any clinicians and clinical teams involved in treatment for Highest Risk Non-Hospitalised Patients (Adults and Children) with Covid-19.

Thank you for your co-operation.

Yours sincerely

**Grace Jamieson**  
**Medicines Policy Team**





# COVID-19 Therapeutic Alert

CEM/CMO/2022/015

28 November 2022

## Treatment of Hospital-Onset COVID-19 In Adults and Children

### Summary

The [published UK-wide policy](#) covering COVID treatment options for adults and children with 'hospital-onset COVID-19' – i.e. those hospitalised for a non COVID indication but who test positive for COVID during the period of their admission - has been updated to provide access to the following antiviral treatment options:

- First-line: nirmatrelvir/ritonavir (Paxlovid) (antiviral, administered orally)
- Second-line: remdesivir (antiviral, administered intravenously)

Exceptionally, sotrovimab may be considered where the available antiviral treatments are deemed unsuitable and its use is supported following multi-disciplinary team (MDT) assessment.

Eligible children and adolescents may only be considered for treatment with remdesivir (for those weighing 40kg and above) or sotrovimab (for those aged 12 years and above AND weighing 40kg and above). For paediatric/adolescent patients paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment.

Patients are eligible to be considered for treatment if the initial criteria below are met:

- Hospitalised for indications other than for the management of acute symptoms of COVID-19<sup>1</sup>

AND

- SARS-CoV-2 infection is confirmed by either:
  - Polymerase chain reaction (PCR) testing OR
  - Lateral flow test

AND

- [Symptomatic with COVID-19](#) and showing no signs of clinical recovery

AND

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<sup>1</sup> This includes patients admitted to community and mental health hospitals. Where possible patients being considered for intravenous treatment should be transferred to a suitable facility for treatment delivery.

- The patient is a member of a 'highest' risk group (as defined in the Department of Health and Social Care commissioned [Independent Advisory Group Report](#))

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).

Further details, including medicine specific guidance, may be [found in the clinical policy](#). Further information on selecting the most appropriate treatment can be found in [the accompanying clinical guide](#).

## Action

NHS acute trusts / health boards are asked to take the following immediate steps to support the treatment of patients with a hospital-onset COVID-19 infection:

1. Consider prescribing an antiviral treatment to adults in line [with the published policy](#). Exceptionally, sotrovimab may be considered where the available antiviral treatments are deemed unsuitable and its use is supported following multi-disciplinary team (MDT) assessment.
2. Note that eligible children and adolescents may only be considered for treatment with remdesivir (for those weighing 40kg and above) or sotrovimab (for those aged 12 years and above AND weighing 40kg and above). For paediatric/adolescent patients paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment.
3. In the absence of a confirmed virological diagnosis, the treatment should only be used when a multidisciplinary team has a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis.
4. Note that nirmatrelvir/ritonavir is **not recommended during pregnancy**. The use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping nirmatrelvir/ritonavir.
5. Ensure that any patients who receive a COVID antiviral while pregnant are reported to the UK COVID-19 antivirals in pregnancy registry on 0344 892 0909 (available 9:00am to 5:00pm, Monday to Friday, excluding bank holidays) so that they can be followed up. For more information, go to <https://www.medicinesinpregnancy.org/COVID-19-Antivirals-Pregnancy-Registry/>.
6. **Noting the important role of surveillance, treating clinicians are asked to support testing and / or data requirements as recommended under country specific or UK wide surveillance programmes, where laboratory capacity and resourcing allows.** Sequencing is an important part of surveillance activities to monitor for the development of new variants and drug resistance. Genotype results do not form part of the eligibility criteria for any treatment under this policy and treatment should not be delayed pending these results.

7. Discharge letters to primary care, and other handovers of clinical care, should explicitly record the treatment that has been given, together with the dose and date of administration. The following **SNOMED codes should be used to support evaluation and to inform subsequent treatment decisions**:

#### **Provision of nirmatrelvir/ritonavir**

Procedure code: 427314002 |Antiviral therapy (procedure)|

Presentation:

- 30 tablet pack - 40325111000001108

#### **Administration of remdesivir**

Procedure code: 47943005 |Administration of anti-infective agent (procedure)|

Presentation:

- 100mg powder for solution for infusion, 1 vial – 38376311000001103

#### **Administration of sotrovimab**

Procedure code: 47943005 |Administration of anti-infective agent (procedure)|

Presentation:

- Sotrovimab 500mg/8ml solution for infusion vials – 40219011000001108

8. Adhere to the guidance which has been developed by the Specialist Pharmacy Service (SPS) to support the administration of [antivirals](#) or [monoclonal antibodies](#).
9. In England, trusts who have not yet done so should register (by site) to participate in COVID-19 specific medicine supply arrangements, via Blueteq. Blueteq should also then be used to confirm pre-authorisation for individual patients. HSC Trusts in Northern Ireland should liaise with the Regional Pharmaceutical Procurement Service to register interest. In Scotland, Health Board Directors of Pharmacy should notify NHS National Procurement if they wish to participate. Health Boards in Wales should notify the All Wales Specialist Procurement Pharmacist of their intention to participate.
10. Regular stock updates should be provided to trust / hospital and regional pharmacy procurement lead / chief pharmacists. Hospitals should enter the product onto stock control and prescribing systems as described below:
- Paxlovid - nirmatrelvir (150mg tablets) and ritonavir (100mg tablets), 30 tablet pack
  - Remdesivir 100mg powder for concentrate for solution for infusion
  - Sotrovimab 500mg/8ml solution for infusion vials
11. Hospital pharmacies should continue to appropriately store unused stocks of the casirivimab and imdevimab (Ronapreve) combination monoclonal antibody; further guidance will be provided.

## Product Details

Nirmatrelvir plus ritonavir (Paxlovid) is a combination oral antiviral supplied by Pfizer that works by inhibiting a protease required for viral replication. It is supplied as a pack providing a five-day treatment course containing both nirmatrelvir (150mg tablets) and ritonavir (100mg tablets). Nirmatrelvir plus ritonavir has a conditional market authorisation in Great Britain (under the Medicines and Healthcare products Regulatory Authority (MHRA)), and in Northern Ireland (under the European Medicines Agency (EMA)), for the treatment of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID-19.

