Chief Medical Officer Directorate

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The Scottish Government

Dear Colleague

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

Summary

1. Subsequent to DL (2021) 49 published on 9 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. Within the past week, a number of changes have been made to the UK-wide clinical commissioning policy to reflect both the current understanding on the likely impact of the Omicron variant on the efficacy of the combination nMAB casirivumab and imdevimab and the availability of the nMAB sotrovimab from w/c 20 December.

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

4. This letter is also a means to notify all GP practices of the use of their GP data for the purpose of identification and contact of individuals who may be eligible for direct access to new COVID-19 treatments.

New COVID-19 Treatments

5. Neutralising monoclonal antibodies (nMABs) work by binding to the spike protein on the outside of the COVID-19 virus; this in turn prevents the virus from

DL (2021) 52
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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
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attaching to and entering human cells, so that it cannot replicate in the body.

6. To date, two products have received a conditional marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA): the combination nMAB, Ronapreve (casirivumab and imdevimab) and a second product, sotrovimab (Xevudy).

7. Emerging evidence indicates that the casirivimab and imdevimab combination has significantly decreased efficacy against the Omicron variant; it is therefore no longer recommended for use in non-hospitalised patients. Based on laboratory studies, sotrovimab is expected to be active against the Omicron variant and is now available. Sotrovimab is administered by intravenous infusion.

8. Antivirals work by interfering with replication of the virus. They are most effective when administered early in infection by preventing progression to more severe, or even critical, symptoms.

9. In November, the MHRA granted a conditional marketing authorisation to the first oral antiviral for COVID-19, molnupiravir (brand name: Lagevrio).

10. The Summary of Product Characteristics for these medicines can be found online at www.medicines.org.uk

Patient Eligibility Criteria and Access Routes

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

PANORAMIC National Study

9. COVID-19 oral antivirals will be evaluated through a new national study called PANORAMIC, run by the University of Oxford. It is an open-label randomised control trial; 50% of patients will be randomised to receive an antiviral and 50% will receive the current standard of care.

10. Molnupiravir is currently the only oral antiviral that has received a conditional marketing authorisation. It has been shown in company-led clinical trials to reduce the relative risk of hospitalisation or death by approximately 30% in at risk, non-hospitalised adult patients with mild-to-moderate COVID-19 (Ref: MSD Statement). The national study will enable collection of additional data to address limitations in the company-sponsored trial, for example the effectiveness of the treatments in vaccinated patients. The participants in the company-sponsored clinical trial were unvaccinated.

11. The national study is open to individuals living anywhere in the UK who meet the following criteria:
    - Have received a positive PCR 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.

12. Those eligible can sign up for the trial at the study website (www.panoramictrial.org). 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.

13. 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.

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

14. **From 22 December,** individuals identified as being at very high risk of deterioration, hospitalisation or death from COVID-19 will be able to access new COVID-19 therapies via the NHS, outside of the national study.

15. Adults and children (aged 12 years and above) are eligible to be assessed for treatment if they;
    - Have received a positive PCR test for COVID-19 in the last **five** days; and
    - Symptoms of COVID-19 that started in the last **five** days; and
    - Are a member of one of the patient groups considered at high risk from coronavirus and with a clinical condition prioritised for treatment (list of eligible conditions set out at Appendix 1)

16. The list of eligible individuals was developed by an independent expert working group based on detailed clinical evidence and is designed to support targeting those higher risk patients who have the potential to both be least likely to generate a material immune response to vaccines and be at highest risk of disease progression, hospitalisation and death.

17. 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 will be published on NHS Inform once services go-live on 22 December 2021 (www.nhsinform.scot/covid19treatments) and are set out in Appendix 2.

18. Each Health Board is establishing service arrangements with prescribing capability for centralised medical clinical assessment of individuals who contact the single point of contact telephone number. At this time, there is no expectation that these medicines will be prescribed in primary care unless part of locally agreed service arrangements.

19. Where treatment is required, the clinical commissioning policy (link; last updated 16 December 2021) recommends the nMAB sotrovimab as the first-line treatment option for eligible patients; this is likely to involve the individual travelling to a day clinic at a hospital to receive treatment. Where an nMAB is contraindicated or the

administration of an nMAB is not possible, individuals may be treated with a five-day course of molnupiravir.

20. 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. Only those 12-17 year olds assessed as at exceptionally high risk will be offered an infusion of a monoclonal antibody treatment. Molnupiravir is only authorised for use in adults aged 18 years and over.

21. In the coming weeks, a letter will be sent to individuals who may be eligible to access new COVID-19 therapies via the direct access route to ensure awareness of the new treatment options and to provide advice on how to access services. They will also be sent a home PCR test kit to keep at home to support getting tested quickly if they start experiencing symptoms. Work is also underway to enable the proactive NHS-led contact of eligible individuals on receipt of a positive PCR test, to signpost the availability of these new treatments.

22. In order to be able to contact individuals who may be eligible, data is being extracted from a number of clinical systems, including GP IT systems. Appendix 3 provides formal notification to GP practices on the use of their GP data for the purpose of identification and contact of individuals that may be eligible for direct access to COVID-19 treatments. The Royal College of General Practitioners (RCGP) Scotland and the Scottish General Practice Committee (SGPC) have confirmed their support for this approach.

