The role of Advisory Groups and records of meetings

Note that this document is not necessarily a complete record of the COVID Treatments Advisory Group meeting; only the relevant portions of the meeting record relating to COVID Treatments Advisory Group discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

Conflicts of Interest are described and managed in accordance with section 7.2 of the PTAC Terms of Reference.

The COVID Treatments Advisory Group may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule; or

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule; or

(d) recommend that Pharmac discontinue funding of a pharmaceutical currently on the Pharmaceutical Schedule.

Advisory Groups give advice to Pharmac, including recommendations', based on the Groups' different, if complementary, roles, expertise, experience, and perspectives. Recommendations made by the COVID-19 treatments Advisory Group are in the context of COVID-19 treatments only. Pharmac is not bound to follow the recommendations made below.

The record of this Advisory Group meeting will be reviewed by PTAC at an upcoming meeting.

Excerpt from
Record of the COVID Treatments Advisory Group
Meeting held on 29 August 2022

Attendance

Present
Chair – Associate Professor Marius Rademaker
Professor Brian Anderson
Eamon Dufy
Dr Gillian Hood
Dr Justin Travers
Dr Kerry Benson-Cooper
Mark Ayson (Ministry of Health observer)
Dr Nigel Raymond
Professor Stephen Munn
Dr Tim Cutfield

Apologies
Dr Graham Mills
Dr Jessica Keepa
Dr Jane Thomas
Dr Robyn Manuel

COVID-19 Treatments Update

Application

1.1. The Advisory Group reviewed the update of information for funded COVID-19 treatments

1.2. The Advisory Group took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Discussion

Māori impact

1.3. The Advisory Group noted that Māori have an equivalent or higher number of dispensings of nirmatrelvir with ritonavir (Paxlovid) and of molnupiravir (Lagevrio), per number of notified cases of COVID-19, compared to non-Māori. However, when counted against the estimated number of Māori eligible for funded antivirals, the rates are comparatively lower. The Group considered that this likely still indicates inequitable access for Māori. The Group considered there were two issues potentially contributing to these inequities.

1.3.1. Firstly, people with COVID-19 that are undiagnosed are not included in the eligible population, and is likely that a greater proportion of Māori are underdiagnosed.

1.3.2. Secondly, more Māori face increased barriers accessing health care than other populations.

1.4. The Group considered it unclear whether Māori were more likely to go to a pharmacist instead of their GP, for oral antiviral treatments as the evidence for this was lacking. The Group considered it likely Māori accessed Hauora Māori providers at higher rates than other primary care providers. The Group discussed whether

different mechanisms would be required to enable access to antiviral treatments for Māori. The Group noted that during the COVID-19 vaccine roll out, Hauora Māori providers facilitated the encouragement and administration of vaccines.

1.5. The Group considered how a similar network could be used to enable eligible Māori to access nirmatrelvir with ritonavir at similar rates to non-Māori, at least. The Group noted that Te Aka Whai Ora – Māori Health Authority, was working actively in this space and that the Care in the Community team at Te Whatu Ora (with Te Puni Kokiri and the Department of Prime Minister and Cabinet) also has a campaign to target those likely to be eligible, both online and in print.

Background

1.6. The Advisory Group noted reporting from the Ministry of Health (19 August 2022):

1.6.1. The Group noted that case rates of COVID-19 and wastewater RNA levels have continued to decrease nationally.

1.6.2. The Group noted that the hospital admission rate had continued to decrease since mid-July to a seven-day rolling average of 0.015 per 1000 at 7 August 2022.

1.6.3. The Group noted that from March 2022 to 14 August 2022 the age-standardised cumulative non-incidental COVID-19 hospitalisation rate for Māori was 2.5 times higher than that for both Asian and European/Other ethnicities, and the Māori cumulative age-standardised cumulative mortality rate was 2.2 times higher than European or Other, with even higher adjusted rates for Pacific peoples.

1.6.4. BA.5 continues to be the dominant subvariant accounting for approximately 91% of cases. New variants BA.2.75 and BA.4.6 have been detected in the community.

1.6.5. It is probable that infections and hospitalisations and mortality will decline and plateau, however, as viral immunity, both wild-type and vaccine-stimulated, decreases over time and if new variants become prevalent, it is expected that case rates could continue to fluctuate.