Remdesivir (Veklury) is supplied by Gilead. Delivered intravenously, it has market authorisations for use as a treatment for COVID-19 in both Great Britain (under the Medicines and Healthcare products Regulatory Authority (MHRA)) and in Northern Ireland (under the European Medicines Agency (EMA)) for 1) adults and paediatric patients (at least 4 weeks of age and weighing at least 3 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at start of treatment), and 2) adults and paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19.

Sotrovimab (Xevudy) is supplied by GlaxoSmithKline and Vir Biotechnology. Delivered intravenously, sotrovimab has a conditional marketing authorisation in Great Britain (England, Scotland and Wales) and a marketing authorisation in Europe (under the European Medicines Agency) for the treatment of symptomatic adults and adolescents (aged 12 years and over and weighing at least 40 kg) with acute COVID-19 infection who do not require oxygen supplementation and who are at increased risk of progressing to severe COVID-19 infection. Access to sotrovimab in Northern Ireland is through a Regulation 174 approval or the European Medicines Agency marketing authorisation.

## Co-Administration

There is no interaction expected of the treatments covered under the policy with other treatments available for COVID under published UK clinical access policies.

For further information please visit the University of Liverpool COVID-19 Drug Interactions website (<https://www.covid19-druginteractions.org/checker>).

**Antivirals should not be infused concomitantly in the same IV line with other medications.**

## Monitoring, tracking and follow-up

All handovers of clinical care (including between hospitals if patients are transferred, between levels of care and clinical teams within hospitals, and between hospitals and primary care) should explicitly record the treatment that has been given together with the dose and date of administration. SNOMED codes (see action section, above) should be used in discharge letters to primary care.

Healthcare professionals are asked to report any suspected adverse reactions via the United Kingdom Yellow Card Scheme [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

## Distribution

- NHS Trusts (NHS boards in Scotland and Wales)
- National / Regional Medical Directors
- National / Regional Chief Pharmacists
- Lead/Senior Pharmacists and Regional Procurement Pharmacy Leads
- Trust/Hospital Pathology Directors (to circulate to pathology networks and laboratory staff)
- Trust / Hospital Medical Directors (to circulate to medical and nursing staff managing admitted patients infected with COVID-19)

## Enquiries

### England

Enquiries from NHS trusts in England should in the first instance be directed to your trust pharmacy team who will escalate issues to the Regional Chief Pharmacist and national teams if required. Further information can be requested from the dedicated email address: [england.spoc-c19therapeutics@nhs.net](mailto:england.spoc-c19therapeutics@nhs.net).

### Northern Ireland

Enquiries from hospitals in Northern Ireland should in the first instance be directed to your hospital pharmacy team who will escalate issues to the Regional Pharmaceutical Procurement Service or Pharmaceutical Directorate at the Department of Health if required. Further information can be obtained by contacting [RPHPS.Admin@northerntrust.hscni.net](mailto:RPHPS.Admin@northerntrust.hscni.net)

### Scotland

Enquiries from hospitals in Scotland should in the first instance be directed to your hospital pharmacy team who will escalate issues to either NHS National Procurement or the Scottish Government's Medicines Policy Team if required. Contact should be made using the following emails: [nss.nhssmedicineshortages@nhs.scot](mailto:nss.nhssmedicineshortages@nhs.scot) or [medicines.policy@gov.scot](mailto:medicines.policy@gov.scot)

### Wales

Enquiries from hospitals in Wales should in the first instance be directed to the health board's Chief Pharmacist who will escalate issues to the Pharmacy and Prescribing Team at Welsh Government if required. Enquiries to the Welsh Government should be directed to: [COVID-19.Pharmacy.Prescribing@gov.wales](mailto:COVID-19.Pharmacy.Prescribing@gov.wales).

## Rapid Policy Statement

# Interim Clinical Commissioning Policy: Treatments for hospital-onset COVID-19

Publication date: 28 November 2022

Effective from: 28 November 2022

## Commissioning position

The following treatments are recommended to be available for admitted adults and children with hospital-onset COVID-19 infection in accordance with the criteria set out in this document.

- First-line: nirmatrelvir/ritonavir
- Second-line: remdesivir (antiviral)

Sotrovimab (neutralising monoclonal antibody (nMAB)): may be considered by exception where the available antiviral treatments above are contraindicated or determined to be unsuitable following multi-disciplinary team (MDT) assessment.

Further information on selecting the most appropriate treatment can be found in the [Clinical Guide which accompanies this policy](#).

Combination treatment with an antiviral and nMAB is **NOT** routinely recommended.

## Background

Antiviral medications inhibit viral replication and prevent progression of infection. 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.

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 World Health Organization (WHO) updated its 'Therapeutics and COVID-19: Living guideline' on 16 September 2022 and the WHO recommendations (conditional and strong) have been considered in the development of this policy. ([WHO](#), September 2022).

The following products have conditional marketing authorisation for the treatment of patients with COVID-19:

### 1) Nirmatrelvir/ritonavir

#### Evidence

[Final results](#) from the EPIC HR trial indicate that the dual oral antiviral nirmatrelvir/ritonavir resulted in a relative risk reduction of hospitalisation or death by 89% (within 3 day of symptom onset) and 88% (within 5 days of symptom onset) compared to placebo in non-hospitalised,

high-risk adults with COVID-19 (Hammond et al, 2022). The WHO has made a strong recommendation for nirmatrelvir-ritonavir for patients with non-severe COVID-19 at highest risk of hospitalisation ([WHO](#), September 2022).

#### Marketing authorisation

Nirmatrelvir/ritonavir administered orally has conditional marketing authorisation in Great Britain (England, Scotland and Wales) for the treatment of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID-19. Access to nirmatrelvir/ritonavir in Northern Ireland for this indication is through a Regulation 174 approval or the European Medicines Agency marketing authorisation.

## **2) Remdesivir**

#### Evidence

Remdesivir administered intravenously over 3 days to non-hospitalised patients within 7 days of COVID-19 symptom onset and had risk factors for disease progression<sup>1</sup>, resulted in a relative risk reduction of 87% in hospitalisation or death at day 28 (Gottlieb et al, 2021). The WHO has made a conditional recommendation for remdesivir for patients with non-severe COVID-19 at highest risk of hospitalisation ([WHO](#), September 2022). The WHO has made a conditional recommendation for remdesivir in patients with severe COVID-19, and a conditional recommendation against remdesivir in patients with critical COVID-19 ([WHO](#), September 2022).

