Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/022 16 December 2021

Neutralising monoclonal antibodies in the treatment of COVID-19 in hospitalised patients

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. Ronapreve is a combination nMAB containing equal amounts of casirivimab and imdevimab. Sotrovimab (Xevudy) is an nMAB that both blocks viral entry into healthy cells and clears cells infected with SARS-CoV-2.

The UK-wide clinical commissioning policy has now been revised to reflect the availability of the nMAB sotrovimab (from the week commencing 20 December) and the current understanding of the likely impact of the Omicron variant on the efficacy of the combination nMAB casirivimab and imdevimab.

Patients eligible under the policy are:

1) Patients hospitalised for acute COVID-19 illness who are PCR positive and antibody seronegative: may be treated at the off-label total dose of 2.4g of casirivimab and imdevimab, subject to specific requirements relating to local hospital Omicron variant prevalence and/or individual patient genotyping results
2) Patients with hospital-onset COVID-19 (please see policy for additional criteria): to be treated with a total dose of 1.2g casivirimab and imdevimab (if genotyping is available and confirms infection with a non-Omicron variant) or otherwise with sotrovimab

Providers are recommended to continue to use the casirivimab and imdevimab combination in the treatment of patients in Group 1 up to the point at which the Omicron variant accounts for more than 50% of the local hospital prevalence. After this threshold has been reached, where genotyping results are available and confirm non-Omicron variant infection the casivirimab and imdevimab combination can continue to be used. Where genotyping is not available or genotyping confirms Omicron infection, nMABs can only be offered as part of a formal trial

Action

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

1. **Organisations are recommended to consider prescribing a monoclonal antibody for adults, and children aged 12 and over and weighing at least 40 kg, in line with the published policy**

   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.

2. As nMAB therapies should be given to eligible patients as early as possible to maximise benefit, **organisations should ensure that anti-s spike antibody testing[1] is undertaken for all patients hospitalised due to COVID at, or as soon as possible after, the point of admission**. **Patients with hospital-onset COVID treated with an nMAB should also be antibody tested, with appropriate consent, to support further treatment evaluation and surveillance *(antibody status does not affect treatment eligibility in this, second, cohort)*.** If there are concerns or questions around laboratory sensitivity or thresholds these should be discussed in the first instance with local laboratory leads who will have access to comparative and performance data from external quality assessment (EQA) scheme participation. Supporting laboratory networks should ensure that the maximum turnaround time for anti-s antibody tests is no greater than 24 hours from the sample being taken to the result being returned. Positive and negative antibody tests should be reported via the Second Generation Surveillance System (SGSS) to enable reimbursement of associated assay costs in England (parallel reimbursement will be available in the other devolved administrations).

3. **Noting the critical role of surveillance, treating clinicians are strongly encouraged to 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. Discharge letters to primary care should explicitly record that a monoclonal antibody treatment 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**:

   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

[1] Patients may be tested for anti-S1 or anti-S2 antibodies using any validated quantitative or qualitative anti-S assay that measures either IgG or total antibody levels. Serostatus should be established in line with the pre-determined thresholds relevant to the assay being used by the testing laboratory. Quantitative assays with pre-specified thresholds for seropositivity should return clear binary (i.e. either ‘negative’ or ‘positive’) results based on these thresholds. For quantitative assays without a formal threshold for serostatus, clinical decision-making should guide treatment decisions.

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

5. Any organisation treating patients with the casirivimab and imdevimab antibody combination as an off-label product will be required to assure itself that the necessary internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the health board / trust drugs and therapeutics committee, or equivalent.

6. Organisations should adhere to the procedures outlined in the institutional readiness document which has been developed by the Specialist Pharmacy Service to support product storage, preparation and administration.

7. 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.

8. Organisations should note that following initial nationally determined allocations to participating hospitals, ongoing supplies to each hospital 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 admissions) where required.

9. 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**.

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:

    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

    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

    OR

    Sotrovimab 500mg/8ml solution for infusion vials

Product Details

Ronapreve is supplied to the UK by Roche. It is a combination neutralising monoclonal antibody (casirivimab plus imdevimab) used to inhibit viral replication in individuals who have not yet mounted an adequate antibody response to the SARS-COV-2 virus following either exposure or vaccination. The casirivimab plus imdevimab combination for intravenous and subcutaneous use is authorised for use in the treatment and prophylaxis of COVID positive individuals aged 12 and above and weighing at least 40 kg. Supply of the casirivimab and imdevimab combination is subject to the same requirements in both Great Britain and Northern Ireland, and the product information in the Summary of Product Characteristics should be considered applicable across the UK.

Sotrovimab (Xevudy) is supplied by GlaxoSmithKline and Vir Biotechnology. Delivered intravenously, sotrovimab 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 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 a licensing determination by the European Medicines Agency.

Off Label Use of the Casirivimab and Imdevimab Combination Antibody

The casirivimab plus imdevimab combination product is authorised as a treatment for COVID-19 but the published policy includes an off-label use at a dose of 2.4g. As such, clinicians prescribing this treatment should follow trust / hospital 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

Co-Administration

There is no interaction of the monoclonal antibodies covered under the policy expected for either dexamethasone or hydrocortisone, remdesivir, or tocilizumab or sarilumab.

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

Monoclonal antibodies 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 that a monoclonal antibody 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 or search for MHRA Yellow Card in the Google Play or Apple App Store8.

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.

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.