Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/021 16 December 2021

Neutralising monoclonal antibodies (nMABs) or antivirals for non-hospitalised patients with COVID-19

Summary

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. Sotrovimab (Xevudy) is an nMAB that both blocks viral entry into healthy cells and clears cells infected with SARS-CoV-2.

Recent evidence suggests that nMABs and oral antivirals significantly improve clinical outcomes in non-hospitalised patients with COVID-19 who are at highest risk of progression to severe disease and/or death. Key findings are:

- Sotrovimab administered intravenously to non-hospitalised patients with mild-to-moderate disease and at least one risk factor for disease progression decreased the risk of hospitalisation or death by 85% (Gupta et al, 2021)

- Final results from the Phase 3 MOVe-OUT trial show that the oral antiviral molnupiravir resulted in a relative risk reduction of 30% in the composite primary outcome of hospitalisation or death at day 29 (6.8% in the molnupiravir group vs 9.7% in the placebo group, p=0.0218).

The UK-wide clinical commissioning policy extends access to nMAB therapy to non-hospitalised patients who are considered to be at highest risk of progression to severe disease, hospital admission or death, and now also takes into account the availability of sotrovimab (from week commencing 20 December) and current understanding on the likely impact of the Omicron variant on the efficacy of the casirivimab and imdevimab combination antibody treatment. Antiviral treatment may be offered to patients in this cohort if aged 18 and above where an nMAB is contraindicated or treatment with an nMAB is not possible.

Please refer to the published (revised) policy for further details of eligibility and for additional guidance.

Action

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 intravenous infusion of the monoclonal antibody sotrovimab[1] at a total dose of 500mg to adult patients, and children aged 12 and over and weighing at least 40 kg, in line with the published policy <*MHRA to add link*> to non-hospitalised patients where*:***

    - SARS-CoV-2 infection is confirmed by polymerase chain reaction (PCR) testing within the last 5 days

      AND

    - Onset of symptoms of COVID-19[2] is within the last 5 days

      AND

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

    CMDUs and the devolved nation equivalents are asked to ensure that patients eligible for an nMAB who cannot travel to a treatment site are able to access the treatment via alternative routes.

    Eligible patients aged 18 and above may be treated with the oral anti-viral molnupiravir at a dose of 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days if an nMAB is contraindicated or treatment with an nMAB is not possible. Patients should be strongly encouraged to complete the 5-day course. Treatment must not be extended beyond 5 days. In respect of oral antiviral treatment, arrangements should be made to ensure the patient can access the treatment without having to attend the service in person (e.g. courier delivery or medicine collected on behalf of the patient, depending on options available within the treatment window). This may include delivery to patients already admitted or resident in another facility.

2. As molnupiravir is **not recommended** during pregnancy, all individuals of childbearing potential who are prescribed molnupiravir (where an nMAB is contraindicated) should be advised to use effective contraception for the duration of treatment and for 4 days after the last dose of molnupiravir. 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/.

3. **Noting the critical nature of surveillance, actively support additional testing or data requirements as requested under country specific or UK wide surveillance programmes, in line with further guidance to be issued.**

4. 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**:

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[1] Or the combination antibody Ronapreve (casirivimab and imdevimab) at a total dose of 1.2g whilst local prevalence of the Omicron variant remains below 50%. Symptom onset should be within the last **7** days.

[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

Administration of Sotrovimab

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

Presentation:

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

Administration of Ronapreve

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

Presentations:

- Casirivimab 300 mg per 2.5 mL (120 mg/mL) with Imdevimab 300 mg per 2.5 mL (120 mg/mL) 2 vial pack - 40025711000001108
- Casirivimab 1332 mg per 11.1 mL (120 mg/mL) with Imdevimab 1,332 mg per 11.1 mL (120 mg/mL) 2 vial pack – 39654011000001101

Provision of Molnupiravir

Procedure code: 427314002 |Antiviral therapy (procedure)|

Presentation:

- Molnupiravir 200mg capsules, 40 capsule – 40251211000001109

5. Organisations should adhere to the procedural guidance which has been developed by the Specialist Pharmacy Service to support monoclonal antibody storage, preparation and administration.

6. 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.

7. Organisations should 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.

8. Organisations should 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**.

9. Regular stock updates should be provided to trust / hospital and regional pharmacy procurement lead / chief pharmacists. Providers should enter the products onto stock control and prescribing systems as described below:

    - Casirivimab 300 mg per 2.5 mL (120 mg/mL) with Imdevimab 300 mg per 2.5 mL (120 mg/mL) with the dose description as: 2 vial pack
      AND/OR
    - Casirivimab 1332 mg per 11.1 mL (120 mg/mL) with Imdevimab 1,332 mg per 11.1 mL (120 mg/mL) with the dose description as: 2 vial pack
    - 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).

nMABs 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 Store8.

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.