

Molnupiravir for treating COVID-19

Technology appraisal guidance

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Your responsibility

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Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

Contents

1 Recommendation.....	4
Why the committee made this recommendation.....	4
2 Information about molnupiravir.....	5
Marketing authorisation indication.....	5
Dosage in the marketing authorisation.....	5
Price.....	5
3 Committee discussion.....	6
The condition.....	6
Clinical management of COVID-19.....	8
Clinical effectiveness.....	11
Economic model.....	17
Utility values.....	21
Administration costs.....	22
Severity.....	23
Cost-effectiveness estimates.....	23
Other factors.....	25
Conclusion.....	26
4 Implementation.....	27
5 Evaluation committee members and NICE project team.....	28
Evaluation committee members.....	28
Chair.....	28
NICE project team.....	28
6 Update information.....	30

1 Recommendation

- 1.1 Molnupiravir is recommended as an option for treating mild to moderate COVID-19 in adults who have a positive SARS-CoV-2 test, only if:
- they have 1 or more risk factors for progression to severe COVID-19 (as defined in [section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir and tocilizumab for treating COVID-19](#)) and
 - nirmatrelvir plus ritonavir is contraindicated or unsuitable.

Why the committee made this recommendation

Usual treatment for mild to moderate COVID-19 in people at risk of developing severe COVID-19 includes nirmatrelvir plus ritonavir. There are no other treatment options when this medicine cannot be used.

The company asked for molnupiravir to be considered only in the community setting for people with mild to moderate COVID-19 who are at risk of developing severe COVID-19 and cannot have nirmatrelvir plus ritonavir. This does not include everyone it is licensed for.

Some results from clinical trials and real-world evidence for the people molnupiravir is licensed for suggest that it reduces the likelihood of hospitalisation or death compared with no treatment.

Molnupiravir is cost effective for people who are immunocompromised. There is a substantial overlap between these people and those with risk factors defined in [section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir and tocilizumab for treating COVID-19](#). So, molnupiravir is recommended for people with these risk factors.

2 Information about molnupiravir

Marketing authorisation indication

- 2.1 Molnupiravir (Lagevrio, Merck Sharp & Dohme) is indicated 'for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults with a positive SARS-CoV-2 diagnostic test and who have at least one risk factor for developing severe illness'.

Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for molnupiravir](#).

Price

- 2.3 The list price for molnupiravir is £590 per pack containing 40 capsules (excluding VAT; company submission).

3 Committee discussion

The [evaluation committee](#) considered evidence submitted by Merck Sharp & Dohme, a review of this submission by the external assessment group (EAG) and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

The condition

Impact of COVID-19 and access to treatment

3.1 COVID-19 is an acute respiratory illness caused by the SARS-CoV-2 virus. It can range from mild to severe. In severe COVID-19, excessive immune response to the virus may cause severe complications that are associated with hospitalisation and death. The need for organ system support, particularly respiratory support, is also a key feature of severe COVID-19 and can be associated with substantial longer-term morbidity. COVID-19 may also cause long-term symptoms that continue or develop after acute infection. This is called 'long COVID' and causes health problems that fluctuate and can last several months or years. A patient expert explained how long COVID affects all aspects of their life. It means that they have constant fatigue, pain and often became breathless after only moderate activity. They explained that, even if they have good days when they can be more active, this then results in them being particularly exhausted the day after. Many people are at increased risk of hospitalisation or death from COVID-19, including people:

- who are immunocompromised, for example, people with primary immunodeficiency
- having chemotherapy
- who have had a transplant and may have medication to prevent organ rejection
- with comorbidities such as heart disease, respiratory disease, diabetes or neurological conditions.

Some people who are immunocompromised are at risk of persistent viral infection if their immune system cannot control the virus. A second patient expert explained that people at higher risk of severe COVID-19 use a range of behaviours to try and avoid infection. For most people, this includes using face masks and avoiding crowds. But, for people at the highest risk (such as people who have had a lung transplant), this might involve almost complete self-isolation. Patient-expert submissions highlighted the need for treatment options for COVID-19, particularly in people at high risk. They explained that there are very few treatment options available, some of which are difficult to access. A clinical expert also highlighted variation in clinical management depending on severity. They thought that molnupiravir might address an unmet need for an alternative oral treatment option for COVID-19. The committee noted that the risk of COVID-19 infection is significantly lower than during the pandemic phase. It understood that the risk of hospitalisation and death, and other longer-term impacts of COVID-19, result in severe mental burden, and infection can still have serious physical effects. It concluded that people at high risk of severe COVID-19 would welcome new and effective treatment options.

