Department of Health & Social Care

NHS

# COVID-19 Therapeutic Alert

CEM/CMO/2022/001 27 January 2022

## Antivirals or neutralising monoclonal antibodies (nMABs) for non-hospitalised patients with COVID-19

## Summary

Antiviral treatments inhibit the development and replication of viruses such as SARS-CoV-2. Neutralising monoclonal antibodies (nMABs) bind to specific sites on the spike protein of the SARS-CoV-2 virus particle, blocking its entry into cells and therefore inhibiting its replication.

Recent evidence suggests that antivirals and neutralising monoclonal antibodies (nMABs) significantly improve clinical outcomes in non-hospitalised patients with COVID-19 who are at high risk of progression to severe disease and/or death.

The updated UK-wide clinical commissioning policy **(for implementation from 10 February 2022)** applies to non-hospitalised patients with COVID-19 who are symptomatic and showing no evidence of clinical recovery. It provides the following treatment options:

- First-line**:** PF-07321332(Nirmatrelvir) plus Ritonavir (antiviral) OR Sotrovimab (nMAB), as clinically indicated
- Second-line: Remdesivir (antiviral)
- Third-line: Molnupiravir (antiviral)

Either PCR tests or formally registered positive lateral flow tests[1] (registered via gov.uk or via 119) may now be considered to meet the eligibility requirement on confirmed COVID infection.

Further information on selecting the most appropriate treatment can be found in the clinical guide associated with this policy.

Please also refer to the published (revised) policy for a summary of the supporting evidence, further details on eligibility (and exclusion criteria) and for additional guidance.

## Action

[1] Individuals who are symptomatic, and those with a positive lateral flow test result are strongly encouraged to continue to take a confirmatory PCR test.

Providers locally commissioned to provide **C**OVID **M**edicines **D**elivery **U**nit (CMDU) services and any equivalent arrangements in the devolved nations are asked to:

1. **Consider prescribing and administering an antiviral or monoclonal antibody treatment in line with the published policy and associated clinical guide to non-hospitalised patients where*:***

    - SARS-CoV-2 infection is confirmed by either:
        - Polymerase chain reaction (PCR) testing; OR
        - Lateral flow test (registered via gov.uk or via 119)

    AND

    - Symptomatic with COVID-19[2] and showing no signs of clinical recovery

    AND

    - The patient is member of the 'highest' risk group as set out in the policy

    Children aged 12-17 years may only be considered for treatment with sotrovimab or remdesivir. For paediatric/adolescent patients (aged 12-17 years inclusive), paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment.

2. PF-07321332(nirmatrelvir) plus ritonavir, and molnupiravir, are **not recommended during pregnancy.** All individuals of childbearing potential who are prescribed molnupiravir should be advised to use effective contraception for the duration of treatment and for 4 days after the last dose of molnupiravir. 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 Paxlovid.

3. 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 so that they can be followed up. For more information, go to http://www.uktis.org/.

4. Where possible, take samples for relevant serology testing prior to planned treatment with sotrovimab. However, serology results are **not** a requirement for treatment with nMABs under the criteria specified in the policy.

5. **Support additional testing or data requirements where requested under country specific or UK wide surveillance programmes, in line with current guidance.**

[2] The following are considered symptoms of COVID-19: feverish, chills, sore throat, cough, shortness of breath or difficulty breathing, nausea, vomiting, diarrhoea, headache, red or watery eyes, body aches, loss of taste or smell, fatigue, loss of appetite, confusion, dizziness, pressure or tight chest, chest pain, stomach ache, rash, sneezing, sputum or phlegm, runny nose

6. Ensure clinicians prescribing remdesivir for individuals aged 12-17 years, as an off-label product, follow local governance procedures in relation to the prescribing of off-label medicines.

   Further guidance on the prescribing of off-label medicines can be found below:

   - https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities
   - https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines
   - https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Professional%20standards/Prescribing%20competency%20framework/prescribing-competency-framework.pdf

7. Ensure discharge letters to primary care 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 PF-07321332(Nirmatrelvir) plus 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

   **Provision of Molnupiravir**

   Procedure code: 427314002 |Antiviral therapy (procedure)|

   Presentation:
   - Molnupiravir 200mg capsules, 40 capsule – 40251211000001109

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 (and medicine) specific supply arrangements, via Blueteq™. Blueteq should also then be used to confirm pre-authorisation for individual patients and to capture a limited dataset essential for surveillance of antiviral resistance. Training for antimicrobial stewardship teams will be provided via webinar by UKHSA jointly with NHS England and NHS Improvement. 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. Note that following initial nationally determined allocations to participating sites, ongoing supply will be replenished on the basis of relative use / need. Ongoing ordering will be through existing (business as usual) routes, supported by volume-based caps (reflecting estimated eligible patient volumes) if required.

11. Note that initial supply of COVID medicines may be available within 'emergency supply' packaging, which differs from the planned Great Britain (GB) packaging / labelling aligned to the product's GB licence (or the equivalent product packaging / labelling aligned to a Regulation 174 authorisation or European Medicines Agency marketing authorisation as applicable in Northern Ireland). **To preserve available supply, providers must ensure that packs with shorter use by dates are used first**.

12. Provide regular stock updates to trust / hospital and regional pharmacy procurement lead / chief pharmacists. Providers should enter the products onto stock control and prescribing systems as described below:

    - PF-07321332(nirmatrelvir) (150mg tablets) plus Ritonavir (100mg tablets), 30 tablet pack
    - Remdesivir 100mg powder for concentrate for solution for infusion
    - Sotrovimab 500mg/8ml solution for infusion vials
    - Molnupiravir 200mg capsules, 40 capsules

## Co-Administration

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

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

## Monitoring, tracking and follow-up

Monitoring of longer-term progress is strongly recommended via recruitment of patients receiving COVID therapies to the ISARIC-CCP study.

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 (including congenital malformations and or neurodevelopmental delays following treatment during pregnancy) via the United Kingdom Yellow Card Scheme 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)
- Primary Care (including out of hours providers)
- Community Pharmacies
- 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.

**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

**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 or 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.