#### Marketing authorisation

Remdesivir delivered intravenously has conditional marketing authorisation for use as a treatment for COVID-19 in Great Britain (under the Medicines and Healthcare Products Regulatory Authority (MHRA)) and a full marketing authorisation in Northern Ireland (under the European Medicines Agency (EMA)) for the following indications:

- treatment of COVID-19 in adults and paediatric patients (at least 4 weeks of age and weighing at least 3 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at start of treatment), for a treatment duration of 5-10 days.
- treatment of COVID-19 in adults and paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19 within 7 days of symptom onset, for a treatment duration of 3 days.

## **Sotrovimab**

#### Evidence

Interim analysis of the COMET-ICE trial, which studied sotrovimab administered intravenously to non-hospitalised patients with mild-to-moderate disease and at least one risk factor for disease progression, showed a relative risk reduction in hospitalisation or death at day 29 by 85% in patients treated with sotrovimab compared with placebo (Gupta et al, 2021a). The final analysis of this study has shown a relative risk reduction in hospitalisation or death at day 29 by 79% in patients treated with sotrovimab compared with placebo (Gupta et al, 2021b). In September 2022, the WHO made a strong recommendation against the use of sotrovimab patients with COVID-19 ([WHO](#)).

Having taken account of existing evidence and pharmacokinetic and pharmacodynamic data

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<sup>1</sup> Risk factors for progression to severe disease included the following: hypertension, cardiovascular or cerebrovascular disease, diabetes mellitus, obesity (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>), immunocompromised state, chronic mild or moderate kidney disease, chronic liver disease, chronic lung disease, current cancer, and sickle cell disease.



(PK/PD), sotrovimab should only be used as described in this policy.

### Marketing authorisation

Sotrovimab delivered intravenously has conditional marketing authorisation in Great Britain (England, Scotland and Wales) for the treatment of symptomatic adults, and adolescents (aged 12 years and over and weighing at least 40kg) with acute COVID-19 infection who do not require oxygen supplementation and who are at increased risk of progressing to severe COVID-19 infection. Access to sotrovimab in Northern Ireland for the above indication is through a Regulation 174 approval or via the European Medicines Agency marketing authorisation.

## **Eligibility criteria**

Patients are eligible to be considered for treatment if the initial criteria below are met:

- Hospitalised for indications other than for the management of acute symptoms of COVID-19<sup>2</sup>

AND

- SARS-CoV-2 infection is confirmed by either:
  - Polymerase chain reaction (PCR) testing OR
  - Lateral flow test

AND

- [Symptomatic with COVID-19](#) and showing no signs of clinical recovery

AND

- The patient is a member of a 'highest' risk group (as defined in the Department of Health and Social Care commissioned [Independent Advisory Group Report](#))

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 multi-disciplinary team [MDT] assessment).

Eligible patients may be considered for treatment with one of the following:

- First-line: nirmatrelvir/ritonavir (antiviral)
- Second-line: remdesivir (antiviral)

Sotrovimab (nMAB) (by exception) following MDT assessment

Remdesivir may be used in all children weighing over 40kg in patients with no supplemental oxygen requirement. For patients with COVID-19 pneumonia and a supplemental oxygen requirement, children must be older than 4 weeks of age and weighing at least 3kg.

Children and adolescents aged 12-17 years inclusive may be considered for treatment with sotrovimab.

For paediatric/adolescent patients, paediatric MDT assessment should be used to determine clinical capacity to benefit from a treatment. Additional criteria can be found in the Department of Health and Social Care commissioned [Independent Advisory Group Report](#).

Further information on selecting the most appropriate treatment can be found in the Clinical Guide which accompanies this policy.

Combination treatment with an antiviral and nMAB is **NOT** routinely recommended.

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<sup>2</sup> This includes patients admitted to community and mental health hospitals. Where possible patients being considered for intravenous treatment should be transferred to a suitable facility for treatment delivery

Patients who have previously received treatment with an antiviral or nMAB, and who meet the eligibility criteria within this policy, may receive treatment under this policy for a subsequent infective episode, if clinically appropriate.

Where patients are ineligible for treatment under this policy, recruitment to the [RECOVERY trial](#), which is studying the use of sotrovimab and oral antivirals in the hospitalised population with COVID-19, should be supported.

### **First-line: Nirmatrelvir/ritonavir**

If the initial criteria for hospital-onset COVID-19 are met patients are eligible to be considered for treatment with **nirmatrelvir/ritonavir** if:

- Treatment is commenced within 5 days of symptom onset<sup>3</sup>

AND

- The patient does NOT have a history of advanced decompensated liver cirrhosis or stage 4-5 chronic kidney disease (CKD)<sup>4</sup>

AND

- Nirmatrelvir/ritonavir treatment has been deemed safe following guidance from the appropriate specialty team(s) – see the accompanying [Clinical Guide](#) for treatment with antivirals and nMABs.

### **Second-line: Remdesivir**

If the initial criteria for hospital-onset COVID-19 are met patients are eligible to be considered for treatment with **remdesivir** if:

- Treatment with nirmatrelvir/ritonavir is contraindicated or not possible

AND

- Treatment is commenced within 7 days of symptom onset

### **Sotrovimab (by exception)**

If the initial criteria for hospital-onset COVID-19 are met patients are eligible to be considered for treatment with **sotrovimab** by exception if:

- Treatment with remdesivir and nirmatrelvir/ritonavir are both contraindicated or not possible

AND

- Treatment is delivered within 5 days of symptom onset<sup>3</sup>

AND

- Endorsement of treatment has been sought and approved by a relevant MDT

Patients who have received an nMAB within a post-exposure prophylaxis (PEP) or pre-exposure prophylaxis (PrEP) trial (such as the PROTECT-V trial) who meet the eligibility criteria of this policy can still receive treatment with a sotrovimab if this is deemed the most appropriate treatment option.