The rapidly evolving SARS-CoV-2 virus

3.2 The global COVID-19 pandemic caused unprecedented challenges to the healthcare system. This is reflected in the evidence collected on COVID-19 and the treatments for it. The SARS-CoV-2 virus evolved during the pandemic, as did the healthcare system's ability to respond to the virus. New variants and subvariants (variants of concern) emerged, the properties of which differed, such as levels of transmissibility and disease severity. The clinical experts explained that the situation around COVID-19 changed during the pandemic, with:

- increasingly effective supportive care
- growing numbers of people having vaccination
- rising natural immunity.

The committee understood that, since the beginning of the pandemic, overall hospitalisation and mortality rates from COVID-19 have fallen because of

improved clinical management. It also noted the changing nature of SARS-CoV-2 and the context of the pandemic. It thought that the shift to an endemic situation might affect the generalisability of the evidence for this evaluation (see [section 3.6](#)).

Clinical management of COVID-19

Defining high-risk populations

3.3 The risk of developing severe COVID-19 is associated with age, sex, and various other factors and comorbidities. In the UK, factors for defining high risk of progression to severe COVID-19 are listed in:

- the [independent advisory group report commissioned by the Department of Health and Social care](#) definition (from here, the McInnes definition)
- the [Therapeutics Clinical Review Panel risk of severe COVID-19 outcomes report](#) definition (from here, the Edmunds definition) list.

Both of these definitions have been used to inform recent clinical decision making. The McInnes report definition covers adults with a range of health conditions (see [section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir and tocilizumab for treating COVID-19 \[from here, TA878\]](#)). The Edmunds definition covers the same factors as the McInnes definition and also age over 70 years, diabetes, having a body mass index of over 35 and heart failure. The committee noted that the marketing authorisation for molnupiravir is for people with at least 1 risk factor for developing severe illness. It thought that, in practice, the marketing authorisation population would include anyone covered by the Edmunds or McInnes definitions.

Treatments for mild to moderate COVID-19

3.4 Current clinical management for COVID-19 in adults includes nirmatrelvir plus

ritonavir (see [TA878](#)) and remdesivir (see [NICE's technology appraisal guidance on remdesivir and tixagevimab plus cilgavimab for treating COVID-19 \[from here TA971\]](#)). They are options for treating COVID-19 for people who do not need supplemental oxygen and have an increased risk for progression to severe COVID-19 (risk factors as defined in [section 5 of TA878](#)). Remdesivir is recommended as an option for treating COVID-19 in hospitals only. Molnupiravir is, at the time of this evaluation, available through an NHS Interim Clinical Commissioning Policy for COVID-19 in people at high risk according to the McInnes definition, if nirmatrelvir plus ritonavir and sotrovimab are contraindicated or unavailable. People who have symptoms and are not showing signs of a clinical recovery should start treatment as soon as possible after testing positive for COVID-19. But the clinical and patient experts at the committee meeting highlighted the variability in access to the treatment options for COVID-19. The clinical experts explained that this variability in access to treatment was because of several factors including:

- geographical location
- different clinical approaches
- differences between clinical specialties in managing COVID-19 in people at risk
- variability in self-tested and healthcare-professional-tested lateral flow tests.

A patient expert explained that, among people at high risk, there was variation in access to treatment. They added that people who are more knowledgeable about the healthcare system may be more likely to access antiviral treatments. The committee considered the treatment options available and acknowledged that there is variability in the access to them.

Proposed positioning of molnupiravir

3.5 At the first committee meeting, the company's positioning was for people covered by the Edmunds or McInnes criteria for whom nirmatrelvir plus ritonavir is contraindicated, or sotrovimab is contraindicated, unfeasible or undesirable. So, this is when the only alternative would be no treatment. The company thought

that this positioning would be in line with the NHS Interim Clinical Commissioning Policy for COVID-19 (see [section 3.4](#)). The company considered that the strongest clinical evidence was for molnupiravir compared with no treatment. A clinical expert said that the population at highest risk of severe COVID-19 (defined by the McInnes criteria), who could not have either nirmatrelvir plus ritonavir or sotrovimab, was likely small. They said that contraindication would be the most common reason for not having nirmatrelvir plus ritonavir because of the risk of drug-to-drug interactions with chemotherapy for cancer or medication to prevent organ transplant rejection. They thought that not being able to have sotrovimab would likely be because of people not being able to travel to hospitals or clinics for an infusion. The patient expert said that people should be able to have sotrovimab in their own homes. But both they and the clinical expert acknowledged that access to this type of administration was very variable. The patient expert was also concerned that a positive recommendation for molnupiravir (administered orally) in the population for whom sotrovimab was unfeasible might mean that the NHS would be even less likely to provide home administration of sotrovimab. They thought that, if molnupiravir was inferior to sotrovimab, this could disadvantage some people.