1.7. The Advisory Group noted that the funding of COVID-19 treatments remains separate to that of other medicines funded by Pharmac and assessment of these medicines has been completed outside of Pharmac's usual process for funding medicines.

Oral Antivirals

1.8. The Advisory Group noted that there was a substantial revision to the antiviral access criteria as of 18 July 2022. The Group noted that there was an increase in the rate of dispensing of oral antivirals after this date and this higher rate had been maintained since then, although case numbers had declined in recent months.

1.9. The Group noted that molnupiravir and nirmatrelvir with ritonavir had been reclassified as 'Pharmacist Only' medicines which allowed pharmacists to initiate these treatments without a prescription. The Group noted that there was an online course for pharmacists to complete prior to being able to provide either molnupiravir or nirmatrelvir with ritonavir to patients without a prescription. The Group noted that the reclassification was a temporary change for six months and would be re-reviewed by Medsafe. The Group noted that this decision was in part to ensure these treatments remained accessible over the weekends, and to provide options for population groups who might not be able to easily access a GP, noting that time from symptom onset to receiving these medicines is short (within five days) and has a direct effect on the clinical outcomes.

1.10. The Group considered that Māori and Pacific peoples in general face more barriers accessing their GP and considered that pharmacists may be more accessible, which may improve uptake amongst these groups. The Group noted the evidence for improvement of uptake with pharmacy prescribing was lacking. The Group noted that pharmacist prescribing was implemented early in Quebec, Canada which now managed the majority of its dispensing of nirmatrelvir with ritonavir via this mechanism.

1.11. The Advisory Group noted there was ample stock available for remdesivir (Veklury) for use, via Te Whatu Ora Hospitals.

Casirivimab with imdevimab (Ronapreve), and sotrovimab (Xevudy)

1.12. The Group noted that stock for casirivimab with imdevimab was available but due to its predicted reduced efficacy against currently circulating variants was not being used. The Group noted that stock is due to expire in April 2023.

1.13. The Advisory Group noted that sotrovimab was not Medsafe approved. The Group noted that the FDA had removed the emergency approval for sotrovimab in some US States, where the proportion of Omicron BA.2 is over 50%, due to the predicted appreciably reduced efficacy against the BA.2 subvariant. The Group decided that, until the Medsafe approval status of sotrovimab was resolved, the Group would make no further recommendations regarding access criteria for sotrovimab.

Tixagevimab with cilgavimab (Evusheld)

1.14. The Advisory Group noted that the access criteria for tixagevimab with cilgavimab for pre-exposure prophylaxis had been finalised by Pharmac and was due for release on 25 August 2022. The Group noted the change to the criteria since its recommendation from the June 2022 meeting where the recommended international dosing of tixagevimab with cilgavimab was doubled to 300 mg of both tixagevimab with cilgavimab. The Group noted that this was not a Medsafe approved dose.

1.15. The Advisory Group noted the planned roll out of tixagevimab with cilgavimab for community administration, in addition to hospital administration, for a small group that are not able to access it within secondary care. The Group noted that private secondary care practitioners would likely be able to access tixagevimab with cilgavimab through a similar mechanism to that of community administration. The Group noted that secondary care specialists would be leading this roll out and considered that communication with these prescribers would be required to allow this to roll out smoothly.

1.16. The Advisory Group considered the collection of information for the use of tixagevimab with cilgavimab for pre-exposure prophylaxis, could include using the National Immunisation Register (NIR) to provide a mechanism for clinicians to record when tixagevimab with cilgavimab had been administered. The Group considered that this should be raised with the Ministry of Health as a formal recommendation.

1.17. The Advisory Group considered the complexity of the prescription and administration of these medicines, particularly in primary care, and the impact that this would have on the delivery of the services. The Group considered that the access to these medicines is complex and would require cross-system effort to reduce inequities.

1.18. The Advisory Group noted that although there are no targets for the number of treatments to be prescribed or administered, an assessment of the impact of the funding criteria on the groups accessing the medicines would be a useful way to assess the success of the criteria and the implementation.

Tocilizumab and baricitinib

1.19. The Advisory Group noted that the tocilizumab supply issue has been resolved. The Group noted that baricitinib was listed on Section H of the Pharmaceutical Schedule in response to the shortage of tocilizumab. The Group considered the ongoing availability of baricitinib for people with severe COVID-19 and the preference of clinicians to use baricitinib over tocilizumab for the inhibitory effect on immune-modulation given the shorter half-life , the increased proportion of hospitalised patients with bacterial co-infection in the current wave of cases, and the ease of oral administration. The Group noted that the use of baricitinib is low for those with severe COVID-19 in the context of Omicron variant infection resulting in lower ICU admissions and previous estimations of use were based on earlier variants.

