From the Chief Medical Officer
Professor Sir Michael McBride

Department of Health
An Roinn Sláinte
Männystrie O Poustie
www.health-ni.gov.uk

HSS(MD) 28/2022

FOR ACTION
Chief Executives, Public Health Agency/HSC Trusts/NIAS
Deputy Secretary SPPG
GP Medical Advisers, SPPG
All General Practitioners and GP Locums (for onward distribution to practice staff)
OOHs Medical Managers (for onward distribution to staff)

PLEASE SEE ATTACHED FULL CIRCULATION LIST

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Dear Colleague

COVID-19 THERAPEUTIC ALERT: ANTIVIRALS AND NEUTRALISING MONOCLONAL ANTIBODIES (nMABs) IN THE TREATMENT OF HOSPITAL-ONSET COVID-19

This letter supersedes HSS(MD) 11/2022

The published policy has been updated, effective from **13 June 2022**, to link to the published report of the Independent Advisory Group commissioned by the Department of Health and Social Care (DHSC) to advise on the groups of patients likely to be at highest risk of deterioration, hospitalisation or death from a COVID infection. The report confirms the groups of 'highest' risk patients who are potentially eligible for COVID treatments under this policy. Clinicians are asked to note that figure 1 of the report refers to adults (aged 18 years and over) and figure 2 refers to children (aged 12-17 years).

There are no other material changes to the policy.

Actions required

HSC Trusts 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**

[1] Nirmatrelvir/ritonavir (Paxlovid) should only be prescribed for adults

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/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 nirmatrelvir/ritonavir (Paxlovid).

3. Ensure that any patients who receive a COVID antiviral while pregnant are advised to report 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/.

4. **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.

5. Discharge letters to primary care should explicitly record the treatment that has been given, together with the dose and date of administration.

6. 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 HSC Trust drugs and therapeutics committee, or equivalent

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

8. HSC Trusts in Northern Ireland should liaise with the Regional Pharmaceutical Procurement Service to register interest in COVID-19 specific supply arrangements. Allocations of COVID-19 therapeutics for use within the HSC will be determined regionally, informed by nationally determined allocations, with ongoing supplies to each hospital 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-19 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 (EMA) 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. Provide regular updates on the stock position to HSC Trust Heads of Pharmacy and Medicines Management, pharmacy procurement leads and the Regional Pharmaceutical Procurement Service. 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.

The Strategic Planning and Performance Group is asked to:

12. Continue to work with HSC Trusts and the Regional Pharmaceutical Procurement Service to monitor uptake of treatment, pending consideration for routine commissioning in line with extant Managed Entry arrangements

The Public Health Agency is asked to:

13. Continue to work with HSC Trusts and the Business Services Organisation to report positive and negative tests to enable retrospective reimbursement of associated assay costs.

Summary

The policy has been updated, effective from 13 June 2022, to link to the published report the Independent Advisory Group commissioned by the Department of Health and Social Care (DHSC) to advise on the groups of patients likely to be at highest risk of deterioration, hospitalisation or death from a COVID infection. The report confirms the groups of 'highest' risk patients who are potentially eligible COVID treatments under this policy. Clinicians are asked to note that figure 1 of the report

refers to adults (aged 18 years and over) and figure 2 refers to children (aged 12-17 years).

There are no other material changes to the policy.
In summary, available treatment options under the policy for eligible patients with hospital-onset COVID-19 are:

- First-line: nirmatrelvir/ritonavir (Paxlovid), (antiviral)
- Second-line: remdesivir (antiviral)
- Third-line: sotrovimab (nMAB)

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[2]

  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 multidisciplinary team [MDT] assessment).

[2] 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.

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

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 HSC trust 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

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. See action section above for 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

Further enquiries should in the first instance be directed to your hospital pharmacy team.

Yours sincerely

PROFESSOR SIR MICHAEL McBRIDE
Chief Medical Officer

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Chief Pharmaceutical Officer

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