The committee noted that the proposed positioning was not in line with the NHS interim commissioning policy (see [section 3.4](#)). This policy states that molnupiravir should only be used when nirmatrelvir plus ritonavir and sotrovimab are contraindicated or clinically unsuitable in the group at highest risk for severe COVID-19, as defined by the McInnes criteria. The committee noted that nirmatrelvir plus ritonavir is recommended by NICE for people covered by the Edmunds criteria. But, in practice, few people have access to it because of the funding variation that is in place. The committee thought that people covered by the McInnes criteria who cannot have either of the available treatments remain at increased risk of poor outcomes and have the greatest unmet need. It concluded that this population (from now, the 'highest unmet need' population) was the most appropriate for decision making. But it thought that there was uncertainty around exactly how the subpopulation who could not have nirmatrelvir plus ritonavir or sotrovimab was defined. It concluded that it would need to see additional evidence that better defined the highest unmet need population, including why these treatments would be contraindicated and why sotrovimab might not be feasible or desired. It also concluded that it needed to see updated evidence on the clinical effectiveness of molnupiravir in this highest unmet need

population (see [sections 3.7 to 3.9](#)).

At the second committee meeting, the company maintained its positioning. That is, for people covered by the Edmunds or McInnes criteria for whom nirmatrelvir plus ritonavir is contraindicated, or for whom sotrovimab is contraindicated, unfeasible or undesirable. It explained that sotrovimab would be contraindicated, unfeasible or undesirable in cases of complex comorbidities, haematological disease, severe kidney or liver disease, or when people have difficulties accessing sotrovimab because of geographical location. The company also explained that it had presented analyses for 4 subpopulations. These subpopulations were people:

- aged over 70
- for whom nirmatrelvir plus ritonavir is contraindicated
- who are immunocompromised, and
- who have severe chronic kidney disease (CKD).

The committee reiterated its conclusion from the first meeting. This is that the company's positioning is broader than the population the committee considers to have the highest unmet need, because the company's positioning includes the Edmunds criteria.

As of May 2025, the recommendation for nirmatrelvir plus ritonavir was updated because it was no longer cost effective for the Edmunds population. As of February 2026, sotrovimab was no longer available to the NHS because it was discontinued by the company.

Clinical effectiveness

Generalisability of the clinical-effectiveness evidence

3.6 The committee recalled the:

- evolving nature of the SARS-CoV-2 virus

- move from a pandemic to an endemic setting with improved clinical management for COVID-19
- reduced hospitalisation and death rates (see [section 3.2](#)).

It questioned whether there could be issues of generalisability with evidence that was generated at different points in time. The clinical experts thought that a key period in time was late 2021 to early 2022. Around this time, the Omicron variant became dominant in the UK and most people started to have the third dose of a COVID-19 vaccine. In early 2022, there was also wider rollout of antiviral treatments. The clinical experts thought that the situation in late 2021 to early 2022 and beyond was broadly similar to the situation today. They added that they would expect similar results if studies from early 2022 were done again now. They acknowledged that there are different variants of Omicron, which might behave differently, but are all broadly similar. The clinical experts thought that studies done from late 2021 onwards would likely be generalisable to the endemic situation at the time of this evaluation. The committee noted this. It thought that it was likely that studies done from 2022 onwards would be generalisable to the current clinical setting. But it thought that it was plausible that there would be some uncertainty when using these studies to reflect clinical practice. The committee thought that there could also be generalisability issues based on geographical location and the risk level used for study recruitment. It noted that the network meta-analyses (NMAs) of real-world evidence (RWE; see [section 3.9](#)) only included 1 UK study ([Zheng et al. 2023](#)). The committee concluded that it would take generalisability into account in its decision making.

Randomised clinical trial evidence

- 3.7 In the company submission, evidence from 2 randomised controlled trials (RCTs), MOVE-OUT and PANORAMIC, was used to inform some model parameters in the company's economic model (see [section 3.11](#)). Move-OUT (n=1,433) was a company-sponsored, phase 2 and 3, multicentre (including 6 UK centres), double-blind RCT comparing molnupiravir with placebo. It included adults who:

- were not in hospital
- tested positive for SARS-CoV-2
- presented with mild to moderate symptomatic COVID-19
- had at least 1 risk factor for progression to severe COVID-19.