### **Exclusion criteria**

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<sup>3</sup> Treatment commencement may be extended up to a maximum of 7 days from symptom onset if clinically indicated (treatment commencement beyond 5 days from symptom onset is off-label).

<sup>4</sup> Nirmatrelvir/ritonavir may be considered in hospitalised patients with stage 3 CKD. Dose modification is required. See the Summary of Product Characteristics and the section on dosing in the policy for more information.

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

- Require hospital-level care for the management of acute COVID-19 illness
- New supplemental oxygen requirement specifically for the management of COVID-19 symptoms
- Children weighing less than 40kg
- Known hypersensitivity reaction to the active substances or to any of the excipients of the products as listed in the respective Summary of Product Characteristics.

The following additional **exclusion criteria** applies to patients being considered for treatment with **nirmatrelvir/ritonavir**:

- Children aged less than 18 years
- Pregnancy
- The patient is taking any of the medications listed as 'do not use' in the [Specialist Pharmacy Service \(SPS\) guidance for nirmatrelvir/ritonavir](#).

The following additional **exclusion criteria** apply if considering for treatment with **remdesivir**:

- Estimated glomerular filtration rate (eGFR) <30 mL/min (except in patients with end-stage renal disease on haemodialysis)
- Alanine transaminase (ALT)  $\geq$  5 times the upper limit of normal.

Remdesivir should be discontinued in patients who develop **any** of the following:

- ALT  $\geq$  5 times the upper limit of normal during treatment with remdesivir (remdesivir may be restarted when ALT is < 5 times the upper limit of normal)
- ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR).

For treatment with remdesivir, an individual clinical decision should be made as to whether pre-treatment urea and electrolytes and liver function tests are required based upon whether recent bloods are available or the patient is considered at risk of undiagnosed liver or kidney disease.

If the patient experiences clinical deterioration such that hospitalisation and low-flow supplemental oxygen is required, the patient may be considered for treatment with a 5-day course of remdesivir as outlined in the [UK Clinical Commissioning Policy](#) for remdesivir in patients hospitalised due to COVID-19.

## Dose

The recommended dose of nirmatrelvir/ritonavir is 300mg (two 150mg tablets) nirmatrelvir with 100mg (one 100mg tablet) ritonavir taken together orally twice daily for 5 days. In patients with moderate renal impairment (CKD stage 3), the dose of nirmatrelvir/ritonavir should be reduced to nirmatrelvir/ritonavir 150 mg/100 mg (1 tablet of each) twice daily for 5 days. The remaining tablet of nirmatrelvir should be disposed of in accordance with local requirements.

The recommended dose of remdesivir for this cohort is 200mg intravenously on day 1 followed by 100mg intravenously on days 2 and 3.

The recommended dose of sotrovimab is 500mg to be administered as a single intravenous infusion<sup>5</sup>.

## Administration

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<sup>5</sup> No dose adjustment is recommended in patients with renal or hepatic impairment.

### Nirmatrelvir/ritonavir

Nirmatrelvir/ritonavir should be given as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 5 days of onset of symptoms<sup>3</sup>. Clinicians should assure themselves that patients are able to swallow the oral tablets.

Refer to the [Specialist Pharmacy Services guidance](#) and [University of Liverpool COVID-19 Drug Interactions Checker](#) for further information.

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 their healthcare provider.

### Remdesivir

200mg of remdesivir (day 1 loading dose) and 100mg of remdesivir (days 2 and 3 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. Treatment should be initiated as soon as possible after diagnosis of COVID-19 and within 7 days of symptom onset.

Renal and liver function should be monitored carefully during treatment with remdesivir as clinically appropriate.

### Sotrovimab

8mls of sotrovimab (62.5mg/ml) should be added to a 100ml pre-filled infusion bag containing 0.9% sodium chloride and administered over 30 minutes. Treatment should be initiated as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset<sup>3</sup>.

Sotrovimab should not be infused concomitantly in the same intravenous line with other medication.

Preparation and administration of sotrovimab should be initiated and monitored by a qualified healthcare provider using aseptic technique. Administration should be under conditions where management of severe hypersensitivity reactions, such as anaphylaxis, is possible. Individuals should be monitored post intravenous infusion according to local medical practice. Refer to the Specialist Pharmacy Services [institutional readiness document](#) for further information on the handling, reconstitution and administration of the product.

## **Cautions**

Please refer to the Summary of Product Characteristics (SmPC) for [nirmatrelvir/ritonavir](#), [remdesivir](#) and [sotrovimab](#) for special warnings and precautions for use.

### Nirmatrelvir/ritonavir

Nirmatrelvir/ritonavir has a risk of serious adverse reactions due to interactions with other medicinal products (see the [SPS guidance](#) 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.

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.

Patients should be advised of the possible gastro-intestinal side-effects of treatment with nirmatrelvir/ritonavir (e.g. nausea, vomiting). If such side-effects are experienced, anti-emetics should be considered that are not contra-indicated. If nirmatrelvir/ritonavir treatment cannot be tolerated, an alternative treatment can be considered within the options and criteria of this policy. Combination treatment should not be provided<sup>6</sup>.

### Remdesivir

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. Patients should be monitored for hypersensitivity reactions during and following administration of remdesivir as clinically appropriate. If signs and symptoms of a clinically significant hypersensitivity reaction occur, administration of remdesivir should be discontinued immediately and appropriate treatment initiated.

### Sotrovimab

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.

### **Genotyping and sequencing of samples**

Sequencing is an important part of surveillance activities to monitor for the development of new variants and drug resistance. Therefore, in patients being considered for treatment with antivirals or nMABs, samples pre-treatment and where part of the clinical pathway, post-treatment, should be prioritised for sequencing. Genotype results do not form part of the eligibility criteria for treatment with antivirals or nMABs in this policy and treatment should not be delayed pending these results.

### **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.

Further information on the timing of COVID-19 vaccination following administration of nMABs is

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<sup>6</sup> Unless as part of a formal clinical trial

available at the following sites:

- [Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](https://www.covid19-druginteractions.org/)
- [Interactions information for COVID-19 vaccines – SPS – Specialist Pharmacy Services](#)

## **Pregnancy and women of childbearing potential**

Clinicians should refer to the SmPCs 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 antiviral while pregnant are reported to the UK COVID-19 antivirals in pregnancy registry on 0344 892 0909 (available 9:00am to 5:00pm, Monday to Friday, excluding bank holidays) so that they can be followed up. For more information, go to <https://www.medicinesinpregnancy.org/COVID-19-Antivirals-Pregnancy-Registry/>. Clinicians are advised to refer to the SmPC for nirmatrelvir/ritonavir and remdesivir for more information on use during pregnancy or lactation.