23. 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 clinical records alone. **If you receive a query from someone who may be eligible for direct access to these treatments, they should be referred to your Health Board's single point of contact telephone number.**

24. 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

25. 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 very 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 the eligible individuals.

Reporting Suspect Adverse Reactions

26. 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

27. 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. 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

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. We would like to sincerely thank you for your support as we roll out these important new treatment options, reducing the risk of hospitalisation and mortality for those patients at higher risk following COVID infection.

Yours sincerely,

Professor 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
Sickle cell disease	All patients with a diagnosis of sickle cell disease
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 a haematologic malignancy (cancer of the blood)	• Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant
	• Autologous HSCT recipients in the last 12 months
	• Individuals with haematological malignancies who have
	  ○ received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or
	  ○ anti-CD20 monoclonal antibody therapy in the last 12 months
	• Individuals with chronic B-cell lymphoproliferative disorders receiving systemic treatment or radiotherapy within the last 3 months
	• Individuals with chronic B-cell lymphoproliferative disorders with hypogammaglobulinaemia or reduced peripheral B cell counts
	• Individuals with acute leukaemias and clinically aggressive lymphomas who are receiving chemotherapy or within 3 months of completion at the time of vaccination
	• Individuals with haematological malignancies who have received anti-CD38 monoclonal antibody or B-cell maturation agent (BCMA) targeted therapy in the last 6 months
	• Individuals with chronic B-cell lymphoproliferative disorders not otherwise described above

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 • 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
Primary 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)
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 (16 December 2021)

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

Appendix 3: GP Data Extract to Support Identification and Contact of Patients Eligible for Direct Access to COVID-19 Treatments

1. This letter is a means to notify all GP practices of the use of their GP data for the purpose of identification and contact of individuals who may be eligible for direct access to new COVID-19 treatments. This is instead of each individual GP Practice, as joint controller, approving the extraction of data, which in this public health emergency is not feasible.

2. The Information Commissioner's Office (ICO) recognises the need for us to make rapid decisions about how to process personal data to respond effectively to the crisis and that normal compliance procedures may need to be adapted during this COVID-19 pandemic. Changes to our normal compliance procedures includes the use of this letter as a means to notify all GP Practices of the use of their GP data rather than seeking agreement from each GP Practice, as joint controller of data. The Royal College of General Practitioners (RCGP) Scotland and the Scottish General Practice Committee (SGPC) have confirmed their support for this.

3. The required data will be regularly extracted from all GP practices at an individual patient level using the established supplier, Albasoft, under the direction of NHS National Services Scotland (NSS). Once GP practice data is extracted, Public Health Scotland (PHS) will become the primary data controller and will be responsible for the integrity of the data outside of GP IT systems. Appropriate security and information assurances are already in place to control this data in a managed and secure way. Data will at all times be held in line with the PHS Records Management Policy.

4. The data being extracted is the CHI numbers of patients who meet the following clinical criteria groups. Searches are undertaken for READ codes or certain medications within patient records. From the CHI number, PHS will be able to cross match against other data searches and obtain demographic details for the patient. The data extract will include a 'tick' to indicate which of the following groups the patient is identified in (some may have more than one) but no specific Read code or other information is extracted.

Clinical conditions taken from GPIT

- Downs Syndrome – only for age 12-18 inclusive
- Sickle Cell Disease
- Metastatic / Secondary Cancer
- Lung cancer – diagnosed in last 2 years
- B-cell lymphoproliferative disorders
- Primary Immune Deficiencies – includes Common variable deficiencies, Hyper IgM syndromes, Good's syndrome, Severe Combined Immunodeficiency(SCID), APECED syndrome, Primary immunodeficiency, Primary agammaglobulinaemias.
- Renal Disease (equivalent to CKD4 – 5)
- Stem Cell transplants in last year
- Rare Neurological Diseases (Huntingtons Chorea, Myasthenia Gravis, Multiple Sclerosis, Motor Neurone Disease)

Medication searches from GPIT

- prescription of cyclophosphamide, tacrolimus, cyclosporin or mycophenolate in the last 26 weeks
- prescription of a steroid (other than prednisolone) in the last 26 weeks

- recording of Biologics in the last 26 weeks (recognised this will be limited)
- recording of B cell depleting therapies in the last 52 weeks (recognised this will be limited)

5. The data will be used by PHS, working alongside NSS, to create a list of individuals that may be eligible for direct access to the new COVID-19 treatments within five days of receiving a positive PCR test and symptom onset.

6. The Chief Medical Officer will also write directly to these individuals to make them aware of their potential eligibility. Their name and address will also be passed to the UK Health Security Agency (UKHSA) in order for home PCR test kits to be delivered to these individuals to have ready at home. It is crucial that the new COVID-19 treatments are started as soon as possible and within 5 days of both symptom onset and receiving a positive PCR test.

7. The only other direct contact will be from their local Health Board with regards to treatment. Initially PHS and NSS will use the data to provide a list of eligible individuals to local Health Boards and work is underway to, in the near future, set up an automated system that will flag these individuals to the Health Board if they test positive for COVID-19. Boards may contact individuals directly to assess eligibility and arrange treatment.