Lothian NHS Board

Lothian NHS Board
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Edinburgh
EH3 9DN
Main Switchboard: 0131 242 1000

www.nhslothian.scot

Date 05/03/2026
Your Ref
Our Ref 11133

Enquiries to Richard Mutch
Extension 35687
Direct Line 0131 465 5687
loth.freedomofinformation@nhs.scot
richard.mutch@nhs.scot

Dear

**FREEDOM OF INFORMATION – COVID-19 AND ANTIVIRAL THERAPY**

I write in response to your request for information in relation to Covid-19 and antiviral therapy.

Question:

- In early 2022 antivirals were introduced to reduce the impact of Covid-19 on patients. Please can you explain your process for dealing with phone calls from renal transplant patients who were calling to report their Covid illness, including that part of the process where patients were considered for antivirals and levels of immunosuppresants were reviewed/modified for each patient involved.

- I'd also be grateful if you are able to tell me how many renal patients were involved in this process from 1 January 2022 through to 30 June 2022.

- I presume calls to renal dept and covid lines would all have been logged with data recoverable. If so, both of those centres. If not, whichever of those two call points was logged with data recoverable

Answer:

Attached below is an email from 21/12/2021 describing the pathway for the management of antiviral therapy in the out-patient setting. Patients deemed at high risk, including renal transplant, were sent a letter advising them of actions to take if they had Covid, directing them to entry point for antiviral therapy. This part of the process was independent of the transplant unit. Members of the transplant unit were informed of this process.

We are not aware of a separate written protocol/procedure in the transplant unit describing what to do if a patient phoned with a query about Covid, but this would be in keeping with other specific conditions where we would not expect there to be a specific protocol/procedure.

If there had been contact with a patient and a discussion around change in immunosuppression then we would expect this to be documented in individual electronic patient records, and not an external record of this this contact allowing for answer to the

question. I am not aware of any separate record that would allow us to tally the number of calls, or indeed identify who made a call.

We do not have access to this in a centrally extractable format. Under the Freedom of Information Act NHS Lothian is not required to create new records to enable it to respond to your enquiry. This information is not collated or held in aggregate form and it would be necessary to review all case files relating to patients over the period you have requested to assemble the information you seek. Even if NHS Lothian did this – and there would be significant cost implications in doing so – it would be unable to respond in full to your request. The information requested is therefore exempt under section 12.1 – Cost.

Calls are not recorded in the transplant unit. As per Section 17 of the Freedom of information (Scotland) Act 2002 formally I must advise that we do not hold this information.

I hope the information provided helps with your request.

If you are unhappy with our response to your request, \you do have the right to request us to review it. Your request should be made within 40 working days of receipt of this letter, and we will reply within 20 working days of receipt. If our decision is unchanged following a review and you remain dissatisfied with this, you then have the right to make a formal complaint to the Scottish Information Commissioner within 6 months of receipt of our review response. You can do this by using the Scottish Information Commissioner's Office online appeals service at www.itspublicknowledge.info/Appeal. If you remain dissatisfied with the Commissioner's response you then have the option to appeal to the Court of Session on a point of law.

If you require a review of our decision to be carried out, please write to the FOI Reviewer at the email address at the head of this letter. The review will be undertaken by a Reviewer who was not involved in the original decision-making process.

FOI responses (subject to redaction of personal information) may appear on NHS Lothian's Freedom of Information website at: https://org.nhslothian.scot/FOI/Pages/default.aspx

Yours sincerely

**ALISON MACDONALD**
**Executive Director, Nursing**
Cc: Chief Executive
Enc.

NHS Lothian

From: [redacted]
Sent: Tuesday, December 21, 2021 4:08:10 PM
To:
[redacted]
Subject: Fw: Covid-19 limited deployment pathway for outpatients - further UPDATE with important changes, please read. Pathway goes live 22 Dec 2021
Sent on behalf of Dr Caroline Whitworth
*****
To keep you all updated, and please share with relevant colleagues:

(Sarah - please forward to all CDs, Jenny - please forward for all Primary care colleagues)