Eligibility and Access

1.20. The Advisory Group noted that the 75 to 79-year-old group has the highest nirmatrelvir with ritonavir and molnupiravir courses dispensed. The Group noted that the dispensing rates for oral antiviral treatments increase as age increases across all reported ethnicities. The Group noted that there are higher rates of prescribing nirmatrelvir with ritonavir than molnupiravir.

1.21. The Advisory Group noted that the reported dispensing rate was presented as a percentage of those who had reported a positive test to the Ministry of Health. The Group considered that actual usage rates are lower as there would be a group of people who have undiagnosed COVID-19 infection (ie. not tested) or who have not reported their positive test results. The Group considered the impact this has on interpreting the reported dispensing rates and the likely access barriers contributing to this. The Group considered that engagement with this non-testing and/or non-reporting group and with Māori and Pacific communities would be required to understand how best to improve their current access rates. The Group noted the role of Te Aka Whai Ora in commissioning and operational components of reducing barriers for Māori.

1.22. The Group noted that the dispensing rate in Māori and Pacific peoples, in general, was equivalent to or higher than other ethnicities combined over all age groups except those aged over 100 years.

1.23. The Group considered that data on hospitalisation as a result of COVID-19 infection and those who were treated prior to hospital admission compared to those that were not treated would be useful to gain insights into what impact antiviral treatments were having. The Group noted that Te Whatu Ora is conducting an audit to collect this information.

1.24. The Advisory Group noted estimates of the proportions of the population that were eligible for treatment with oral antivirals. The Group noted that, with the recent widening of access criteria, those over 75 years old were eligible regardless of comorbidities and ethnicity. The Group noted that there was an upward trend in the case dispensing rates (ie “access” rates) within this age group over the four weeks since the wider July criteria were implemented. The Group noted access rates in those aged 65-74 years old, where access rates were higher in Māori and Pacific peoples than other ethnicities combined. However, when comparing access to eligibility for treatment, Māori and Pacific peoples had lower eligibility-adjusted access rates than non-Māori and non-Pacific peoples. The Group noted that in those aged 50-64 years old, access rates again were higher in Māori and Pacific peoples. The Group noted that further information would be provided to them by Pharmac staff after this meeting for further consideration.

Excerpt from
Record of the COVID Treatments Advisory Group Meeting held on 29 August 2022

Molnupiravir for COVID-19 data update

Application

2.1. The Advisory Group reviewed the updated information for molnupiravir in the treatment of COVID-19.

2.2. The Advisory Group took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

2.3. The Advisory Group **deferred** its **recommendation** on changing the access criteria until further information is available.

Discussion

Previous consideration of molnupiravir for COVID-19

2.4. Molnupiravir was initially considered for the treatment of mild to moderate COVID-19 at the October 2021 COVID-19 Treatment Advisory Group meeting. The Group recommended molnupiravir be prioritised for treatment of mild to moderate COVID-19 in community and hospital under access criteria targeting identified at risk patient groups. While no clinical benefits had been observed with molnupiravir use in the inpatient setting among patients with moderate-to-severe COVID-19, early initiation of molnupiravir within 5 days of symptom onset in non-hospitalised patients with mild-to-moderate COVID-19 and high risk factors for progression to severe disease has been associated with relative risk reduction of hospitalisation or death by 30% (following initial reports of it providing 50% reductions).

2.4.1. The Advisory Group noted that these clinical trials were conducted prior to the emergence of Omicron variant, and the clinical efficacy of oral antivirals against this currently dominant variant of concern had only been inferred from experimental evidence. Real-world evidence of oral antiviral use in patients with SARS-CoV-2 infection of Omicron variant was lacking.

2.5. Molnupiravir was considered again at the COVID-19 Treatment Advisory Group meeting in April 2022 where the efficacy of funded oral antivirals was re-assessed in the context of the emerging Omicron variant(s). This was then discussed further at the May 2022 meeting. Since the initial outbreak of SARS-CoV-2, a number of variants have emerged with different infectivity profiles, clinical characteristics, and susceptibility to treatments. The Advisory Group noted that at the time the BA.2 subvariant of Omicron was the dominant strain of SARS-CoV-2 in New Zealand. At this time the Advisory Group considered that antiviral treatments molnupiravir retained in-vitro activity against BA.1 and BA.2.

