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URGENT MESSAGE TO:

1. Directors of Pharmacy
2. Medical Directors NHS Boards

16 December 2021

Dear Healthcare Professional,

COVID THERAPEUTIC ALERT – INTERIM CLINICAL COMMISSIONING POLICY ON THE USE OF NEUTRALISING MONOCLONAL ANTIBODIES OR ANTIVIRALS FOR NON-HOSPITALISED PATIENTS WITH COVID-19.

Please see attached CMO letter and interim clinical commissioning policy regarding the use of neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19 for dissemination to relevant healthcare professionals.

for onward transmission as detailed below:-

Could all Directors of Pharmacy please forward this alert to:-

- Community Pharmacists
- Hospital Pharmacists
- Primary Care Pharmacists

Please could Medical Directors arrange to forward this alert on to:-

- General Practitioners
- Accident & Emergency Departments
- Nurses
- Consultants in Communicable Diseases
- Directors of Public Health
- Relevant Clinics
- Chief Executives of NHS Board

Thank you for your co-operation.

Yours sincerely

IRENE FAZAKERLEY
Medicines Policy Team

Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/021 16 December 2021

Neutralising monoclonal antibodies (nMABs) or antivirals for non-hospitalised patients with COVID-19

Summary

Neutralising monoclonal antibodies (nMABs) bind to specific sites on the spike protein of the SARS-CoV-2 virus particle, blocking its entry into cells and therefore inhibiting its replication. Sotrovimab (Xevudy) is an 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 non-hospitalised patients with COVID-19 who are at highest risk of progression to severe disease and/or death. Key findings are:

- Sotrovimab administered intravenously to non-hospitalised patients with mild-to-moderate disease and at least one risk factor for disease progression decreased the risk of hospitalisation or death by 85% (Gupta et al, 2021)

- 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).

The UK-wide clinical commissioning policy extends access to nMAB therapy to non-hospitalised patients who are considered to be at highest risk of progression to severe disease, hospital admission or death, and now also takes into account the availability of sotrovimab (from week commencing 20 December) and current understanding on the likely impact of the Omicron variant on the efficacy of the casirivimab and imdevimab combination antibody treatment. Antiviral treatment may be offered to patients in this cohort if aged 18 and above where an nMAB is contraindicated or treatment with an nMAB is not possible.

Please refer to the published (revised) policy for further details of eligibility and for additional guidance.

Action

Providers locally commissioned to provide **C**OVID **M**edicines **D**elivery **U**nit (CMDU) services and any equivalent arrangements in the devolved nations are asked to:

1. **Consider prescribing and administering an intravenous infusion of the monoclonal antibody sotrovimab[1] at a total dose of 500mg to adult patients, and children aged 12 and over and weighing at least 40 kg, in line with the published policy <*MHRA to add link*> to non-hospitalised patients where*:***

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

      AND

    - Onset of symptoms of COVID-19[2] is within the last 5 days

      AND

    - The patient is a member of the 'highest' risk group as set out in the policy

    CMDUs and the devolved nation equivalents are asked to ensure that patients eligible for an nMAB who cannot travel to a treatment site are able to access the treatment via alternative routes.

    Eligible patients aged 18 and above may be treated with the oral anti-viral molnupiravir at a dose of 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days if an nMAB is contraindicated or treatment with an nMAB is not possible. Patients should be strongly encouraged to complete the 5-day course. Treatment must not be extended beyond 5 days. In respect of oral antiviral treatment, arrangements should be made to ensure the patient can access the treatment without having to attend the service in person (e.g. courier delivery or medicine collected on behalf of the patient, depending on options available within the treatment window). This may include delivery to patients already admitted or resident in another facility.

2. As molnupiravir is **not recommended** during pregnancy, all individuals of childbearing potential who are prescribed molnupiravir (where an nMAB is contraindicated) should be advised to 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/.

3. **Noting the critical nature of surveillance, actively support additional testing or data requirements as requested under country specific or UK wide surveillance programmes, in line with further guidance to be issued.**

4. Ensure discharge letters to primary care explicitly record the treatment that has been given, together with the dose and date of administration. The following **SNOMED codes should be used to support evaluation and to inform subsequent treatment decisions**:

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[1] Or the combination antibody Ronapreve (casirivimab and imdevimab) at a total dose of 1.2g whilst local prevalence of the Omicron variant remains below 50%. Symptom onset should be within the last **7** days.

[2] 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

Administration of Sotrovimab

Procedure code: 47943005 |Administration of anti-infective agent (procedure)|

Presentation:

- Sotrovimab 500mg/8ml solution for infusion vials – 40219011000001108

Administration of Ronapreve

Procedure code: 47943005 |Administration of anti-infective agent (procedure)|

Presentations:

- Casirivimab 300 mg per 2.5 mL (120 mg/mL) with Imdevimab 300 mg per 2.5 mL (120 mg/mL) 2 vial pack - 40025711000001108
- Casirivimab 1332 mg per 11.1 mL (120 mg/mL) with Imdevimab 1,332 mg per 11.1 mL (120 mg/mL) 2 vial pack – 39654011000001101

Provision of Molnupiravir

Procedure code: 427314002 |Antiviral therapy (procedure)|

Presentation:

- Molnupiravir 200mg capsules, 40 capsule – 40251211000001109

5. Organisations should adhere to the procedural guidance which has been developed by the Specialist Pharmacy Service to support monoclonal antibody storage, preparation and administration.