You may have seen an interim Clinical Commissioning Policy published 8 Dec, from the 4 nations' CMOs regarding use of neutralising monoclonal Abs (nmAb) or antiviral agents in ultra-high risk patients in the 'limited deployment' pathway.
This is for patients over 12* years of age presenting with symptoms and a positive PCR in the last 5 days, in the diagnostic categories listed below in Appendix 1.
Very recent data has now suggested that for patients with Omicron variant, one of the proposed nMAb options Ronapreve IV/SC was likely to have no neutralising effect. As a consequence a new Interim Commissioning Policy has been produced - attached, published 16 December. A new CMO letter (DL (2021) 52 - attached - is being sent to all Health care professionals today.

As a consequence we are planning to use Sotrovimab IV as the first line nMAb.

The majority (approx 90%) of eligible patients (see Appendix 1 below) will be identified by PHS and those patients should receive a letter informing them of that eligibility within the next 2 weeks, and what to do if they develop symptoms and have a positive PCR. We expect this letter to be posted to patients by PHS ~31 Dec 2021. However we are very aware that the list of eligible patients will both MISS some eligible patients and include patients who are NOT eligible.

The letter will advise them to look at NHS Inform website where the single point of contact - Tel number 0300 790 6769 ( open 09:00 – 17:00) for patients resident in NHS Lothian will be published once the pathway goes live. National messaging and media will also point

patients to NHS Inform page, where patients can look at the inclusions and see whether they should be eligible.

If patients are within 5 days of symptom onset, ongoing symptoms, and within 5 days of taking a PCR (and positive) and they fall into one of the groups listed below in Appendix 1 then they would be eligible for either a nmAb or antiviral Rx through the limited deployment pathway.

This limited deployment pathway has a confirmed starting date of 22 Dec 2021.

This pathway will not undertake clinical assessment of patients who are unwell with Covid-19.
Referrals for clinical assessment of patients who are unwell with possible or confirmed covid, should go through normal routes.

Please don't refer patients into this pathway.
Please direct eligible patients to the contact number (0300 790 6769) advertised on NHS Inform where they will be triaged, ONCE the pathway goes live on 22 Dec 2021.
If eligible patients meet criteria, they will be either invited to an appropriate site (ED RHCYP or WGH RIDU OPAT) for outpatient IV nMAb treatment or receive oral antiviral Rx. The latter can be delivered to their home.

Patients with a positive PCR AND ongoing symptoms could NOW also be directed to the PANORAMIC trial - Platform Adaptive trial of NOvel antiviRals for eArly treatMent of covid-19 In the Community. Patients can sign-up themselves at https://www.panoramictrial.org/ from now. This trial can include the patients listed in Appendix 1, but has wider inclusion.

If patients are suitable for the limited deployment pathway, from 22 Dec it is more appropriate to direct them to the limited deployment pathway via NHS Inform rather than to PANORAMIC. All patients testing positive, do receive a number of text messages including a text referring them to a site with a list of clinical trials (including PANORAMIC).

It is also important to be realistic with patients as to what these treatment options may or may not achieve. There remains some uncertainty about actual benefit - published data are from trials performed before vaccination and before Omicron, and suggested NNT for benefit (a combined endpoint of avoiding admission or death) with Sotrovimab is ~17, and for Molnupravir ~33. These numbers may be quite different in a largely vaccinated population with Omicron. Hence the need for the PANORAMIC trial. There are also uncertain risks about giving treatment beyond 5 days.

* ultra-high risk patients over 12 are eligible for Sotrovimab, and those over 18 are eligible for either Sotrovimab or Molnupravir (latter contra-indicated in pregnancy)

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 advisory group commissioned by the Department of Health and Social Care (DHSC).

| Cohort | Description |
| --- | --- |
| Down's syndrome | 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)<br>All patients receiving chemotherapy within the last 3 months<br>Patients receiving group B or C chemotherapy 3-12 months prior to illness.<br>[Details about Group B and C CTx included in attached DL (2021)52]<br>Patients receiving radiotherapy within the last 6 months |
| Patients with a haematologic malignancy | Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant<br>Autologous HSCT recipients in the last 12 months<br>Individuals with haematological malignancies who have<br>o received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or<br>o anti-CD20 monoclonal antibody therapy in the last 12 months<br>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 Bcell 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 o 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)