2.5.1. The Group considered that antiviral treatments are likely to retain in-vitro efficacy against current and future variants of SAR-CoV-2 given they target proteins which are well preserved across the variants. The Group considered antiviral treatments are appropriate for use in the general population.

2.6. The Group noted that compared to nirmatrelvir with ritonavir, molnupiravir was expected to be easier to prescribe as it does not have ritonavir's propensity to

multiple drug interactions. The Group raised concerns that this could lead to molnupiravir being prescribed by clinicians instead of nirmatrelvir with ritonavir, even though the available initial clinical phase 3 trial data published by Bernal et al 2022 and Hammond et al 2022 indicated that nirmatrelvir with ritonavir reduced the risk of COVID-19 related hospitalisation or death compared to placebo by ~89%, and compared to molnupiravir by ~30% .

Māori Impact

2.7. The Advisory Group noted that prior to the availability of oral antivirals there was proactive action to engage with Māori communities for the administration of remdesivir infusions, specifically within the Auckland region, and considered this service could be re-purposed for those who have a contra-indication to nirmatrelvir with ritonavir. A Member noted that Auckland region has very limited capacity for infusions and little flexibility within that service. The Group noted while the decrease in COVID-19 case numbers and the resulting reduced pressure on the hospitals is positive, the inequity of access for Māori to molnupiravir and nirmatrelvir with ritonavir continues to be of concern given Māori are at higher risk of severe COVID-19 than non-Māori.

Health Need

2.8. The Advisory Group noted that molnupiravir does not target the spike protein, so evolving changes in this protein in emerging and future variants of COVID-19 would not be expected to alter anti-viral activity. The Group noted that molnupiravir has in vitro effect against Omicron variant(s). The Group noted molnupiravir is not Medsafe approved for people under 18 years old and FDA recommends that molnupiravir not be used in those under 18 due to concerns about maturation of bone and cartilage. The Group noted reports that molnupiravir may cause foetal harm, based on animal studies.

2.9. The Advisory Group noted that, like many other treatments for COVID-19, the adverse effect profile of molnupiravir is not well known, due to the novelty of the drug, but nonetheless noted specifically flu-like symptoms, extremity pain, as well as the RNA mutation mechanism having a theoretical effect on the development of new variants. The Group considered that because of these potential adverse effects that those patients considered for funding should gain a clear benefit from this drug.

2.10. The Advisory Group noted that the earlier a course of molnupiravir was started the better. The Group noted that people treated within 3 days of the start of their symptoms fared better than those that started treatment from day 3 to day 5.

Health Benefit

2.11. The Advisory Group considered that the prior evidence for benefit was reported in unvaccinated people during Delta variant dominance. The Group noted the respective risk of harm between Delta and Omicron variants, where the risk of pneumonitis is lower in Omicron. The Group also noted that those who are vaccinated would be expected to have greater protection against being infected with lower viral loads of SARS-CoV-2; in addition, previous evidence signals that treatment with molnupiravir in people with a low viral load was not superior to placebo.

2.12. The Advisory Group considered a secondary analysis of the MOVe-OUT study (Johnson et al. Ann Intern Med. 2022;175(8):1126-34). The Group noted this was a randomised control trial comparing those who were treated with molnupiravir or placebo and their rates of hospitalisation. The Group noted reported findings of reduced hospitalisation and death through day 29 (Phase 3 all randomised population) compared with placebo (6.8% v 9.7%; 95% CI: 0.1%-5.9%). The Group

noted the secondary analysis from this trial reported the frequency of acute care visits (7.2% v 10.6%; RRR 32.1% [CI, 4.4%-51.7%]), COVID-19-related acute care visits (6.6% v 10.0%; RRR 33.8% [CI 5.6%-53.6%]) were less in the molnupiravir treated group. Molnupiravir-treated participants had a decreased need for respiratory interventions compared to placebo-treated participants (RRR 34.3% [95% CI, 4.3%-54.9%]) with similar findings in participants who were hospitalised after randomisation. Participants were not immunised against COVID-19. The Group noted that it was reported that people with a low viral load or who previously had COVID-19 infection did not demonstrate benefit from treatment. The Group noted that in a supplier-provided data update, based on the study above, it was reported that the immunocompromised subgroup included participants with active cancer, HIV, those on immunosuppressant therapies, prior systemic corticosteroid treatment and transplant recipients, and noted other information from the supplier that of those treated with molnupiravir 8.0% were hospitalised or died through day 29 compared to 25% of those in the placebo group (RRR 68%; 95% CI -36.0% to 3.6%).