The trial reported a 6.8% (95% confidence interval [CI] -11.3 to -2.4) reduction in all-cause hospitalisation or death for molnupiravir compared with placebo in the interim analysis and 3% (95% CI -5.9 to -0.1) reduction in the final analysis. PANORAMIC (n=26,411) was a large, UK-only, primary care, open-label, multigroup, prospective, platform-adaptive trial comparing molnupiravir with usual care. It included people with COVID-19 symptoms and a positive SARS-CoV-2 test who were not in hospital and were 50 years or over, or 18 years or over and had comorbidities. The primary outcome was all-cause hospitalisation or death at day 29 (odds ratio 1.06, 95% CI 0.81 to 1.41). The committee noted that MOVE-OUT was done from May to October 2021. It recalled the clinical expert testimony about generalisability (see [section 3.6](#)). The committee thought that MOVE-OUT was not generalisable to current clinical practice, so was not appropriate to inform the model (see [section 3.13](#)). A clinical expert said that PANORAMIC was done in a population that had high levels of vaccination at a time when Omicron was becoming the dominant variant. The committee thought that PANORAMIC, being a large UK-based study done between December 2021 and April 2022 was likely to be generalisable to clinical practice (see [section 3.6](#)). It noted that it was a very large trial with the potential to provide reliable subgroup analyses. A clinical expert, an investigator on PANORAMIC, confirmed that inclusion criteria in PANORAMIC were broad. But, because the trial was so large, various subgroup analyses were still possible, including in people with diabetes, people with lung disease and people who were immunocompromised. The committee concluded that the overall population of PANORAMIC was not likely to reflect the highest unmet need population for molnupiravir (see [section 3.5](#)). But it would like to see PANORAMIC subgroups explored to inform the clinical effectiveness of molnupiravir compared with no treatment in the highest unmet need population.

NMAs of RCT evidence

3.8 The company did NMAs of RCTs to enable molnupiravir to be compared indirectly with nirmatrelvir plus ritonavir, sotrovimab, remdesivir and no treatment. A total of 11 RCTs were included in the NMAs. The results of NMAs of RCTs for hospitalisation or death showed that molnupiravir was not statistically significantly superior to any comparator other than no treatment. The company did not use the NMAs of RCTs to inform the economic model because the trials were largely done before Omicron was the dominant variant (see [section 3.7](#)). The EAG agreed that the NMAs of RCTs had significant limitations including the:

- likely lack of generalisability
- fact that the company had not adequately assessed the sensitivity of the NMAs of RCTs to risk of bias
- fact that only fixed-effects models had been submitted, which meant that the uncertainty in the NMAs was possibly underestimated.

The committee considered the various limitations of the NMAs of RCTs and concluded that they were of limited use for decision making.

RWE and NMAs

3.9 The company also did pairwise NMAs of RWE studies comparing molnupiravir with nirmatrelvir plus ritonavir, sotrovimab, remdesivir or no treatment when sufficient RWE studies were available for each of these comparisons. The company identified 30 RWE studies, 17 of which were thought to be appropriate for inclusion in the NMA. The studies were of varying design, risk profile for severe COVID-19, geographical location, sample size, recruitment time period and outcomes. The results of these NMAs did not provide evidence that molnupiravir was significantly superior to any active comparator for any hospitalisation and death outcomes. But it showed statistically significant superiority for all-cause hospitalisation or all-cause death when compared with no treatment. But there was no evidence that molnupiravir was clinically superior to no treatment for COVID-19-related hospitalisation or death. The EAG highlighted several uncertainties associated with the NMAs of RWE. These were:

- uncertainty around the appropriate time cut-off to ensure relevance of studies to clinical practice, and generalisability of the NMA results
- a lack of UK studies included in the NMAs
- limitations of the clinical-effectiveness results of the NMAs because of a lack of results for outcomes for COVID-19 symptom progression or resolution, virological outcomes or the need for respiratory support
- uncertainty in the clinical significance of statistically significant reductions in hospitalisation rate.

The EAG also identified a UK study ([Tazare et al. 2023](#)) that was not identified by the company's literature review. This was a study using the OpenSAFELY database. It noted that this study reported no statistically significant difference between molnupiravir and no treatment for the outcome of COVID-19-related hospitalisation or death. The committee noted the uncertainties highlighted by the EAG and the additional study identified. It thought that the best available RWE evidence it had seen so far was likely to be Tazare et al. It also thought that, because of the updated positioning (see [section 3.5](#)):

- the only relevant comparison was with no treatment
- there was substantial uncertainty around whether the NMAs of RWE showed any significant benefit for hospitalisation or death outcomes for this comparison.

At the first committee meeting, the committee noted that the NMAs of RWE might not appropriately reflect the highest unmet need population. This was because the studies included people with a range of different risks for severe COVID-19 and the highest unmet need population was specific to people with the highest risk (see [section 3.5](#)). So, it concluded that it would need to see either evidence that showed the NMAs of RWE reflected the highest unmet need population, or an updated NMA of RWE or new RWE evidence to inform the modelling of the highest unmet need population.