### Nirmatrelvir/ritonavir

There are no human data on the use of nirmatrelvir/ritonavir during pregnancy to inform the drug-associated risk of adverse developmental outcomes, women of childbearing potential should avoid becoming pregnant during treatment with nirmatrelvir/ritonavir. Nirmatrelvir/ritonavir is **not recommended** during pregnancy and in women of childbearing potential not using effective contraception.

Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping nirmatrelvir/ritonavir.

### Remdesivir

There are no or limited amount of data from the use of remdesivir in pregnant women. Remdesivir should be **avoided** in pregnancy unless clinicians believe the benefits of treatment outweigh the risks to the individual (please see SmPC for further information).

### Sotrovimab

There are no data from the use of sotrovimab in pregnant women. The SmPC for sotrovimab states that sotrovimab may be used during pregnancy where the expected benefit to the mother justifies the risk to the foetus.

## **Co-administration**

Please see the [SPS guidance](#) for potential interactions involving nirmatrelvir/ritonavir.

There is no interaction expected between remdesivir or nMABs with the drugs listed below. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (<https://www.covid19-druginteractions.org/checker>).

### 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<sup>7</sup>. nMABs and antivirals should not be regarded as an alternative to corticosteroids.

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<sup>7</sup> Updated WHO guidance on the use of systemic corticosteroids in the management of COVID-19 can be found [here](#).

## Remdesivir

The Clinical Commissioning Policy for the use of [remdesivir in patients hospitalised with COVID-19 can be found here](#).

## 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](#).

## **Safety reporting**

Any suspected adverse reactions from treatment with the drugs in this policy should be reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: <https://coronavirus-yellowcard.mhra.gov.uk/>.

## **Governance**

### **Off-label use of medication**

Any provider organisation treating patients with off-label products will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the health board/hospital/trust's drugs and therapeutics committee, or equivalent.

### **Data collection requirement**

Provider organisations in England should register all patients using prior approval software (alternative arrangements in Scotland, Wales and Northern Ireland will be communicated) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Clinicians are also required to ensure that any data collection requirements are met for the purpose of ongoing surveillance, audit and relevant evaluation, including of clinical effectiveness, around the use of nMABs (see 'Surveillance and service evaluation' section below).

### **Effective from**

This policy will be in effect from 28 November 2022

### **Policy review date**

This is an interim rapid clinical policy statement, which means that the full process of policy production has been abridged: public consultation has not been undertaken. This policy may need amendment and updating if, for instance, new trial data emerges, supply of the drug changes, or a new evidence review is required. A NICE Technology Appraisal or Scottish Medicines Consortium (SMC) Health Technology Assessment or All Wales Medicines Strategy Group (AWMSG) appraisal of nirmatrelvir/ritonavir, remdesivir or sotrovimab for COVID-19 would supersede this policy when completed.

### **Surveillance and service evaluation**

There is an urgent need to generate more evidence and greater understanding around the use of antivirals and nMABs in the treatment of patients with COVID-19. Both surveillance and service evaluation are necessary to gain knowledge around the following: factors of relevance in determining antiviral and nMAB treatment; the impact of antiviral and nMAB treatment in the community and hospital settings on the immune/virologic response and clinical recovery; and the public health sequelae of antiviral and nMAB use, such as generation of new mutations and/or variants.

Treating clinicians are asked to ensure that all PCR tests undertaken as part of routine clinical care should do this through the hospital laboratory where these samples should be retained for sequencing. Please note that during times of high prevalence, labs will prioritise sending samples from clinical priority groups only. To aid with this, clinicians should ensure PCR samples from clinical priority groups are clearly labelled as such. Further serial sampling for specific patient groups may be requested as part of UKHSA genomic surveillance purposes, or country specific programmes.

Clinicians must ensure that any additional data collection requirements are met for the purpose of relevant surveillance, audit and evaluation around the use of antivirals and nMABs. It is expected that there will be ongoing monitoring (involving sample collection) of selected patients treated with antivirals and nMABs (led by UKHSA, for instance around the potential generation of new variants), as well as academic research to generate new knowledge around clinical effectiveness and other relevant aspects of public health.

## Equality statement

Promoting equality and addressing health inequalities are at the heart of the four nations' values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010 or equivalent equality legislation) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

## Definitions

<b>COVID-19</b>	Refers to the disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus
<b>Neutralising monoclonal antibody</b>	Synthetic antibodies that bind to a virus and inhibit its ability to infect host cells and replicate
<b>Spike protein</b>	The part of the SARS-CoV-2 virus that binds to the host cell, which then facilitates its entry into the cell

## References

1. Gottlieb RL, Vaca CE, Paredes R, et al. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. *N Engl J Med.* 2021;NEJMoa2116846.  
[doi:10.1056/NEJMoa2116846](https://doi.org/10.1056/NEJMoa2116846)
2. Gupta A, Gonzalez-Rojas Y, Juarez E, et al. Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab. *N Engl J Med.* 2021;10.1056/NEJMoa2107934.  
[doi:10.1056/NEJMoa2107934](https://doi.org/10.1056/NEJMoa2107934)
3. Gupta A, Gonzalez-Rojas Y, Juarez E, et al. Effect of the Neutralizing SARS-CoV-2 Antibody Sotrovimab in Preventing Progression of COVID-19: A Randomized Clinical Trial. Preprint available at: <https://www.medrxiv.org/content/10.1101/2021.11.03.21265533v1>
4. Hammond J, Leister-Tebbe H, Gardner A, et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. *N Engl J Med.* 2022;10.1056/NEJMoa2118542.