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• 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

Evidence for Sotrovimab:

Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab (nejm.org)

Thank you

Dr CE Whitworth
Medical Director (Acute)

Group B

Group C

10-50% risk of grade 3/4 febrile neutropenia or lymphopenia

>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

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· 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

· 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

Chief Medical Officer Directorate

T: 0300 244 4000
E: medicines.policy@gov.scot

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**
**21 December 2021**

**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

Tel: 0300 244 4000
E-mail:
medicines.policy@gov.scot

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)<br>• All patients receiving chemotherapy within the last 3 months<br>• Patients receiving group B* or C** chemotherapy 3-12 months prior<br>• 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<br>• Autologous HSCT recipients in the last 12 months<br>• Individuals with haematological malignancies who have<br>  ○ received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or<br>  ○ anti-CD20 monoclonal antibody therapy in the last 12 months<br>• Individuals with chronic B-cell lymphoproliferative disorders receiving systemic treatment or radiotherapy within the last 3 months<br>• Individuals with chronic B-cell lymphoproliferative disorders with hypogammaglobulinaemia or reduced peripheral B cell counts<br>• Individuals with acute leukaemias and clinically aggressive lymphomas who are receiving chemotherapy or within 3 months of completion at the time of vaccination<br>• Individuals with haematological malignancies who have received anti-CD38 monoclonal antibody or B-cell maturation agent (BCMA) targeted therapy in the last 6 months<br>• 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)<br>○ Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals<br>○ Not been vaccinated prior to transplantation<br>• Non-transplant patients who have received a comparable level of immunosuppression<br>• 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).<br>• Patients with a liver transplant<br>• Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis)<br>• 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<br>• IMID with active/unstable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate.<br>• IMID with stable disease on either corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate.<br>• IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate<br>• IMID with stable disease on either corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate.<br>• 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)<br>• Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig)<br>• Hyper-IgM syndromes<br>• Good's syndrome (thymoma plus B-cell deficiency)<br>• Severe Combined Immunodeficiency (SCID)<br>• Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) |

| | |
|---|---|
| | • Primary immunodeficiency associated with impaired type I interferon signalling<br>• 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<br>• 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<br>• Motor neurone disease<br>• Myasthenia gravis<br>• 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.

Rapid Policy Statement

# Interim Clinical Commissioning Policy: Neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19

Published on: 16 December 2021
Effective from: 20 December 2021

## Commissioning position

The proposal is: Sotrovimab is recommended to be available as a treatment option through routine commissioning for non-hospitalised adults and children (aged 12 years and above) with COVID-19 treated in accordance with the criteria set out in this document. Where treatment with sotrovimab is contraindicated or not possible, eligible patients may be offered an antiviral as an alternative.

## Background

nMABs are synthetic monoclonal antibodies that bind to the spike protein of SARS-CoV-2, preventing subsequent entry of the virus into the host cell and its replication. This effectively 'neutralises' the virus particle. The following nMAB has conditional marketing authorisation (or regulation 174 emergency use authorisation in Northern Ireland) for use in the treatment of COVID-19 in the UK:

- **Sotrovimab (Xevudy®)**: a dual-action nMAB that both blocks viral entry into healthy cells and clears cells infected with SARS-CoV-2

Recent evidence suggests that nMABs and oral antivirals significantly improve clinical outcomes in unvaccinated[1] non-hospitalised patients with COVID-19 who are at high risk of progression to severe disease and/or death. Key findings are as follows:

- Sotrovimab administered intravenously to non-hospitalised patients with mild-to-moderate disease and at least one risk factor for disease progression resulted in a relative risk reduction in hospitalisation or death by 85% (Gupta et al, 2021).

[1] This evidence has only been collected in unvaccinated populations – further research on vaccinated populations is needed.

- Final results from the Phase 3 MOVe-OUT trial show that the oral antiviral molnupiravir resulted in a relative risk reduction of 30% in the composite primary outcome of hospitalisation or death at day 29 (6.8% in the molnupiravir group vs 9.7% in the placebo group, p=0.0218).