2.13. The Advisory Group considered evidence from three unpublished cohort studies from Hong Kong provided by the supplier prior to peer review and publication comparing people who were treated with antivirals (molnupiravir and nirmatrelvir with ritonavir) to those who were not:

2.13.1. Wong et al. [Preprint 2022, 13 July posting]
A territory-wide retrospective cohort study assessing the real-world effectiveness of molnupiravir and nirmatrelvir/ritonavir among COVID-19 inpatients during Hong Kong's Omicron BA.2 wave from 26 February to 26 April 2022. Participants were hospitalised patients not requiring oxygen therapy. The study outcomes included a composite outcome of disease progression (all-cause mortality, initiation of invasive mechanical ventilation [IMV], or intensive care unit admission), individual outcomes and lower viral load of cycle threshold value of more than or equal to 30 cycles.

2.13.1.1. In a supplier-provided data update, based on the unpublished study above, it was reported that in the molnupiravir arm of the study a relative risk reduction of 45% and absolute risk reduction of 7.4% with a number needed to treat of 14 for composite progression outcome cumulatively through to day 30. All-cause mortality was reported at a relative risk reduction of 44% and absolute risk reduction of 7% cumulatively through to day 30.

2.13.2. Wong et al. [Preprint 2022, 26 May]
An unpublished, territory-wide retrospective cohort study assessing the real-world effectiveness of molnupiravir and nirmatrelvir/ritonavir against mortality, hospitalisation, and in-hospital outcomes among community-dwelling, ambulatory COVID-19 patients during the BA2.2 wave in Hong Kong from 26 February to 3 May 2022. Investigators reported low vaccination rates in all groups. Based on relative efficacy, this study was supportive of current guidelines prioritising nirmatrelvir/ritonavir use over molnupiravir in community-dwelling COVID-19 patients who are at high risk of hospitalisation or progression to severe disease, should the former be accessible and clinically appropriate.

2.13.3. Yip et al. Clin Infect Dis. [Epub ahead of print 2022, 29 August]
A territory-wide retrospective cohort study considered the impact of the use of oral antivirals agents on the risk of hospitalisation in community COVID-19 patients. Non-hospitalised COVID-19 patients who attended designated outpatient clinics between 16 February and 31 March 2021 were identified. The primary endpoint was hospitalisation. The secondary endpoint was a composite of intensive care unit admission, invasive mechanical ventilation use, and/or

death. Of 93,883 patients, 83,154 (88.6%), 5,808 (6.2%), and 4,921 (5.2%) were oral antiviral non-users, molnupiravir users, and nirmatrelvir/ritonavir users respectively. The complete vaccination rate was reported as 36.1% for molnupiravir treated, 42.6% nirmatrelvir with ritonavir treated and 55.9% antiviral non-users. Compared to non-users, oral antiviral users were older and had more comorbidities, lower complete vaccination rate, and more hospitalisations in the previous year. Molnupiravir users were older, and had more comorbidities, lower complete vaccination rates, and more hospitalisations in the previous year than nirmatrelvir/ritonavir users. At a median follow-up of 30 days, 1,931 (2.1%) patients were admitted to hospital and 225 (0.2%) patients developed the secondary endpoint (composite of intensive care unit admission, invasive ventilation use and death). After propensity score weighting, molnupiravir use (weighted hazard ratio 1·17, 95% CI 0·99-1·39, *P*=0·062) was not associated with a reduced risk of hospitalisation than non-users. The use of molnupiravir was not associated with a lower risk of the secondary endpoint as compared to non-users. In the subgroup of patients aged ≥60 years or aged <60 years with comorbidities, molnupiravir use was not associated with a reduced risk of hospitalisation than non-users.