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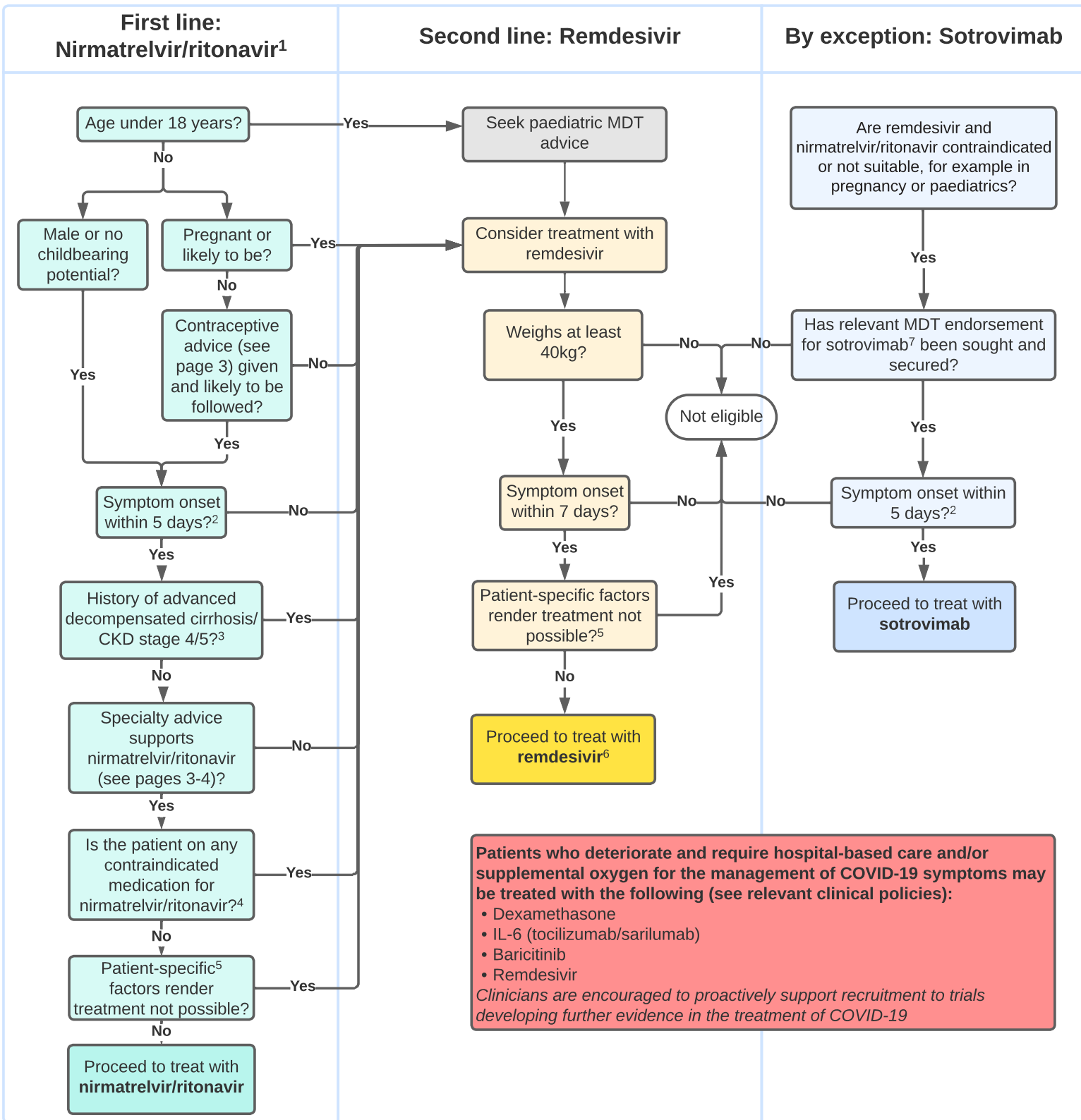
5. Hoffmann M, Kruger N, Schulz S, et al. The Omicron variant is highly resistant against antibody-mediated neutralisation – implications for control of the COVID-19 pandemic. Preprint available at: <https://www.biorxiv.org/content/10.1101/2021.12.12.472286v1>
6. World Health Organization (WHO), 2022. Therapeutics and COVID-19: Living guideline. Available at: [Therapeutics and COVID-19: Living guideline](https://www.who.int/publications/m/item/therapeutics-and-covid-19-living-guideline) (who.int)

# UK Interim Clinical Commissioning Policy

## Therapies for adult and paediatric patients with symptomatic hospital-onset COVID-19

### Consider access to this clinical pathway under the following conditions:

- Hospitalised for indications other than for the management of acute symptoms of COVID-19
- Onset of symptoms of COVID-19 within the last 5 days (for nirmatrelvir/ritonavir and sotrovimab) or 7 days (for remdesivir), remains symptomatic and with no signs of clinical recovery
- SARS-CoV-2 infection is confirmed by either PCR or lateral flow test
- The patient is a member of the 'highest' risk group (as defined in the Department of Health and Social Care commissioned Independent Advisory Group report) OR COVID-19 infection presents a material risk of destabilising a pre-existing condition or compromising recovery from a procedure (as determined by MDT assessment)
- The patient is not requiring new supplementary oxygen specifically for the management of COVID-19 symptoms



<sup>1</sup> May also be known as paxlovid

<sup>2</sup> Treatment commencement may be extended up to a maximum of 7 days from symptom onset if clinically indicated (this would be off-label)

<sup>3</sup> Nirmatrelvir/ritonavir may be considered in hospitalised patients with stage 3 CKD. Dose modification is required. See the Summary of Product Characteristics and the section on dosing in the policy for more information.

