NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Molnupiravir for treating COVID-19

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of molnupiravir within its marketing authorisation for treating COVID-19.

Background

COVID-19 is the acute respiratory illness caused by the SARS-CoV-2 virus. It can range from mild or moderate to severe. It begins with infection, or the viral replication phase, with symptoms such as cough, fever and breathlessness. This disease stage is when viral shedding occurs and people are at the peak of infectiousness.[1] Supplemental oxygen and hospitalisation may not be required at the mild or moderate stage. If the disease is not adequately controlled, excessive immune response can lead to more severe complications such as hospitalisation and death.[1] Some people are at a higher risk of severe COVID-19 outcomes because of underlying risk factors. These risk factors have been defined within an independent advisory group report commissioned by the Department of Health and Social Care. Data from the UK also suggest that mortality due to COVID-19 is strongly associated with older age, male gender, deprivation and Black, Asian and minority ethnic family background.[2] Some people may develop post-COVID syndrome, defined by the NICE's rapid guideline on managing the long-term effects of COVID-19 as symptoms continuing for more than 12 weeks after the initial COVID-19 infection.

The COVID-19 pandemic rapidly evolved globally, with countries facing different stages of the spread of disease. In England and Wales between 1 March 2020 and 22 September 2023, 206,804 deaths occurred involving COVID-19.[3] The gradual mutation of SARS-CoV-2 has led to various variants of concern, each with different transmissibility, morbidity, and mortality effects.

NICE recommends the use of nirmatrelvir plus ritonavir and sotrovimab as options for treating COVID 19 for people who do not need supplemental oxygen and have an increased risk for progression to severe COVID 19, as defined in the independent advisory group report (TA878):

- Nirmatrelvir plus ritonavir is recommended in adults
- Sotrovimab is recommended in adults and young people aged 12 years and over and weighing at least 40 kg, only if:
    - nirmatrelvir plus ritonavir is contraindicated or unsuitable.

NICE evaluation of remdesivir and tixagevimab plus cilgavimab for treating COVID-19 is ongoing to address appeal points raised following consideration of these technologies alongside those recommended in the multiple technology appraisal TA878 [ID6261]. NICE has restarted its evaluation of molnupiravir for treating COVID-19 to address appeal points raised in the multiple technology appraisal TA878 [ID6340].

NHS England has an Interim Clinical Commissioning Policy on remdesivir and molnupiravir for people non-hospitalised with COVID-19. The policy recommends the following:

- First-line: nirmatrelvir plus ritonavir (as per the published TA878)
- Second-line: sotrovimab (as per the published TA878)
- Third-line: remdesivir (where supply is available and subject to additional criteria set out in the policy)
- Fourth-line: molnupiravir (subject to meeting additional criteria set out in the policy)

The technology

Molnupiravir (Lagevrio, Merck Sharp & Dohme) is an antiviral medication. It is administered orally. Molnupiravir has a marketing authorisation in the UK for the treatment of mild to moderate COVID-19 in adults with a positive SARS-COV-2 diagnostic test and who have at least one risk factor for developing severe illness.

Intervention(s)	Molnupiravir
Population(s)	Mild to moderate COVID-19 in adults with a positive SARS-COV-2 diagnostic test and who have at least one risk factor for developing severe illness
Subgroups	If evidence allows the following subgroups will be considered: ○ People with risk factors for severe COVID-19 as described in TA878 ○ People with broader risk factors for severe COVID-19 than those described in TA878 which may include: ○ Age as a risk factor (for example age over 50 years with one risk factor for severe illness or age over 70 years) ○ Specific risk factors (for example a body mass index (BMI) of 35 kg/m2 or more, diabetes, or heart failure)
Comparators	Established clinical management without molnupiravir including: • Nirmatrelvir plus ritonavir • Sotrovimab for people for whom nirmatrelvir plus ritonavir is contraindicated or unsuitable • Remdesivir (subject to NICE evaluation)

Outcomes	The outcome measures to be considered include: • mortality • requirement for respiratory support • time to recovery • hospitalisation (requirement and duration) • time to return to normal activities • virological outcomes (viral shedding and viral load) • symptoms of post-COVID-19 syndrome • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The use of molnupiravir is conditional on the presence of a positive SARS-COV-2 diagnostic test. The economic modelling should include the costs associated with diagnostic testing for positive SARS-COV-2 in people with COVID-19 who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. The impact of vaccination status or SARS-CoV-2 seropositivity on the clinical evidence base of the intervention, generalisability to clinical practice and interaction with other risk factors will be considered in the context of the appraisal. The impact of different variants of concern of COVID-19 on the clinical evidence base of the intervention will be considered in the context of the appraisal.
Related NICE recommendations	**Related technology appraisals:**

	Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 (2023) NICE technology appraisal guidance 878. **Related technology appraisals in development:** Nirmatrelvir plus ritonavir for treating COVID-19 (partial rapid review of TA878). NICE technology appraisal guidance [ID6262] Expected publication date: 13 September 2023 Molnupiravir, remdesivir and tixagevimab plus cilgavimab for treating COVID-19. NICE technology appraisal guidance [ID6261] Publication date to be confirmed **Related NICE guidelines:** COVID-19 rapid guideline: managing COVID-19 (2021, updated 2023) NICE guideline NG191. **Related interventional procedures:** Exploratory economic modelling of SARS-CoV-2 viral detection point of care tests and serology tests. NICE diagnostics guidance. Publication date to be confirmed
Related National Policy	Department of Health and Social Care (September 2023) Independent report - Defining the highest risk clinical subgroups upon community infection with SARS-CoV-2 when considering the use of neutralising monoclonal antibodies (nMABs) and antiviral drugs Department of Health and Social Care (May 2023) Interim Clinical Commissioning Policy: remdesivir and molnupiravir for non-hospitalised patients with COVID-19 Department of Health and Social Care (Dec 2022, updated March 2023) Commissioning Framework: COVID-19 Therapeutics for Non-Hospitalised Patients Department of Health and Social Care (Nov 2022) Interim Clinical Commissioning Policy: Treatments for hospital-onset COVID-19 The NHS Long Term Plan (2019) NHS Long Term Plan

Questions for consultation

Where do you consider molnupiravir will fit into the existing care pathway for COVID-19?

- What subgroups (if any) need to be considered?

What technologies are established clinical management?

Have all the comparators been considered?

Have all relevant outcomes been considered?

Would molnupiravir be a candidate for managed access?

Do you consider that the use of molnupiravir can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

What additional COVID-19 NHS testing costs (if any) need to be considered for people who might be eligible for treatment with molnupiravir?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which molnupiravir is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Cevik M, Kuppalli K, Kindrachuk J et al. (2020) Virology, transmission, and pathogenesis of SARS-CoV-2. The BMJ.
2. The King's Fund (2021) Deaths from Covid-19 (coronavirus). Accessed October 2023.
3. The UK Health Security Agency COVID-19 dashboard, Deaths in United Kingdom. Accessed October 2023.