6. In England, trusts who have not yet done so should register (by site) to participate in COVID-19 (and medicine) specific supply arrangements, via Blueteq™. Blueteq should also then be used to confirm pre-authorisation for individual patients and to capture a limited dataset essential for surveillance of antiviral resistance. Training for antimicrobial stewardship teams will be provided via webinar by UKHSA jointly with NHS England and NHS Improvement. HSC Trusts in Northern Ireland should liaise with the Regional Pharmaceutical Procurement Service to register interest. In Scotland, Health Board Directors of Pharmacy should notify NHS National Procurement if they wish to participate. Health Boards in Wales should notify the All Wales Specialist Procurement Pharmacist of their intention to participate.

7. Organisations should note that following initial nationally determined allocations to participating sites, ongoing supply will be replenished on the basis of relative use / need. Ongoing ordering will be through existing (business as usual) routes, supported by volume-based caps (reflecting estimated eligible patient volumes) if required.

8. Organisations should note that initial supply of COVID medicines may be available within ‘emergency supply’ packaging, which differs from the planned Great Britain (GB) packaging / labelling aligned to the product’s GB licence (or the equivalent product packaging / labelling aligned to a Regulation 174 authorisation or European

Medicines Agency marketing authorisation as applicable in Northern Ireland). **To preserve available supply, providers must ensure that packs with shorter use by dates are used first**.

9. Regular stock updates should be provided to trust / hospital and regional pharmacy procurement lead / chief pharmacists. Providers should enter the products onto stock control and prescribing systems as described below:

    - Casirivimab 300 mg per 2.5 mL (120 mg/mL) with Imdevimab 300 mg per 2.5 mL (120 mg/mL) with the dose description as: 2 vial pack
      AND/OR
    - Casirivimab 1332 mg per 11.1 mL (120 mg/mL) with Imdevimab 1,332 mg per 11.1 mL (120 mg/mL) with the dose description as: 2 vial pack
    - Sotrovimab 500mg/8ml solution for infusion vials
    - Molnupiravir 200mg capsules, 40 capsules

Co-Administration

For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

nMABs should not be infused concomitantly in the same IV line with other medications.

Monitoring, tracking and follow-up

Monitoring of longer-term progress is strongly recommended via recruitment of patients receiving COVID therapies to the ISARIC-CCP study.

All handovers of clinical care (including between hospitals if patients are transferred, between levels of care and clinical teams within hospitals, and between hospitals and primary care) should explicitly record the treatment that has been given together with the dose and date of administration. SNOMED codes (see action section, above) should be used in discharge letters to primary care.

Healthcare professionals are asked to report any suspected adverse reactions (including congenital malformations and or neurodevelopmental delays following treatment during pregnancy) via the United Kingdom Yellow Card Scheme www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store8.

Distribution

- NHS Trusts (NHS boards in Scotland and Wales)
- Primary Care (including out of hours providers)
- Community Pharmacies
- National / Regional Medical Directors
- National / Regional Chief Pharmacists
- Lead/Senior Pharmacists and Regional Procurement Pharmacy Leads

- Trust/Hospital Pathology Directors (to circulate to pathology networks and laboratory staff)
- Trust / Hospital Medical Directors (to circulate to medical and nursing staff managing admitted patients infected with COVID-19)

Enquiries

England

Enquiries from NHS trusts in England should in the first instance be directed to your trust pharmacy team who will escalate issues to the Regional Chief Pharmacist and national teams if required. Further information can be requested from the dedicated email address: england.spoc-c19therapeutics@nhs.net.

Northern Ireland

Enquiries from hospitals in Northern Ireland should in the first instance be directed to your hospital pharmacy team who will escalate issues to the Regional Pharmaceutical Procurement Service or Pharmaceutical Directorate at the Department of Health if required Further information can be obtained by contacting RPHPS.Admin@northerntrust.hscni.net

Scotland

Enquiries from hospitals in Scotland should in the first instance be directed to your hospital pharmacy team who will escalate issues to either NHS National Procurement or the Scottish Government's Medicines Policy Team if required. Contact should be made using the following emails: nss.nhssmedicineshortages@nhs.scot or medicines.policy@gov.scot

Wales

Enquiries from hospitals in Wales should in the first instance be directed to the health board's Chief Pharmacist who will escalate issues to the Pharmacy and Prescribing Team at Welsh Government if required. Enquiries to the Welsh Government should be directed to: COVID-19.Pharmacy.Prescribing@gov.wales.

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) • 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	• 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

[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 • 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
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