## Marketing authorisation

### Sotrovimab

Sotrovimab delivered intravenously 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 for the above indication is through a Regulation 174 approval or a licensing determination by the European Medicines Agency.

### Molnupiravir

Molnupiravir administered orally has conditional marketing authorisation in Great Britain (England, Scotland and Wales) for use in the treatment of mild to moderate COVID-19 in adults (aged 18 years and over) with a positive SARS-CoV-2 diagnostic test and who have at least one risk factor for developing severe illness. Access to molnupiravir in Northern Ireland for this indication is through a Regulation 174 approval or a licensing determination by the European Medicines Agency.

## Eligibility criteria

Patients must meet all of the eligibility criteria and none of the exclusion criteria. Pre-hospitalised patients are eligible for treatment[2] if:

- SARS-CoV-2 infection is confirmed by polymerase chain reaction (PCR) testing within the last 5 days

  AND

- Onset of symptoms of COVID-19[3] [4] within the last 5 days

  AND

- A member of a 'highest' risk group (as defined in Appendix 1).

The eligible patients as outlined in this policy should initially be considered for treatment with an nMAB (sotrovimab). Where an nMAB is contraindicated or the administration of an nMAB is not possible, patients may be treated with a five-day course of molnupiravir if the onset of symptoms is in the last 5 days.

Patients who have received an nMAB within a post-exposure prophylaxis (PEP) or pre-exposure prophylaxis (PrEP) trial (such as the PROTECT-V trial) who meet the eligibility criteria of this policy can still receive treatment with an nMAB.

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[2] For paediatric/adolescent patients (aged 12-17 years inclusive), paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment

[3] The following are considered symptoms of COVID-19: feverish, chills, sore throat, cough, shortness of breath or difficulty breathing, nausea, vomiting, diarrhoea, headache, red or watery eyes, body aches, loss of taste or smell, fatigue, loss of appetite, confusion, dizziness, pressure or tight chest, chest pain, stomach ache, rash, sneezing, sputum or phlegm, runny nose

[4] For patients who have been symptomatic (within the specified time period) but are no longer symptomatic, clinical judgement should determine suitability for treatment

### Exclusion criteria

Patients are not eligible for nMAB treatment in the community if they meet any of the following:

- Require hospitalisation for COVID-19
- New supplemental oxygen requirement specifically for the management of COVID-19 symptoms
- Children weighing less than 40kg
- Children aged under 12 years[5]

### Serology testing

Where possible, all patients should have samples taken for serology testing against SARS-CoV-2 prior to treatment with an nMAB. However, serology results are **not** a requirement for treatment with nMABs under the criteria specified in this policy.

### Cautions

Please refer to the Summary of Product Characteristics (SmPC) for sotrovimab and molnupiravir for special warnings and precautions for use.

Sotrovimab

Hypersensitivity reactions, including serious and/or life-threatening reactions such as anaphylaxis, have been reported following infusion of sotrovimab. Hypersensitivity reactions typically occur within 24 hours of infusion. Signs and symptoms of these reactions may include nausea, chills, dizziness (or syncope), rash, urticaria and flushing. If signs and symptoms of severe hypersensitivity reactions occur, administration should be discontinued immediately and appropriate treatment and/or supportive care should be initiated.

If mild to moderate hypersensitivity reactions occur, slowing or stopping the infusion along with appropriate supportive care should be considered.

Molnupiravir

The most common adverse reactions (≥1% of subjects) reported during treatment and during 14 days after the last dose of molnupiravir were diarrhoea (3%), nausea (2%), dizziness (1%) and headache (1%) all of which were Grade 1 (mild) or Grade 2 (moderate).

### COVID-19 vaccines

Concomitant administration of an nMAB with COVID-19 vaccines has not been studied. Refer to local/national guidelines for vaccine administration and guidance on the risks associated with administration of a SARS-CoV-2 vaccine.

Further information on the timing of COVID-19 vaccination following administration of an nMAB is available at the following sites:

- Liverpool COVID-19 Interactions (covid19-druginteractions.org)
- Interactions information for COVID-19 vaccines – SPS – Specialist Pharmacy Services

[5] Molnupiravir is only licensed for adults aged 18 years and above.

