Deployment of COVID-19 treatments for highest risk non-hospitalised patients
Frequently Asked Questions

Who is this treatment for?
The treatment is recommended as an option for non-hospitalised adults and children (aged 12 years and above) with COVID-19. A full list of who is eligible is given at the end of this document.

How will patients be identified?
Patients are being identified centrally by NHS Digital and being shared with local COVID-19 Medicine Delivery Units (CMDU). The CMDU for Hampshire and the Isle of Wight is University Hospital Southampton NHS Foundation Trust (UHS).

Where will the treatment be given?
The treatment will be administered by a nurse visiting the patient's home. The medication is only available via UHS. Several homecare providers are currently planning this activity, all established in home chemotherapy or antibiotic delivery.

What form does the treatment take?
The primary route is injectable neutralising monoclonal antibody therapy (nMAB). The first available nMAB, Rovapreve (casirivimab and imdevimab) have been used in acute trusts since September 2021.

In addition, sotrovimab, the second licensed nMAB, is expected to be ready for use in early 2022.

Early trial estimates indicate that one hospitalisation is avoided for every 15 – 18 patients treated with nMAB therapy.

Alongside these injectable therapies, a new oral antiviral agent, molnupiravir, will be offered where nMABs cannot be offered either due to contraindications or significant practical problems in the delivery of the nMAB therapy.

Are there any side effects?
At present there have been very low levels of adverse reactions.

<u>Casirivimab and imdevimab</u>
Hypersensitivity reactions, including anaphylaxis, have been reported with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions (IRRs) have been observed with IV administration of casirivimab and imdevimab. IRRs observed in clinical studies were mostly mild to

moderate in severity and were typically observed during or within 24 hours of infusion. The commonly reported signs and symptoms for these reactions included nausea, chills, dizziness (or syncope), rash, urticaria and flushing.

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

Can these treatments be used for pregnant women or women of childbearing potential?

The community study investigating casirivimab and imdevimab in non-hospitalised patients with mild-to-moderate COVID-19 included pregnant women, although data on outcomes in this cohort are not yet available.

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-19 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.

Can nMabs be obtained from a community pharmacy?

No, the only stock in Hampshire and the Isle of Wight is kept at UHS and the only way it can be accessed is via this service.

Do patients need monitoring?

Patients will be monitored for deterioration, and several services such as the COVID-19 Oximetry @ Home and frailty services would be well placed to provide monitoring. Additional planning is underway to ensure that the CMDU processes link and utilise these teams in post-infusion monitoring. All therapies provided by CMDUs must be highlighted to GPs and registered on the Blueteq national registration and approval system.

What doses will be given?

Casirivimab and imdevimab
The recommended dose of casirivimab and imdevimab is 1.2g (600mg each of casirivimab and imdevimab) to be administered either as a single intravenous infusion or by subcutaneous injection.

Molnupiravir
The recommended dose of molnupiravir is 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days. Treatment must not be extended beyond 5 days.

Molnupiravir should be started 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.

Who is eligible?

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 and other genetic disorders	Patients with Down's syndrome and other genetic conditions that might reasonably be expected to reduce immune competence, beyond the primary immune deficiency syndromes
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) • Patients receiving chemotherapy within the last 12 months • 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 • 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: o Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin) o 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) • Severe Combined Immunodeficiency (SCID) • Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
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

Are there any exclusion criteria for these groups?

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

- Require hospitalisation for COVID-19
- Require supplemental oxygen
- Children weighing less than 40kg
- Children aged under 12 years