In response to consultation, the company did not update the NMA of RWE. Instead, it argued that current real-world use of molnupiravir is in people with

the highest unmet need. So, it considered the RWE NMA appropriate. It highlighted 2 studies, Xie et al. (2023) and Ahmad et al. (2024), that it thought were particularly important for the committee to consider. But the EAG noted that the relevance of these studies to the NHS was uncertain. The clinical experts agreed, highlighting differences in healthcare systems and potential confounding factors associated with retrospective analysis. The EAG's overall conclusion was that the company's response broadly reiterated the existing clinical-effectiveness evidence provided in its submission. This did not specifically resolve the uncertainties relating to the RWE studies raised by the committee. The committee agreed with this assessment.

Risk of novel mutations and risk of resistance with molnupiravir

3.10 The committee was aware that molnupiravir has a mechanism of action that alters the RNA of the virus. This causes novel mutations of SARS-CoV-2 that may potentially be transmitted if the virus is not fully cleared. The clinical experts explained that viral clearance is necessary to avoid transmitting the virus and any viral mutations generated by the mechanism of action of molnupiravir. This could increase the risk of new SARS-CoV-2 variants developing and potentially reduce the efficacy of molnupiravir. The EAG noted that limited results for the virological outcomes from MOVE-OUT were reported by the company in its clarification response compared with the expected virological endpoints of the trial. The EAG highlighted that virological outcomes were only analysed in the NMAs of RCTs. These showed improved clearance compared with no treatment, although the results were subject to limitations (see [section 3.7](#)). A clinical expert said that molnupiravir has been shown to drive a pattern of mutagenesis that is identifiable in global circulating virus, particularly in areas where molnupiravir has been used. They noted that, in PANORAMIC, viral load was higher in the molnupiravir arm than the usual-care arm on day 14. The clinical expert said that there is an increased risk of immune-escape variants arising and persisting in people who are immunocompromised. This is because their immune systems are less likely to clear the virus fully. The committee noted that, with the new positioning of molnupiravir (see [section 3.5](#)), the highest unmet need population is likely to have a larger proportion of people who are immunocompromised. It thought that there is a theoretical risk that molnupiravir use might increase the risk of new variants emerging and drug resistance. The committee thought that this was not

something that could not be captured in the modelling, but that it could consider this in its decision making as a non-health factor.

Economic model

Company's modelling approach

3.11 The company developed a hybrid economic model comprising:

- a decision tree for the acute phase of COVID-19 (30 days), and
- a Markov model to follow people who survive the acute phase through their lifetime.

In the acute phase of the model, people in the outpatient setting started treatment with molnupiravir or had no treatment. They then stayed in the outpatient setting, or were admitted to hospital because of severe COVID-19. In hospital, they could be in a general ward, a high dependency unit or an intensive care unit with mechanical ventilation (the highest level of care). The treatment effects of molnupiravir included preventing progression to hospitalisation and reducing symptom duration. In hospital, the treatment effect of inpatient drugs (remdesivir and tocilizumab) was applied. People surviving the acute phase of COVID-19 and being discharged from hospital entered the Markov model. They could then either recover or experience long-term sequelae.

There was one key difference between the company and EAG base-case modelling. The company assumed an acute mortality rate of 24.98% for the subgroup of people who are immunocompromised, based on INFORM. The EAG highlighted that the mortality rate for people who are immunocompromised was likely a key model driver, particularly in a subgroup with a higher proportion of such people. Instead, it preferred a 10.39% acute mortality rate for this subgroup based on [TA971](#).

The EAG highlighted that it was unclear how appropriate it was to assume that remdesivir is used to treat COVID-19 in people admitted to hospital

because of the condition. Clinical advice to the EAG noted that [NICE's COVID-19 rapid guideline on managing COVID-19](#) and TA971 lack detail on where in the treatment pathway remdesivir should be used or whether it is indicated for mild or severe symptoms. It also noted that they rarely use remdesivir in their clinical practice. The EAG also highlighted that the economic model did not capture the pathway of people with incidental COVID-19 (see [section 3.5](#)). This was because of a lack of specific data for this group, which was likely to be significant in size. But, overall, the EAG thought that the company's model structure was appropriate for decision making, and in line with previous cost-effectiveness studies for molnupiravir and other outpatient COVID-19 treatments. The committee concluded that the company's economic model structure was appropriate for decision making.