2.14. The Advisory Group considered the level of confounding by indication in real-world retrospective cohort studies, makes determining a valid comparator group more difficult, as it is likely those treated with antivirals in the real world setting are at higher risk of severe disease than those in the randomised controlled clinical trials. The Group considered that the available information on the methods used to adjust for this confounding was not clear. The Group noted that when measuring for differences in initiation of invasive mechanical ventilation and admission to ICU outcomes in hospital inpatients with COVID-19 (Wong et al. July 2022) and in the risk of hospitalisation in people attending COVID-19 outpatient clinics (Yip et al. 2022) that molnupiravir did not appear to be superior to placebo. The Group considered that nirmatrelvir with ritonavir was probably superior to molnupiravir based on the unpublished data presented but noted that these comparisons are not based on head-to-head direct comparison trials. The Group considered that the adjustment for confounding within each of these studies was not clear and this reduced the value of this data at the current time. The Group also considered the vaccination rate in the populations assessed (Wong et al. May 2022, Yip et al. 2022), noting that higher vaccination rates were associated with lower death rates overall, consequently the absolute reduction in deaths was relatively small in both molnupiravir and nirmatrelvir with ritonavir treatment groups in the context of the currently dominant Omicron variant of COVID-19.

2.15. The Advisory Group considered that this new information relating to molnupiravir re-enforces that nirmatrelvir with ritonavir has reported likely higher efficacy compared to molnupiravir. The Group considered that the unpublished data provided could be confounded by indication due to differences in baseline risk of people being selected for treatment. The Group considered that this confounding was adjusted for by propensity analysis but was not able to interpret the extent this adequately controlled for known and unknown confounders. The Group considered it is unlikely treatment with molnupiravir would significantly prevent severe acute COVID-19 lung disease in the current context of low incidence and prevalence in a predominantly Omicron variant of COVID-19 in New Zealand.

2.16. The Advisory Group noted the published results of a randomised control trial examining the efficacy and safety of molnupiravir against Omicron variant infection (Zhou et al. Front Pharmacol. 2022). The primary endpoint was time to viral RNA clearance (9 days vs 10 days median, *P*=<0.01) and at day 10 of the molnupiravir treated group 76.3% were returning a negative PCR test compared to the placebo

group returning 51.6% negative (*P*=0.02). The Group noted that there was no statistically significant difference between the clinical outcomes of the molnupiravir and placebo group.

2.17. The Advisory Group considered that to justify the use of molnupiravir the patient would need a high risk of severe disease. The Advisory Group considered that the current access criteria for molnupiravir were likely allowing it to be prescribed to people that may have several risk factors but are not high-risk enough to receive benefit from treatment. The Group considered the targeting of access to these high-risk people who are not able to take nirmatrelvir with ritonavir would likely be of benefit.

2.18. The Group noted that a hierarchy for COVID-19 treatments could be included within community and hospital guidelines. The Group considered that changing the access criteria specifically for molnupiravir to target treatment to the highest risk people was less likely to be effective compared to changing prescribing guidelines.

2.19. The Advisory Group considered results from an unpublished retrospective observational study provided by the supplier investigating the prevalence of people who are taking medications with potential interactions with nirmatrelvir with ritonavir). It was reported that there was a 60% prevalence of potential severe to moderate drug interactions with nirmatrelvir with ritonavir. The Group noted that they had previously estimated this as 30-40% of eligible patients in New Zealand. The Group noted that drug interactions were assessed against the Liverpool DDI checker, Paxlovid US FDA factsheet and Lexicomp database to give an overall rating of low to severe interaction. The Group considered that it was unclear as to the clinical significance of these interactions and that an unknown proportion of these interactions could be mitigated to allow these people to receive nirmatrelvir with ritonavir.

2.20. The Group considered the COVID-19 environment in New Zealand compared to the rest of the world. The Group noted that New Zealand has a high risk, COVID-19 naïve population compared to other populations that have not used the same strategies to control case numbers as New Zealand has. The Group noted that the United Kingdom is likely to have a different level of immunity due to differences in the incidence and prevalence of COVID-19 over the last 3 years. On this basis, the Group considered the potential effects of this limiting the relevance of any findings to the New Zealand population, particularly those who are not vaccinated and have not had an infection. The Group considered that potentially some benefit, at least for a short period, could be assumed as New Zealand moves toward an endemic phase. The Group noted that the current dominant Omicron subvariant was less virulent compared to previously dominant variants of COVID-19, so considered that extrapolation from emerging evidence was difficult when accounting for variant evolution and differences in severity of symptoms. The Group noted the COVID-19 mortality rate in New Zealand was estimated as 1 in 1000 cases. Given this, it was considered that due to the low risk of death overall that use of molnupiravir should be targeted and confined to those with a higher risk of severe disease, as the risk of side-effects in people of lower risk would out-weigh the potential benefit.

