Chief Medical Officer Directorate

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The Scottish Government

Dear Colleague

FURTHER INFORMATION FOR HEALTHCARE PROFESSIONALS - TARGETED DEPLOYMENT OF COVID-19 MEDICINES FOR NON-HOSPITALISED PATIENTS

DL (2022) 04
16 February 2022

Summary

1. Subsequent to DL (2021) 52 published on 21 December 2021, this letter provides updated and further information for healthcare professionals on new treatment options for COVID-19 which are being made available to individuals at higher risk of hospital admission or death from COVID-19.

2. To be most effective, these treatments need to be administered as soon as practically possible after receiving a positive COVID-19 test result and symptom onset. These treatments are in addition to vaccinations, which still remain the best way to protect everyone.

3. We would be grateful for your help in supporting eligible patients to access these treatments in the event that they start experiencing symptoms and receive a positive COVID-19 test result.

Patient Eligibility Criteria and Access Routes

4. As set out in more detail below, there are two access routes to receive COVID-19 community treatments, both with different eligibility criteria and access arrangements.

Addressees

For action
Medical Directors, NHS Boards and Special Health Boards
Directors of Pharmacy, NHS Boards
and Special Health Boards

For information
Chief Executives, NHS Boards
Chief Executive, NHS 24
Scottish General Practice Committee
Community Pharmacy Scotland
General practitioners and their teams
Community pharmacists and their teams
Out of Hours service providers

Enquiries to:
Medicines Policy Team

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5. To date, two oral antivirals have received a conditional marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA): molnupiravir (brand name: Lagevrio®) and a second combination product, PF-07321332 (also known as nirmatrelvir) plus ritonavir (brand name: Paxlovid®). The Summary of Product Characteristics for these medicines can be found online at www.medicines.org.uk

PANORAMIC National Study (Oral Antivirals)

6. COVID-19 oral antivirals are being evaluated through a national study called PANORAMIC, run by the University of Oxford. It is an open-label randomised control trial. The national study will enable collection of additional data to address limitations in the company-sponsored trial, for example to understand the effectiveness of the treatments in vaccinated patients.

7. The national study is open to individuals living anywhere in the UK who meet the following criteria:
    - Have received a positive PCR of Lateral Flow Test for COVID-19; and
    - Feel unwell with symptoms of COVID-19 that started in the last five days; and
    - Are either aged 50+ years old **or** are aged 18-49 years old with an underlying medical condition that can increase the chance of having severe COVID-19. A list of these underlying medical conditions can be found on the PANORAMIC trial website.

8. Those eligible can sign up for the trial at the study website (www.panoramictrial.org) or by calling the freephone number 0808 156 0017. All participants take part from their own homes, without needing to visit a clinic or hospital. Where a patient is randomised to receive an oral antiviral, these will be home delivered via a central pharmacy.

9. To participate, individuals will be asked to agree to complete a daily diary for 28 days, or receive a phone call from the trial team on days 7, 14 and 28 to discuss their symptoms.

10. The outcomes from the trial will enable the NHS to fully understand how best to make use of these treatments in the future.

11. We would grateful for your support in raising awareness of the study and encouraging individuals who may be eligible to sign-up. Attached is a poster that can be used to support raising awareness; a range of other resources including graphics for use in social media and presentations can be found in the *Share* section of the PANORAMIC Trial Website (Link). Translated resources can be found in the *Community Outreach* section of the PANORAMIC Trial website (Link).

Direct Access to COVID-19 Treatments for Eligible High Risk Individuals

12. Individuals identified as being at very high risk of deterioration, hospitalisation or death from COVID-19 can directly access new COVID-19 therapies via the NHS, outside of the national study.

13. Adults and children (aged 12 years and above) are eligible to be assessed for treatment if they have;
    - Symptoms of coronavirus that started in the last 5 days with no signs of clinical recovery;

- Are a member of one of the patient groups considered at high risk from coronavirus with a clinical condition prioritised for treatment (list of prioritised conditions set out at Appendix 1);
- Coronavirus is confirmed by either a positive PCR test or lateral flow device (LFD) test.

14. Given the short effective treatment window, to avoid delays, a positive LFD result will be accepted to be assessed for treatment. A PCR test is still required to confirm a positive result, and to provide material for sequencing if needed, but there is no need to wait for the result of this PCR test before starting treatment. The PCR test is needed to provide information to monitor a patient's response to any treatment.

15. Each Health Board has established a single point of contact telephone number for eligible high-risk individuals to contact for an assessment of their suitability for treatment. The single point of contact telephone numbers can be found on NHS Inform (www.nhsinform.scot/covid19treatments) and are set out in Appendix 2. In addition, each Board has put in place service arrangements with prescribing capability to support medical clinical assessment of individuals who contact the single point of contact telephone number.