<sup>4</sup> See Specialist Pharmacy Service (SPS) guidance for nirmatrelvir/ritonavir and University of Liverpool COVID-19 Drug Interactions checker

<sup>5</sup> Patient-specific factors could include needle phobia and inability to receive intravenous treatment (remdesivir) or swallowing difficulties with oral tablets (nirmatrelvir/ritonavir)

<sup>6</sup> Please see remdesivir specific exclusion criteria in the clinical commissioning policy

<sup>7</sup> Please see sotrovimab specific exclusion criteria in the clinical commissioning policy

# Clinical Guide: Therapy characteristics when deciding on treatment choice

## Use this guide to assist in decision making on which therapeutic option to use:

- Two products have similar relative risk reduction of reducing hospitalisation: nirmatrelvir/ritonavir and remdesivir
- Molnupiravir has a substantially lower level of efficacy - reserve when the others cannot be used
- Medicines availability will be monitored nationally and regionally, so unless otherwise directed do not consider supply issues in your decision making

Nirmatrelvir/ritonavir (Paxlovid)	Remdesivir (Veklury)
Antiviral (dual therapy)	Antiviral (monotherapy)
Administered <b>orally</b> : 3 tablets twice a day for 5 days	Administered <b>intravenously</b> : one infusion every 24 hours for 3 days
Adults only (aged 18 years and over)	Adults and paediatric patients (weighing at least 40 kg)
Evidence based on treatment within <b>5</b> days of symptom onset	Evidence based on treatment within <b>7</b> days of symptom onset
<b>Not recommended in pregnancy</b>	May be used in <b>pregnancy</b> where benefits of treatment outweigh risks
Breast-feeding should be discontinued during treatment and for 7 days after last dose	No specific advice on discontinuation of breast-feeding during treatment
Contraindicated in severe liver and kidney disease	Not recommended in individuals with ALT $\geq 5$ times the upper limit of normal or eGFR $< 30$ ml/min
Multiple significant drug-drug interactions (see SPS guidance)	No significant drug-drug interactions
88% Relative Risk Reduction of hospitalisation	87% Relative Risk Reduction of hospitalisation

Sotrovimab (Xevudy)	
Neutralising monoclonal antibody	May be used in <b>pregnancy</b> although there is no safety data available
Administered <b>intravenously</b> : single infusion	No specific advice on discontinuation of breast-feeding during treatment
Adults and adolescents (aged 12 years and over and weighing at least 40kg)	No dose adjustment recommended in liver or renal impairment*
Evidence based on treatment within <b>5</b> days of symptom onset	No significant drug-drug interactions

## For the key publications of trial results and licence click here

Nirmatrelvir/ritonavir  
NEJM Feb 2022

Nirmatrelvir/  
ritonavir  
SmPC

Remdesivir  
NEJM Dec 2021

Remdesivir  
SmPC

Sotrovimab  
NEJM Nov 2021

Sotrovimab  
SmPC

Molnupiravir  
NEJM Dec 2021

Molnupiravir  
SmPC

\*there are limited/no data on the use of sotrovimab in patients with a creatinine clearance of  $< 30$ ml/min/1.73m<sup>2</sup> and those with severe elevations ALT (5 -  $< 10$  x upper limit of normal)

## Clinical Guide: Speciality advice for 'highest-risk' cohorts

Speciality-specific advice on the management of patients within each of the highest-risk cohorts (particularly around the use of nirmatrelvir/ritonavir) may be found in the table below. Contact your local specialist team for further guidance on issues not covered by this advice.

Cohort	Advice/guidance
Liver disease	Nirmatrelvir/ritonavir should not be administered to patients with advanced decompensated cirrhosis. Such patients can be identified by questioning or review of medical records. Patients should be asked if they have ever been admitted to hospital with liver disease and if they are currently receiving regular ascitic drainage. A positive response is a contraindication to nirmatrelvir/ritonavir. If blood tests are available a bilirubin >50 at any time is a contraindication to nirmatrelvir/ritonavir, if the jaundice is due to liver disease. Patients receiving rifaximin (only used in very advanced liver disease) should not receive nirmatrelvir/ritonavir.
Solid organ transplant (non-renal)	Nirmatrelvir/ritonavir is currently contraindicated in both Solid Organ and Islet Transplant recipients due to significant harmful drug interactions especially anti-rejection medication. These patients should be triaged to receive sotrovimab.
Renal disease (including renal transplant)	Currently nirmatrelvir/ritonavir is not indicated in the majority of at-risk individuals with renal disease, due to lack of dosing information or drug interactions. These include patients with CKD stage 4 and 5, including those on dialysis, and in transplant patients due to interactions with immunosuppressive therapy. Nirmatrelvir/ritonavir requires dose modification in people with CKD stage 3 (see product information). When nMABs are not indicated or available, clinicians can discuss alternative treatment options such as remdesivir with renal provider clinicians. Remdesivir may be used in patients with an eGFR of $\geq 30\text{ml/min/1.73m}^2$ and in some patients on haemodialysis (discuss with renal clinicians for further guidance).
Solid cancer (including metastases); Haematological disease (including non-malignant conditions)	Specialist cancer and haematology teams are encouraged to establish a central provider email account to receive queries from clinicians treating patients with COVID-19 with antivirals and/or nMABs. For patients who are receiving SACT or complex supportive care for malignancy or stem cell transplantation, please ask whether the patient has already been contacted or reviewed by their specialist haematology/oncology/bone marrow transplant team. If the patient has not already been in contact with their specialist, please establish the location of the provider and consider referral to the respective specialist team via the central provider email where available. Please ask the patient to have details of their current medication available for any following consultation.
Rare neurological conditions	There are no specific needs for specialist neurology services to prescribe nirmatrelvir/ritonavir, though care should be taken with those who have difficulty swallowing or have supported feeding, and for those with behavioural or psychiatric concerns. If a patient is identified as eligible for nirmatrelvir/ritonavir due to neurology risk factors then ask about swallowing difficulties. Disease-specific advice is as follows: <b>Multiple Sclerosis (MS)</b> <ul style="list-style-type: none"> <li>In addition to the medicines listed in the SPS guidance, avoid concurrent use of nirmatrelvir/ritonavir with the following: siponimod, cladribine and modafinil</li> <li>For those patients taking oral or intravenous methylprednisolone discuss the steroid dose with the MS neurology team as nirmatrelvir/ritonavir may increase corticosteroid levels.</li> </ul> <b>Myasthenia Gravis</b> <ul style="list-style-type: none"> <li>This includes muscle specific kinase (MUSK) myasthenia and the Lambert-Eaton Myasthenic Syndrome (LEMS). There are anecdotal reports of myasthenia gravis worsening in association with nirmatrelvir/ritonavir</li> <li>There are no known specific drug interactions. Myasthenia can be aggravated by COVID-19 and COVID-19 vaccination and requires close monitoring given the risk of bulbar and respiratory failure.</li> </ul> <b>Motor Neurone Disease (MND)</b> <ul style="list-style-type: none"> <li>Discuss patients on quinine with an MND physician</li> <li>Levels of riluzole treatment may be increased by nirmatrelvir/ritonavir and should be temporarily suspended following discussion with an MND physician.</li> </ul> <b>Huntington's Disease</b> <ul style="list-style-type: none"> <li>In addition to the medicines listed in the SPS guidance, avoid concurrent use of nirmatrelvir/ritonavir with the following: primidone, tetrabenazine and trihexyphenidyl</li> </ul>
Immunology	Considering commonly prescribed medications in immunology, there are no issues with concomitant immunoglobulin replacement therapy and nirmatrelvir/ritonavir and nMABs. Patients should be informed by specialist clinicians and clinical/patient networks to maintain a list of all medications including those prescribed in hospital. Patients may be taking prophylactic antimicrobials - please refer to the list of contraindicated medications in the SPS guidance for further reference.
Obstetrics and gynaecology	It is recommended that CMDU staff liaise with their Maternity COVID Champion, or dedicated clinician when assessing a pregnant patient with COVID. Please ensure that a full drug history and past medical history is taken as other specialists may also need to be involved, for example renal or transplant teams. Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping nirmatrelvir/ritonavir.
Paediatrics	For paediatric/adolescent patients, paediatric multidisciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from treatment.