## Pregnancy and women of childbearing potential

There are no data from the use of sotrovimab in pregnant women. The SmPC for sotrovimab states that sotrovimab may be used during pregnancy where the expected benefit to the mother justifies the risk to the foetus.

There are no data from the use of molnupiravir in pregnant women. Studies in animals have shown reproductive toxicity. Molnupiravir is **not recommended** during pregnancy. Individuals of childbearing potential should use effective contraception for the duration of treatment and for 4 days after the last dose of molnupiravir. All healthcare professionals are asked to 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/. Clinicians are advised to refer to the SmPC for molnupiravir for more information on use during pregnancy or lactation.

## Dose and administration

Sotrovimab

The recommended dose of sotrovimab is 500mg to be administered as a single intravenous infusion[6]. 8mls of sotrovimab (62.5mg/ml) should be added to a 100ml pre-filled infusion bag containing 0.9% sodium chloride and administered over 30 minutes.

Preparation and administration of sotrovimab should be initiated and monitored by a qualified healthcare provider using aseptic technique. Administration should be under conditions where management of severe hypersensitivity reactions, such as anaphylaxis, is possible. Individuals should be monitored post intravenous infusion according to local medical practice.

Refer to the Specialist Pharmacy Services institutional readiness document for further information on the handling, reconstitution and administration of the product.

Sotrovimab should not be infused concomitantly in the same intravenous line with other medication.

Molnupiravir

The recommended dose of molnupiravir is 800mg (four 200mg capsules) taken orally every 12 hours for 5 days. Treatment must not be extended beyond 5 days. Molnupiravir should be commenced as soon as possible after a diagnosis of COVID-19 has been made and within 5 days of symptom onset.

To reduce the possibility of emerging resistance, patients should be advised to complete the whole course of treatment even if their symptoms improve and/or they feel better.

## Co-administration

There is no interaction expected between sotrovimab or molnupiravir with the drugs listed below. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

Corticosteroids

Administration of systemic dexamethasone or hydrocortisone is recommended in the management of patients with severe or critical COVID-19. Corticosteroids are not suggested in non-severe COVID-19 disease. Updated WHO guidance on the use of systemic

[6] No dose adjustment is recommended in patients with renal or hepatic impairment.

corticosteroids in the management of COVID-19 can be found here. nMABs and antivirals should not be regarded as an alternative to corticosteroids.

Remdesivir

The Clinical Commissioning Policy for the use of remdesivir in hospitalised patients with COVID-19 can be found here.

IL-6 inhibitors

The Clinical Commissioning Policies for the use of IL-6 inhibitors in hospitalised patients with COVID-19 who require supplemental oxygen can be found here.

### Safety reporting

It is vital that any suspected adverse reactions (including congenital malformations and/or neurodevelopmental problems following treatment during pregnancy) are reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/.

## Governance

### Data collection requirement

Provider organisations in England should register all patients using prior approval software (alternative arrangements in Scotland, Wales and Northern Ireland will be communicated) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Clinicians are also required to ensure that any data collection requirements are met for the purpose of ongoing surveillance, audit and relevant research around the use of nMABs and antivirals (see 'Research' section below).

### Clinical outcome reporting

Where available, hospitals managing COVID-19 patients are strongly encouraged to submit data through the ISARIC 4C Clinical Characterisation Protocol (CCP) case report forms (CRFs), as coordinated by the COVID-19 Clinical Information Network (CO-CIN) (https://isaric4c.net/protocols/).

### Effective from

This policy will be in effect from 20 December 2021.

### Policy review date

This is an interim rapid clinical policy statement, which means that the full process of policy production has been abridged: public consultation has not been undertaken. This policy may need amendment and updating if, for instance, new trial data emerges, supply of the drug changes, or a new evidence review is required. A NICE Technology Appraisal or Scottish Medicines Consortium (SMC) Health Technology Assessment or All Wales Medicines Strategy Group (AWMSG) appraisal of nMABs and/or antivirals for COVID-19 would supersede this policy when completed.