16. Updated treatment recommendations came into effect on 10 February 2022. The oral antiviral, Paxlovid® and the intravenously-administered monoclonal antibody, sotrovimab (Brand name: Xevudy®) are jointly recommended as first line treatment options. More information can be found in the UK-wide clinical commissioning policy.

17. COVID-19 is much less likely to progress to severe disease in the 12-17 year-old age group, even in those who might be viewed as at increased risk, relative to their peers. Only those 12-17 year olds assessed as at exceptionally high risk will be offered treatment. The oral antivirals are not authorised for use in adults aged under 18 years so children aged 12-17 years may only be considered for treatment with sotrovimab or the IV antiviral, remdesivir.

18. A number of clinical systems have been searched to seek to identify patients who may be eligible for direct access to the new treatments; this includes GP IT systems and hospital records. A letter has been sent to patients who were identified via these searches to support raising awareness of the new treatment options and the access route. This is supplementing other approaches to raising awareness of the new treatments - it is not necessary for a patient to have received a letter for an eligible individual to access treatment.

19. In a number of Boards, where patients have been identified as potentially eligible, they have also been receiving a text message with details of the service arrangements at the point of receiving a positive test result. This text service will be broadened to all Boards during w/c 14 February. Again, the text is to support raising awareness of the new treatment options and it is not necessary for an eligible patient to have received a text to access treatment.

20. Given limitations in how data is stored in IT systems, it is not feasible to identify 100% of individuals who may be eligible for these new treatments from searches of clinical records alone. If you receive a query from someone who may be eligible for direct access to these treatments (experiencing symptoms **+** positive test **+** a prioritised clinical condition), they should be referred to your Health Board's single point of contact telephone number.

21. Where an individual from this cohort meets the eligibility criteria for both the national study and for direct access to COVID-19 treatments, they should be signposted to the direct access arrangements.

Supply Chain

22. Supply of nMABs and COVID-19 antivirals is being managed by NSS National Procurement (NP). NSS NP will continue to work with Health Boards on stock allocation. Given limited supply, community pharmacies will only be able to access oral antivirals where there is agreement with the Health Board that the pharmacy will support the dispensing of these medicines to eligible individuals.

Reporting Suspect Adverse Reactions

23. Reporting suspected adverse reactions enables the continued monitoring of the benefit/risk balance of medicines. Healthcare professionals are asked to report any suspected adverse reactions via the Coronavirus Yellow Card Reporting site or search for MHRA Yellow Card in the Google Play or Apple App Store.

UK COVID-19 Antivirals in Pregnancy Registry

24. As molnupiravir is 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 four days after the last dose of molnupiravir. Similarly, Paxlovid is not recommended during pregnancy and in women of childbearing potential not using effective contraception. All healthcare professionals are asked to ensure that any individuals 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/.

Actions Required

Medical Directors are asked to distribute this letter to:

- General practices
- Out of Hours Service providers
- Accident & Emergency Departments
- Directors of Public Health
- Relevant clinical specialists
- Prison Health Centre Managers

Pharmacy Directors are asked to distribute this letter to:

- Community pharmacy contractors
- Hospital pharmacy teams
- GP practice pharmacy teams

All healthcare staff are asked to support the signposting of patients who may be eligible for these new treatments.

NHS Inform will be kept updated: www.nhsinform.scot/covid19treatments.

We would like to sincerely thank you for your ongoing support in helping patients to access these important new treatment options, reducing the risk of hospitalisation and mortality for those patients at higher risk following COVID infection.

Yours sincerely,

Professor Sir Gregor Smith

Chief Medical Officer

Professor Alison Strath

Chief Pharmaceutical Officer

Appendix 1: Patient cohorts considered at highest risk from COVID-19 and to be prioritised for treatment with nMABs

The following patient cohorts were determined by an independent Department of Health and Social Care (DHSC) commissioned group of clinical experts using the best available evidence on outcomes in COVID-19.

Cohort	Description
Down's syndrome	All patients with Down's syndrome
Patients with a solid cancer	• Active metastatic cancer and active solid cancers (at any stage) • All patients receiving chemotherapy within the last 3 months • Patients receiving group B* or C** chemotherapy 3-12 months prior • Patients receiving radiotherapy within the last 6 months
Patients with haematological diseases and stem cell transplant recipients	• Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases) • • Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases) • Individuals with haematological malignancies who have received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or radiotherapy in the last 6 months • Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months except patients with chronic phase chronic myeloid leukaemia (CML) in molecular response or first or second line tyrosine kinase inhibitors (TKI). • All patients with myeloma (excluding MGUS) or chronic B-cell lymphoproliferative disorders (e.g. chronic lymphocytic leukaemia, follicular lymphoma) or myelodysplastic syndrome (MDS) who do not fit the criteria above. • All patients with sickle cell disease. • Individuals with non-malignant haematological disorder (e.g. aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (e.g. anti-CD20, anti-thymocyte globulin [ATG] and alemtzumab) within the last 12 months.