2.21. The Advisory Group considered the potential negative implications of narrowing and restricting the access criteria for molnupiravir to those who have are higher risk of severe disease, with a risk that this may result in molnupiravir being misconstrued to be a preferred option for these high-risk people. The Group considered there are two funded and readily available alternatives (nirmatrelvir with ritonavir, and remdesivir) and that the current evidence indicates these are likely more effective than molnupiravir in the current Omicron environment. The Group noted that there are no direct head-to-head trials directly comparing antiviral treatments for COVID-19.

2.22. The Advisory Group considered the barriers to prescribing nirmatrelvir with ritonavir over molnupiravir. The Group considered that more information relating to this was required from prescribers to fully assess the impact the access criteria may have on clinical decision making. The Group considered that there could be a bias towards molnupiravir as it does not have the complex drug interactions characteristics of nirmatrelvir with ritonavir. The Group considered whether funding and capacity in primary care is enough to support the prescribing of this drug given the time it would take to assess the interactions. The Group considered that reducing these barriers, such as confidence in prescribing nirmatrelvir with ritonavir and how to mitigate the potential interactions, and being resourced to either have the time to assess or have clinical support doing so (eg locally available clinical pharmacists) would likely encourage the prescribing of nirmatrelvir with ritonavir over molnupiravir.

2.23. The Advisory Group considered the use of prescriber education as a tool to increase the prescribing of nirmatrelvir with ritonavir compared to molnupiravir for eligible people. The Group considered that the likely barrier is the time it takes to assess the potential drug interactions given the target population is likely receiving medicines (often many) for co-morbidities. The Group noted that there is no tangible information as to the barriers faced by primary care in the prescribing of nirmatrelvir with ritonavir.

2.24. The Group noted that the temporary reclassification of nirmatrelvir with ritonavir and molnupiravir to 'Pharmacist Only' medicines allows the burden of assessment of interactions to be shared between GP's and pharmacists. The Group noted the differences between pharmacist prescribers and those in General Practice. The Group noted that initial data for rates of prescribing molnupiravir by these two groups are similar. The Group noted that this would continue to be monitored.

2.25. The Advisory Group noted while the decrease in case numbers and reduced pressure on the hospitals from COVID-19 is positive, the inequity of access for Māori and Pacific peoples to molnupiravir and nirmatrelvir with ritonavir continues to be of concern given they are at higher risk of more severe disease than non-Māori non-Pacific people. The Group considered that access criteria differentiating nirmatrelvir with ritonavir and molnupiravir by widening access specifically to nirmatrelvir with ritonavir would be more desirable, as restricting access to molnupiravir is likely unacceptable to the public and could limit access to some people who might otherwise benefit. The Group noted that prior to the availability of nirmatrelvir with ritonavir and molnupiravir there was proactive action to engage well with Māori and Pacific communities, specifically within the Auckland region, to increase the administration of remdesivir infusions for these communities. The Group considered this service could be re-purposed for those who have a contraindication to nirmatrelvir with ritonavir.

2.26. The Advisory Group considered that it would be beneficial to formulate clinical guidance to encourage prescribers to prescribe nirmatrelvir with ritonavir and remdesivir in preference to molnupiravir. The Group noted that Pharmac's role is not a supplier of clinical information but suggested collaboration with Te Whatu Ora and Te Aka Whai Ora to support the development of guidance.

2.27. The Advisory Group considered that the information presented was not sufficient to recommend a change to the current access criteria. The Group considered that further information was required including data on deaths from COVID-19 associated illness, information on those who received funded COVID-19 treatments prior to hospitalisation, and further dispensing data. The Group considered that nirmatrelvir with ritonavir prescribing should be encouraged over molnupiravir prescribing. The Group also recommended that collaboration with Te Whatu Ora be used to facilitate increased access.

2.28. The Advisory Group noted the PANORAMIC clinical study, which was evaluating the effectiveness of molnupiravir in preventing hospitalisation or death from of COVID-19 compared to standard of care, had recently stopped recruitment. The Advisory Group considered that it would be useful for it to review the results of the study once they are available, noting it would provide data for molnupiravir in the treatment of the Omicron variant of COVID-19.