University Hospitals Sussex
NHS Foundation Trust

Guidelines and Algorithm for the use of Sotrovimab for non-hospitalised patients with COVID-19

Version:	1.1
Approved by:	Professor Mike Okorie
Clinical Sponsor:	Dr Andrew Leonard
Date approved:	17/12/21
Name of author(s):	Vikesh Gudka
Name of responsible committee:	Medicnes Governance Committee
Date issued:	16/12/21
Review date:	17/03/22
Target audience:	Covid19 Medicines Delivery Unit Medical Assessors
Minor update:	28.01.2022 (Removed closed system photos and changed preparation sheet)

Commissioning position

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.

Sotrovimab (Xevudy®) is 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 unvaccinated1 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).
- 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 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

Eligibility criteria

Patients must meet all of the eligibility criteria and none of the exclusion criteria. Pre-hospitalised patients are eligible for treatment 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 within the last 5 days
  AND
- A member of a 'highest' risk group (as defined in Appendix 1 and 2).

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. See separate Molnupiravir Guidelines.

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.

Exclusion criteria

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

- The pattern of clinical presentation indicates that there is recovery rather than risk of deterioration from infection
- 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
- Known hypersensitivity reaction to the active substances or to any of the excipients of sotrovimab as listed in the respective Summary of Product Characteristics

Cautions

Please refer to the Summary of Product Characteristics (SmPC) for Sotrovimab for special warnings and precautions for use at https://www.medicines.org.uk/emc/product/13097

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.

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.

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 https://www.covid19-druginteractions.org/checker
- Interactions information for COVID-19 vaccines – SPS – Specialist Pharmacy Services https://www.sps.nhs.uk/articles/interactions-information-for-covid-19-vaccines/

Dose and administration

The recommended dose of sotrovimab is 500mg to be administered as a single intravenous infusion. 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 using the clinical area preparation sheet (Appendix 3)

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 for 1 hour.

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

Co-administration

There are no drug interaction expected with Sotrovimab.

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

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/

Reference

1. MHRA CAS Alert CEM/CMO/2021/021 on 16th December 2021 https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103186
2. 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).

Cohort	Description
Down's syndrome	All patients with Down's syndrome
Patients with a solid cancer	• Active metastatic cancer and active solid cancers (at any stage) • All patients receiving chemotherapy within the last 3 months • Patients receiving group B or C chemotherapy 3-12 months prior (see Appendix 2) • Patients receiving radiotherapy within the last 6 months

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

	thymocyte globulin [ATG] and alemtzumab) within the last 12 months.

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

Patients with liver disease	• Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease). • Patients with a liver transplant • Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) • Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Patients with immune-mediated inflammatory disorders (IMID)	• IMID treated with rituximab or other B cell depleting therapy in the last 12 months • IMID with active/unstable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID with stable disease on either corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate
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

Appendix 2: Chemotherapy agents (Groups B and C)

Patients currently on or who have received the following chemotherapy regimens (Groups B and C in the table below) in the last 12 months and are considered to be at higher risk of Grade 3/4 febrile neutropenia or lymphopenia.

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 • 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	• 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

Appendix 3: Clinical Area Preperation Record – Sotrovimab 500mg in 50ml Sodium Chloride 0.9% Infusion Bag.

Specialist Pharmacy Service

Confidential - For NHS use only

NHS

Clinical Area Preparation Record – Sotrovimab 500mg in 50mL Sodium Chloride 0.9% Infusion Bag (Total volume = 58mL)

Set up
Step 1 Remove from the refrigerator: • 1 x Sotrovimab 500mg (62.5mg/mL) Concentrate for Solution for Infusion vial. Select: • 1 x Sodium Chloride 0.9% 50mL Infusion Bag • 1 x 10mL luer lock syringe • 1 x drawing up needle • 1 x 0.2 micron administration filter
Step 2 Visually inspect the Sotrovimab vial • The solution should be clear, colourless or yellow to brown and free from visible particles Should particulate matter or discoloration be observed, the vial must be discarded and replaced with a new vial.
Step 3 Place to the left side of the preparation area: • 1 x Sotrovimab 500mg vial • 1 x Sodium Chloride 0.9% 50ml Infusion Bag
Step 4 Prepare an infusion additive label with the following details: • Sotrovimab 500mg in Sodium Chloride 0.9% (Total volume = 58mL) • Date and time prepared • [Additional details as required by local label format]

Preparation of Infusion Bag
Step 1 Bring the Sodium Chloride 0.9% 50mL Infusion Bag from the left side of the preparation area into the middle, swab the bung with a sterile 70% alcohol wipe and allow to dry.
Step 2 Bring the Sotrovimab 500mg vial from the left side of the preparation area into the middle, swab the bung with sterile 70% alcohol wipe and allow to dry.
Step 3 Gently swirl the vial several times before use without creating air bubbles. **Do not shake or vigorously agitate the vial.**
Step 4 Attach a drawing up needle to a 10mL luer lock syringe and draw up **1 x 8mL** of Sotrovimab 500mg (62.5mg/mL) from the vial
Step 5 Add **8mL** of Sotrovimab (62.5mg/mL) to the Sodium Chloride 0.9% 50mL Infusion Bag. Discard the syringe and needle into a yellow lidded sharps bin
Step 6 Gently rock the infusion bag back and forth 3 to 5 times. ***NB: Do not invert the infusion bag. Avoid forming air bubbles. Do not shake***
Step 7 Attach the pre-prepared label to the bag
Step 8 Ensure the product is administered using an [Insert local in-line or add-on 0.2µm filter used] as a single IV infusion for 30 minutes
Step 9 Record details of the patient who will receive the bag below, and file the completed *Clinical Area Preparation Record* in accordance with local guidance

Patient Name		Hospital No		Date of Birth	