Hospitalisation rates

3.12 The baseline hospitalisation rate is a key driver of cost effectiveness in the economic model. It leads to different estimates of cost effectiveness in the 4 subgroups presented by the company:

- In the aged over 70 subgroup, the company used a hospitalisation rate of 12.84% from Kabore et al. (2023), a Canadian retrospective cohort analysis of people with at least 1 risk factor for progression to severe disease.
- In the group for whom nirmatrelvir plus ritonavir is contraindicated, the company used a rate of 4%. This was based on the committee's preferred assumption in TA878 of the hospitalisation rate for people with advanced renal disease. Nirmatrelvir plus ritonavir would be contraindicated for most of these people.
- In the immunocompromised group, the company used a rate of 22.47%, from a subgroup of severely immunocompromised people from the Kabore et al. (2023) study.
- In the severe CKD group, the company used a rate of 4.4% from the DISCOVER-NOW database, a UK observational study of people covered by the McInnes report.

One of the clinical experts explained that hospitalisation rates for COVID-19 were much lower in the last year than in previous years. They added that while it was hard to know what would happen next year, they considered that with repeated vaccination and better understanding of treatment in primary care, hospitalisation rates would continue to be low. The other clinical expert noted that the hospitalisation rate in the PANORAMIC study of molnupiravir was 0.77%, and people had to be over 50 and have 1 comorbidity. The clinical expert added that the more recent nirmatrelvir plus ritonavir arm is not published yet, but it is expected that the baseline hospitalisation rate will be substantially lower than 0.77%. But people eligible for nirmatrelvir plus ritonavir are likely to be younger and fitter than people eligible for molnupiravir because nirmatrelvir plus ritonavir is contraindicated in more groups. It was later clarified that a more recent (unpublished) analysis of the nirmatrelvir plus ritonavir data from PANORAMIC suggested the baseline hospitalisation rate was likely to be similar to that seen in the molnupiravir arm. Both clinical experts considered that the appropriate hospitalisation rates would be closer to those used in TA878, which were 2.41% to 2.82% for the McInnes high-risk group and 4% for people for whom nirmatrelvir plus ritonavir is contraindicated. One of the patient experts noted that their organisation had some data on hospitalisation rates since the availability of treatments for COVID-19. The relevant rates were 24% for people who had a lung transplant and 13.4% for people who had a heart transplant. They noted that people who had a lung transplant are likely to have among the highest risks of hospitalisation for COVID-19 of any group of people. The EAG considered that the hospitalisation rates for the aged over 70 and immunocompromised groups may be overestimates. It noted that the estimates are similar or higher than the hospitalisation rates reported in the MOVE-OUT trial, which was done during the pandemic. The EAG tested using lower hospitalisation rates of 8% for people aged over 70 and 15.9% for people who are immunocompromised, as reported by Shields et al. (2022). It agreed with the company's base-case inputs for the other subgroups of around 4%. It also provided scenario analysis using a hospitalisation rate of 4% for the immunocompromised group and 0.77% for people aged over 70, based on PANORAMIC. The committee recognised that it was considering a population for whom available treatments were contraindicated. Based on the expert input, it considered that the maximum hospitalisation rate for people

for whom nirmatrelvir plus ritonavir is contraindicated, who are immunocompromised or have severe CKD was likely to be 4%, in line with its considerations in TA878. But because time had passed since then, it could be lower. In TA878 and TA971 the committee had seen rates from OpenSAFELY of 2.41% (untreated but eligible using the McInnes definition) and 1.37% (untreated but eligible without nirmatrelvir plus ritonavir being contraindicated). For people aged over 70, TA878 used the hospitalisation rate for people aged over 70 from PANORAMIC, which was slightly higher than 0.77% for the overall population in PANORAMIC. So, the committee considered it appropriate to consider analyses based on a 0.77% hospitalisation rate for this subgroup.

Treatment effect on hospitalisation

3.13 In its base-case economic model, the company modelled a treatment effect on hospitalisation. It did this using the relative risk of all-cause hospitalisation for molnupiravir compared with no treatment. It used the same value for all 4 subgroups, 0.71, from the NMAs of RWE (see [section 3.9](#)). The EAG highlighted that there were no UK studies included in these NMAs for all-cause hospitalisation. It also explained that the relative risk of COVID-19-related hospitalisation was based on a fixed-effect analysis because of the sparsity of the evidence network. So, the confidence intervals for the relative risks of COVID-19-related hospitalisation did not capture between-study heterogeneity. The EAG thought that it was unclear from a clinical point of view whether the treatment effect for all-cause hospitalisation or COVID-19-related hospitalisation should have been used in the economic model. The EAG also noted that the UK real-world studies, [Zheng et al. \(2023; see section 3.6\)](#) and [Tazare et al. \(2023; see section 3.9\)](#) did not report either of these outcomes. Instead, they reported a composite hospitalisation and death outcome that did not match the parameters in the company's economic model. The EAG thought that it was unclear whether outpatient treatments have any effect on mortality, noting that no such effect was modelled. It thought that, if there was no effect, it would be appropriate to use the composite outcomes from Tazare et al. to inform hospitalisation rates in the model. The EAG used the same approach as the company in its base case.