This policy will be reviewed, if required, as further data emerge on the population prevalence of the omicron variant and any impact it may have on the efficacy of COVID-19 therapies.

## Surveillance and service evaluation

There is an urgent need to generate more evidence and greater understanding around the use of nMABs and antivirals in the treatment of patients with COVID-19. Both surveillance and service evaluation are necessary to gain knowledge around the following: factors of relevance in determining nMAB and antiviral treatment; the impact of nMAB and antiviral treatment in the community and hospital settings on the immune/virologic response and clinical recovery; and the public health sequelae of nMAB and antiviral use, such as generation of new mutations.

Treating clinicians are asked to ensure that all PCR tests undertaken as an inpatient and/or in the community where any patient who is receiving ongoing PCR testing as part of secondary care (for example, through an outpatient clinic) should do this through the hospital laboratory where these samples should be retained for sequencing. Further serial sampling for specific patient groups may be requested as part of UKHSA genomic surveillance purposes, or country specific programmes.

Clinicians must ensure that any additional data collection requirements are met for the purpose of relevant surveillance, audit and evaluation around the use of nMABs and antivirals. It is expected that there will be ongoing monitoring (involving sample collection) of selected patients treated with nMABs and antivirals (led by UKHSA, for instance around the potential generation of new variants), as well as academic research to generate new knowledge around clinical effectiveness and other relevant aspects of public health.

## Equality statement

Promoting equality and addressing health inequalities are at the heart of the four nations' values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010 or equivalent equality legislation) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

## Definitions

| | |
|---|---|
| **COVID-19** | Refers to the disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus |
| **Neutralising monoclonal antibody** | Synthetic antibodies that bind to a virus and inhibit its ability to infect host cells and replicate |
| **Spike protein** | The part of the SARS-CoV-2 virus that binds to the host cell, which then facilitates its entry into the cell |

## References

1. Gupta A, Gonzalez-Rojas Y, Juarez E, et al. Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab [published online ahead of print, 2021 Oct 27]. N Engl J Med. 2021;10.1056/NEJMoa2107934. doi:10.1056/NEJMoa2107934

## 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 advisory group commissioned by the Department of Health and Social Care (DHSC)[7].

| 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)<br>• All patients receiving chemotherapy within the last 3 months<br>• Patients receiving group B or C chemotherapy 3-12 months prior<br>• Patients receiving radiotherapy within the last 6 months |
| Patients with a haematologic malignancy | • Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant<br>• Autologous HSCT recipients in the last 12 months<br>• Individuals with haematological malignancies who have<br>  ○ received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or<br>  ○ anti-CD20 monoclonal antibody therapy in the last 12 months<br>• Individuals with chronic B-cell lymphoproliferative disorders receiving systemic treatment or radiotherapy within the last 3 months<br>• Individuals with chronic B-cell lymphoproliferative disorders with hypogammaglobulinaemia or reduced peripheral B cell counts<br>• Individuals with acute leukaemias and clinically aggressive lymphomas who are receiving chemotherapy or within 3 months of completion at the time of vaccination |

[7] For paediatric/adolescent patients (aged 12-17 years inclusive), paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment

| | |
|---|---|
| | • Individuals with haematological malignancies who have received anti-CD38 monoclonal antibody or B-cell maturation agent (BCMA) targeted therapy in the last 6 months<br>• 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:<br>  ○ Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)<br>  ○ Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals<br>  ○ Not been vaccinated prior to transplantation<br>• Non-transplant patients who have received a comparable level of immunosuppression<br>• 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).<br>• Patients with a liver transplant<br>• Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis)<br>• 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<br>• IMID with active/unstable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate.<br>• IMID with stable disease on either corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate.<br>• 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)<br>• Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig)<br>• Hyper-IgM syndromes<br>• Good's syndrome (thymoma plus B-cell deficiency)<br>• Severe Combined Immunodeficiency (SCID) |

| | |
|---|---|
| | • Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)<br>• Primary immunodeficiency associated with impaired type I interferon signalling<br>• 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<br>• 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<br>• Motor neurone disease<br>• Myasthenia gravis<br>• Huntington's disease |