## Clinical Guide: Speciality advice for 'highest-risk' cohorts

Speciality-specific advice on the management of patients within each of the highest-risk cohorts (particularly around the use of nirmatrelvir/ritonavir) may be found in the table below. Contact your local specialist team for further guidance on issues not covered by this advice.

Cohort	Advice/guidance
IMID	<p><b>Factors to be considered in IMID patients:</b></p> <ul style="list-style-type: none"> <li>• Consistent with existing guidance on management of COVID-19 in patients with IMID, patients should temporarily suspend their conventional DMARD(s), biologic and/or JAK inhibitor until the course of antiviral treatment has been completed and symptoms of COVID-19 are improving (this will usually be between 1-3 weeks). For most patients this will not require specific contact with the specialty team.</li> <li>• Do not stop or decrease corticosteroids</li> <li>• Swallowing difficulties may preclude the use of oral antivirals e.g. in patients with dysphagia due to myositis, oesophageal dysmotility due to scleroderma/systemic sclerosis because of the size of the tablets (approximately 2cm long)</li> <li>• Do not delay antiviral treatment pending specialist advice</li> </ul> <p>The following links on speciality websites may be useful:</p> <ul style="list-style-type: none"> <li>• The British Society for Rheumatology website</li> <li>• <a href="#">COVID-19 guidance   British Society for Rheumatology</a></li> <li>• <a href="#">COVID-19 Guidance &amp; Advice - The British Society of Gastroenterology (bsg.org.uk)</a></li> <li>• British Thoracic Society website: <a href="https://www.brit-thoracic.org.uk/covid-19/">https://www.brit-thoracic.org.uk/covid-19/</a></li> <li>• British Association of Dermatologists Advice for Dermatology HCPs during COVID-19 pandemic: <a href="https://www.bad.org.uk/healthcare-professionals/covid-19">https://www.bad.org.uk/healthcare-professionals/covid-19</a></li> </ul>
HIV/AIDS	<ul style="list-style-type: none"> <li>• It is recommended that each CMDU has details of their local HIV specialist service (both specialist HIV pharmacist and HIV physician) to discuss individuals where advice is needed. Speciality arrangements for referral to HIV specialist advice may be regional in some areas.</li> <li>• The majority of individuals living with HIV and referred to CMDUs for nirmatrelvir/ritonavir treatment should be managed in accordance with the guidance without the need for referral to the specialist centre. There are no antiretroviral treatment (ART) regimens that are a contraindication to nirmatrelvir/ritonavir treatment. No dose adjustment of any ART agent including ritonavir or cobicistat is needed. Interactions with other generalist co-medications prescribed should be assessed according to guidance including by reference to the Liverpool Covid drug interaction website.</li> <li>• Some individuals living with HIV do not disclose their HIV status to their GPs. It is therefore good practice to enquire of individuals during triage if they have any other medical conditions or take any other medications not managed directly by their GP.</li> <li>• CD4 counts are no longer routinely monitored in those with virological suppression and previous counts above 350 cells/mm<sup>3</sup>. These individuals will generally be assessed as not meeting the immunosuppression criteria although some patients may still meet the criteria that take account of other demographic factors and co-morbidities. We suggest using an age threshold of 55 years or older as an appropriate indicator for treatment in these circumstances as this was the inclusion criteria used in clinical studies.</li> </ul>
Down's syndrome <sup>1</sup>	<ul style="list-style-type: none"> <li>• The following issues should be given due consideration when assessing a patient for treatment with a suitable antiviral or nMAB: <ul style="list-style-type: none"> <li>• The individual is likely to have impaired ability to understand the information given and they may be more likely to have hearing and communication difficulties</li> <li>• There is significant potential for co-existence of significant health conditions</li> <li>• There is a need for a corroborated and detailed collateral medical and drug history from an informant</li> <li>• Mental capacity assessment is an essential part of the assessment/triage process in these individuals</li> <li>• Other people cannot consent for an individual's treatment unless they are legally permitted to do so</li> <li>• In patients judged not to have capacity, a process of best interests decision-making should be pursued.</li> </ul> </li> <li>• A person with Down's syndrome may be more likely to be taking medications that are contra-indicated or which may lead to interactions with nirmatrelvir/ritonavir e.g.: <ul style="list-style-type: none"> <li>• For heart conditions and high blood pressure</li> <li>• Antipsychotics, antidepressants, anxiolytics</li> <li>• Anticonvulsants (anti-epileptics)</li> <li>• Statins</li> </ul> </li> <li>• Nirmatrelvir/ritonavir tablets are relatively large (8-9mm diameter) and should not be crushed. Patients with swallowing difficulties will need support to ensure these are taken safely.</li> <li>• Contact the hospital learning disability liaison nurse (if available) or the local specialist learning disability service for clinical advice around psychotropic medications and the implication of contraindications and potential interactions</li> </ul>

<sup>1</sup>This advice may also apply to individuals with other chromosomal abnormalities affecting immune competence.