The committee thought that the treatment effect on hospitalisation for

molnupiravir for all comparisons was very uncertain. It thought that because of the highest unmet need population (see [section 3.5](#)) the only relevant comparison was with no treatment. With current evidence (for the wider population), it was unclear whether molnupiravir reduced hospitalisation compared with no treatment. At the first meeting, the committee concluded that it would like to see various sources of clinical evidence explored, including the RWE NMAs (see [section 3.9](#)), PANORAMIC (see [section 3.7](#)) and single studies including Tazare et al. and the OpenSAFELY database (see [section 3.9](#)). But the company did not provide this in response to consultation on the draft guidance.

Utility values

Source of utility values

3.14 In the company's base case, health-state utility values were informed by a vignette study done by the company. This involved members of the UK public completing EQ-5D-5L questionnaires for each of the model health states. The EAG thought that the utility values derived from the company's vignette study lacked face validity. This was because they were much lower than other sources and included negative values for people in hospital. The EAG also highlighted that the vignette study did not meet NICE's reference case. This was because it used members of the public rather than people with COVID-19 and carers to answer the questionnaire. Instead, the EAG used utilities from [Soare et al. \(2024\)](#) in its base case. This study reported EQ-5D-5L values for people with mild to moderate COVID-19 in the UK, including for pre-COVID, acute COVID, post-COVID and long COVID. The EAG also assumed that:

- a utility of 0.28 applied for people hospitalised with acute COVID-19, reflecting that for people on a general hospital ward ([TA878](#) and [TA971](#))
- a utility of 0 applied for people in an intensive care unit having mechanical ventilation ([TA878](#) and [TA971](#)).

In response to consultation, the company accepted the EAG's utility values for people hospitalised with acute COVID-19 and for people having mechanical ventilation. But it used a value of 0.57 for people with symptoms

having outpatient treatment, based on a UKHSA study (Sandmann et al. 2021) reporting health-related quality of life for "the worst day of COVID". This value was very similar to the EAG's value of 0.59 from Soare et al.

The committee noted that, in Soare et al., there was minimal difference in people's utility values before and after an episode of long COVID. It thought that this was implausible in light of the patient-expert testimony (see [section 3.1](#)). It also noted that this was an opt-in internet study that may have been associated with negative bias and could have underestimated disutility. In response to consultation, the company provided evidence from the OpenPROMPT study, which used the OpenSAFELY database. This reported a utility value for long COVID of 0.49. The EAG acknowledged that applying the utility for long COVID from Soare et al. might be an underestimate, particularly for people with the highest unmet need. So, it accepted the company's revised estimate of 0.49 for this health state. The committee thought that there was broad agreement between the company and EAG on the utility values used in the model and concluded that these were appropriate.

Administration costs

3.15 The company used an administration cost of £31.85, based on a study estimating the costs of oral antiviral delivery in UK clinical practice. The company subtracted the cost of assessing drug–drug interactions from the estimated cost, arguing that this would not need to be done for molnupiravir. In response to consultation on the draft guidance, NHS England commented that in TA878, the committee had considered a range of administration costs from £117 to £410 for nirmatrelvir plus ritonavir and that the same range should be considered in this evaluation. The EAG provided scenario analyses using both of these estimates. As in TA878, the committee was concerned that an administration cost of £410 may be too high for delivering oral antivirals. It recognised that some of the cost of delivering nirmatrelvir plus ritonavir comes from assessing potential drug–drug interactions. It considered that because molnupiravir is being positioned for people for whom nirmatrelvir plus ritonavir is contraindicated, this process would need to be worked through to assess eligibility for molnupiravir. It concluded that an

administration cost of £117 was appropriate.

Severity

3.16 The committee considered the severity of the condition (that is, the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a greater weight to quality-adjusted life years (QALYs; that is, a severity modifier) if technologies are indicated for conditions with a high degree of severity. Both the company and EAG thought that a severity weighting was not appropriate for the COVID-19 disease area. Even for the most vulnerable subgroups of people (immunocompromised or with CKD), in line with the approach taken in [TA971](#), a severity modifier was not applied. So, the committee concluded that NICE's methods on conditions with a high degree of severity did not apply.

Cost-effectiveness estimates

Acceptable ICER

3.17 [NICE's manual on health technology evaluations](#) notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will consider the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also consider other aspects including uncaptured health benefits. The committee noted the high level of uncertainty, which arose from the:

- clinical effectiveness of molnupiravir compared with no treatment in the highest unmet need population (see [sections 3.7 to 3.9](#) and [section 3.13](#))
- hospitalisation rates for people who have not had treatment in the highest unmet need population (see [section 3.12](#))
- risk of virus mutations associated with the mechanism of action and viral

clearance profile of molnupiravir (see [section 3.10](#)).

