

Guidelines and Algorithm for the use of Molnupiravir 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:	Medicines Governance Committee
Date issued:	16/12/21
Review date:	17/03/22
Target audience:	Covid19 Medicines Delivery Unit Medical Assessors
Minor update:	28.01.22 (changes to inclusion/exclusion criteria)

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 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).

Exclusion criteria

- Pregnancy or possibility of being pregnant
- The pattern of clinical presentation indicates that there is recovery rather than risk of deterioration from infection
- Swallowing difficulties. Capsules are 22mm x 7mm, cannot be opened and four capsules need to be taken twice a day for five days
- < 18years of age

Cautions

Please refer to the Summary of Product Characteristics (SmPC) for molnupiravir for special warnings and precautions for use at <https://www.medicines.org.uk/emc/product/13044>

Molnupiravir

The most common adverse reactions ($\geq 1\%$ 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).

Pregnancy and women of childbearing potential

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

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 are no drug interaction expected with molnupiravir.

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

Reference

MHRA CAS Alert CEM/CMO/2021/021 on 16th December 2021

<https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103186>

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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> ○ 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	<ul style="list-style-type: none"> • Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who: <ul style="list-style-type: none"> ○ 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	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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)

	<ul style="list-style-type: none"> • Primary immunodeficiency associated with impaired type I interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
HIV/AIDS	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Multiple sclerosis • Motor neurone disease • Myasthenia gravis • Huntington's disease

