Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2022/005 24 February 2022

Antivirals and 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. Antiviral treatments inhibit the development and replication of viruses such as SARS-CoV-2.

The casirivimab and imdevimab (Ronapreve) combination neutralising monoclonal antibody is no longer available to patients admitted to hospital to manage symptoms of COVID, since it is ineffective against Omicron, which is now the predominant circulating SARS-CoV-2 variant. Patients in this cohort who are potentially suitable for a monoclonal antibody treatment, regardless of antibody status, may instead be considered for entry into the RECOVERY trial, which is studying sotrovimab versus standard of care.

Please also refer to the published clinical guide and the other published UK clinical access policies for treatment options for patients admitted due to COVID infection.

Patients admitted to hospital for a non-COVID related reason but who nonetheless test positive during their hospital stay, and meet additional eligibility criteria, may be considered for treatment with nirmatrelvir plus ritonavir (Paxlovid), as a first-line treatment option. Remdesivir (Veklury) is a licensed second-line treatment option. Sotrovimab (Xevudy) is available as a third-line treatment option in this cohort. Further information to support clinical decision making for patients with hospital-onset COVID-19 can be found in the supporting clinical guide.

Further details on supporting evidence and eligibility, together with further guidance, can be found in the published policy.

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. **Consider prescribing an antiviral or monoclonal antibody treatment to adults, and children aged 12 and over and weighing at least 40kg[1], with hospital-onset COVID infection 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. Note that nirmatrelvir plus ritonavir (Paxlovid) 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 Paxlovid.

3. 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. **Undertake anti-S (spike) antibody testing[2] for all patients hospitalised due to COVID at, or as soon as possible after, the point of admission**. **Patients with hospital-onset COVID should also be tested for anti-S antibody, with appropriate consent, to support further treatment evaluation and surveillance *(antibody status does not affect treatment eligibility under this policy).*** 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 support surveillance and enable reimbursement of associated assay costs in England (parallel reimbursement will be available in the other devolved administrations).

5. Sequencing is an important part of surveillance activities to monitor for the development of new variants. 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. Genotyping results should be reported via the Second Generation Surveillance System (SGSS) to support surveillance and enable reimbursement of associated assay costs in England (parallel reimbursement will be available in the other devolved administrations).

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[1] Paxlovid should only be prescribed for adults

[2] 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.

6. **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.**

7. Discharge letters to primary 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 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

8. Any organisation prescribing remdesivir to children aged 12-17 years and not on supplementary oxygen, 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.

9. Adhere to the guidance which has been developed by the Specialist Pharmacy Service (SPS) to support the administration of antivirals and monoclonal antibodies.

10. 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.

11. 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.

12. 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**.

13. 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:
    - Nirmatrelvir (PF-07321332) (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

14. 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 a section 174 approval covers use in Northern Ireland, 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 a conditional market authorisation 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 adolescents aged 12 and up to less than 18 years and weighing at least 40kg, with pneumonia requiring supplemental oxygen and 2) for adults 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 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 licensing determination made by the European Medicines Agency.

Off Label Use of the Antiviral Remdesivir

The use of remdesivir for COVID-19 in adolescents aged 12-17 years not yet requiring supplemental oxygen is off-label. As such, clinicians prescribing either 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 expected of the treatments covered under the policy with other treatments available for COVID under published UK clinical access policies - 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 and / or antivirals 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 an antiviral or 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 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.

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.