The committee concluded that given these considerable uncertainties, an acceptable cost-effectiveness estimate would be below £20,000 per QALY gained.

Cost-effectiveness estimates

3.18 Because of confidential discounts for subsequent treatments, the exact cost-effectiveness estimates cannot be reported here. The company and EAG base-case analysis both estimated:

- an ICER less than £20,000 per QALY gained for the aged over 70 subgroup
- an ICER between £20,000 and £30,000 per QALY gained for the subgroup for whom nirmatrelvir plus ritonavir is contraindicated
- that molnupiravir is more effective and less expensive in the immunocompromised subgroup
- an ICER between £20,000 and £30,000 per QALY gained for the severe CKD subgroup.

The committee preferred to use an administration cost of £117 for molnupiravir (see [section 3.15](#)), which increased the cost-effectiveness estimates in all subgroups. For the aged over 70 subgroup, the committee considered the scenario analysis using the hospitalisation rate of 0.77% from PANORAMIC. Combined with the higher administration cost, the ICER was more than £100,000 per QALY gained. The committee considered that the hospitalisation rate in this subgroup could be slightly higher than 0.77%, but even so molnupiravir was unlikely to be cost effective. For the subgroups for whom nirmatrelvir plus ritonavir is contraindicated and who have severe CKD, the ICERs were greater than £20,000 per QALY gained. The committee recalled that these estimates were based on hospitalisation rates of 4.0% and 4.4%, which it considered to be the maximum likely hospitalisation rates. With lower hospitalisation rates, the ICERs would increase further so the committee concluded that molnupiravir was unlikely to be cost effective for

these subgroups. For the immunocompromised subgroup, with a hospitalisation rate of 4% and the higher administration cost, the ICER was less than £20,000 per QALY gained. The committee considered that this estimate was uncertain because of uncertainties around molnupiravir's effect on hospitalisation and the appropriate hospitalisation rate. But it considered that because the estimate was sufficiently below £20,000 per QALY gained, molnupiravir was likely to be cost effective for this subgroup.

Other factors

Equality

3.19 The company submission highlighted that molnupiravir supports the need for an easy-to-administer oral treatment for mild to moderate COVID-19. The aim is to provide options for people, particularly people with protected characteristics and to eliminate any residual and unobserved aspects of access inequality. The patient carer organisation said that most people eligible for molnupiravir are disabled in some way by their pre-existing condition. The clinical expert submission noted that molnupiravir is contraindicated during pregnancy, so a pregnancy test should be done before it is used. The committee thought that its recommendations do not have a different impact on people protected by the equality legislation than on the wider population. The committee concluded that there were no equalities issues that could be addressed by its recommendations.

Uncaptured benefits

3.20 The committee considered whether there were any uncaptured benefits of molnupiravir. It did not identify additional benefits not captured in the economic modelling. So, the committee concluded that all additional benefits of molnupiravir had already been considered.

Conclusion

Recommendation

3.21 The committee considered that molnupiravir had only shown cost effectiveness in the immunocompromised subgroup. The committee considered that this subgroup would overlap to a substantial extent with the McInnes criteria, recalling its similar conclusion in TA971. So the committee concluded that molnupiravir was recommended for treating mild to moderate COVID-19 in adults who have a positive SARS-CoV-2 test, only if:

- they have 1 or more risk factors for progression to severe COVID-19 (as defined in [section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir and tocilizumab for treating COVID-19](#)) and
- nirmatrelvir plus ritonavir is contraindicated or unsuitable.

4 Implementation

- 4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.
- 4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.
- 4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has COVID-19 and the healthcare professional responsible for their care thinks that molnupiravir is the right treatment, it should be available for use, in line with NICE's recommendations.
- 4.4 The Scottish Medicines Consortium collaborated with NICE on this guidance. In Scotland, the advice will have the same status for health board consideration as other Scottish Medicines Consortium advice on new medicines.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee C](#).

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The [minutes of each evaluation committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Stephen O'Brien

Chair, technology appraisal committee C

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Zain Hussain

Technical lead

Samuel Slayen and Adam Brooke

Technical advisers

Louise Jafferally

Project manager

Ross Dent

Associate director

6 Update information

February 2026

We removed sotrovimab from recommendation 1.1. This is because GlaxoSmithKline has discontinued manufacturing, supply, distribution and marketing of sotrovimab in the UK. The 'why the committee made these recommendations' section and committee discussion section have also been amended to reflect the updated recommendation.

May 2025

We updated the list price for molnupiravir in section 2.3.

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