Patients with renal disease	• Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who:
	  ○ Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)
	  ○ Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals
	  ○ Not been vaccinated prior to transplantation
	• Non-transplant patients who have received a comparable level of immunosuppression
	• Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 ml/min/1.73m2) without immunosuppression

Patients with liver disease	• Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease). • Patients with a liver transplant • Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) • Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Patients with immune-mediated inflammatory disorders (IMID)	• IMID treated with rituximab or other B cell depleting therapy in the last 12 months • IMID with active/unstable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID with stable disease on either corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate
Immune deficiencies	• Common variable immunodeficiency (CVID) • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) • Hyper-IgM syndromes • Good's syndrome (thymoma plus B-cell deficiency) • Severe Combined Immunodeficiency (SCID) • Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) • Primary immunodeficiency associated with impaired type I interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)

	• Any patient with a secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy
HIV/AIDS	• Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • On treatment for HIV with CD4 <350 cells/mm3 and stable on HIV treatment or CD4>350 cells/mm3 and additional risk factors (e.g. age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, those with alcohol-dependence)
Solid organ transplant recipients	All recipients of solid organ transplants not otherwise specified above
Rare neurological conditions	• Multiple sclerosis • Motor neurone disease • Myasthenia gravis • Huntington's disease

***Group B chemotherapy (10-50% risk of grade 3/4 febrile neutropenia or lymphopenia):** • Etoposide based regimens • CMF • Irinotecan and Oxaliplatin based regimens • Cabazitaxel • Gemcitabine • Chlorambucil • Temozolomide • Daratumumab • Rituximab • Obinutuzumab • Pentostatin • Proteosome inhibitors • IMIDs • PI3Kinase inhibitors • BTK inhibitors • JAK inhibitors • Venetoclax • Trastuzumab-emtansine • Anthracycline-based regimens • Fluorouracil, epirubicin and cyclophosphamide (FEC) • Methotrexate, vinblastine, adriamycin/doxorubicin, cisplatin (MVAC) • Adriamycin/doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD) • Cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) • Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisolone (BEACOPP) • Liposomal doxorubicin • Taxane – 3-weekly • Nab-paclitaxel • Carboplatin-based regimens • Ifosphamide-based regimens • Bendamustine • Cladrabine • Topotecan •Cyclophosphamide/Fludarabine combinations • Ifosphamide, carboplatin, etoposide (ICE) • Gemcitabine, dexamethasone, cisplatin (GDP) • Isatuximab • Polatuzumab • Acalabrutinib • Dexamethasone, cytarabine, cisplatin (DHAP) • Etoposide, methylprednisolone, cytarabine, cisplatin (ESHAP) • Cyclophosphamide, vincristine, doxorubicin, dexamethasone (CVAD) • Dacarbazine-based regimens • Lomustine • Magalizumab • Brentuximab vedotin • Asparaginase-based regimens

****Group C chemotherapy (>50% risk of grade 3/4 febrile neutropenia or lymphopenia):** • All acute myeloid leukaemia/acute lymphocytic regimens • Bleomycin, etoposide and platinum • Highly immunosuppressive chemotherapy (e.g. FluDAP, high dose Methotrexate & • Cytarabine) • Trifluradine/ Tipiracil • KTE-X19 • Gilteritinib

Ref: Interim Clinical Commissioning Policy: Neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19 (27 January 2022)

Appendix 2: Board Single Points of Contact for Referral

The table below provides a single point of contact in each Health Board that individuals can contact following a positive PCR test result if they believe they meet the eligibility criteria. Lines may be operated as an answering machine and call-back service so must **not** be used for general queries or to seek urgent medical advice.

Health Board Area	Single Point of Contact
NHS Ayrshire & Arran	01563 825610
NHS Borders	01896 827015
NHS Dumfries & Galloway	01387 241959
NHS Fife	01592 729799
NHS Forth Valley	01786 434036
NHS Grampian	01224 553555
NHS Greater Glasgow & Clyde	0800 121 7072
NHS Highland	0800 085 1558
NHS Lanarkshire	01355 58 5145
NHS Lothian	0300 790 6769
NHS Orkney	01856 888259
NHS Shetland	01595 743393
NHS Tayside	01382 919477
NHS Western Isles	01851 601151