Record of the COVID Treatments Advisory Group Meeting held on 28 February 2022

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.

Attendance

Present
Chair –Dr Jane Thomas
Professor Brian Anderson
Eamon Dufy
Dr Gillian Hood
Dr Justin Travers
Dr Kerry Benson-Cooper
Associate Professor Marius Rademaker
Dr Nigel Raymond
Dr Robyn Manuel
Professor Stephen Munn
Dr Tim Cutfield

Apologies
Dr Graham Mills
Dr Jessica Keepa

1. Ivermectin for the Treatment of COVID-19

Application

1.1. The Advisory Group reviewed material provided by Pharmac staff regarding the use of ivermectin for the treatment of COVID-19.

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

Recommendation

1.3. The Advisory Group noted that an application had been submitted to Pharmac by a consumer for the funding of ivermectin for the treatment of people infected with SARs-CoV-2 (COVID-19).

1.4. The Advisory Group recommended that ivermectin not be funded for the treatment of COVID-19 at this time, based on the very low certainty of evidence available for ivermectin in this setting.

1.5. The Advisory Group acknowledged the importance of securing a portfolio of treatments for COVID-19 for New Zealand and noted it would welcome any additional information regarding the effectiveness of ivermectin in the treatment of COVID-19.

Discussion

1.6. The Advisory Group noted that no priority ranking (within the context of treatments for COVID-19) was sought by Pharmac, reflecting the rapidly evolving evidence for treatments in COVID-19 and separate funding outside the Combined Pharmaceutical Budget, and therefore did not need to discuss a priority ranking.

1.7. The Advisory Group reiterated this was an area of rapidly evolving evidence and knowledge and identified that its recommendation may need to be reconsidered in the future, noting this was based on currently available data from published studies and could be subject to change should new data become available, warranting further review.

1.8. The Advisory Group noted that ivermectin is a semi-synthetic macrocyclic lactone with a broad-spectrum antiparasitic activity, which binds with high affinity to glutamate-gated chloride channels causing an increase in the permeability of the cell membrane to chloride ions with hyperpolarisation of the nerve or muscle cell.

1.9. The Advisory Group noted that the potential mechanism of action for ivermectin as an antiviral against COVID-19 is currently unknown.

1.10. The Advisory Group noted that ivermectin is available in New Zealand as a 3 mg tablet and dosing for the treatment of parasitic infections is in multiples of 3 mg depending on body weight and the severity of infection being treated.

1.11. The Advisory Group noted that the dosing of ivermectin in clinical trials for the treatment of COVID-19 is variable and was approximately 150 mcg to 200 mcg per kg twice per day for up to 5 days.

1.12. The Advisory Group noted that in routine, single dose treatments of parasitic infections, side effects from ivermectin are relatively uncommon, however the Group acknowledged that safety data for the use of ivermectin as a preventative treatment over longer periods of time (as it would be used in the treatment of COVID-19) was not available.

1.13. The Advisory Group considered clinical evidence for ivermectin for the treatment of COVID-19:

1.13.1. The Group noted that a number of meta-analyses had been undertaken to evaluate the effectiveness of ivermectin in the treatment of COVID-19. The Group noted an article by Rothrock, Weber Giordano et al 2022, which concluded that the poor design of these meta-analyses and the limitations of the component studies were sufficiently appreciable to invalidate findings that use of ivermectin was associated with reduced mortality from COVID-19.

1.13.2. The Group noted a Cochrane review of trials up to 26 May 2021 (Popp et al. CDSR 2021;7:CD015017). The authors reported very low to low certainty of evidence for the efficacy and safety of ivermectin for prevention of SARS-CoV-2 infection or the treatment of patients hospitalised or in outpatient settings with COVID-19, and concluded that the available evidence did not support the use of ivermectin in the treatment of COVID-19. The Group noted this review did not include the most recent studies, and considered that treatments for COVID-19 is a rapidly evolving area and data continues to emerge.

1.13.3. The Group noted a sub group meta-analysis of trials for ivermectin in COVID-19 to assess the effects of stratifying by trial quality on the overall results (Hill, Mirchandani and Pilkington et al. 2022), which reported that when all 12 studies evaluated in the meta-analysis were included, the use of ivermectin in the treatment of COVID-19 was associated with a 51% increase in survival. However,

excluding all trials considered to be fraudulent or at risk of bias, resulted in no material increase in survival associated with ivermectin use.

1.14. The Advisory Group considered recent studies for ivermectin in the treatment of COVID-19 which were undertaken subsequent to Popp et al 2021 and not identified by Hill, Mirchandani and Pilkington et al 2022 as being at risk of bias. These included:

1.14.1. Efficacy and safety of ivermectin in the treatment of COVID-19 Buonfrate et al 2022 COVER Study: A randomised, investigator-initiated, double-blind, multicentre, phase II, dose-finding, proof-of-concept clinical trial to assess the efficacy and safety of high doses of ivermectin in reducing viral load in individuals with early SARS-CoV-2 infection in outpatient settings. Patients were randomly assigned to receive placebo (arm A) 600 mg/kg/day (Arm b) or 1200 mg/kg/day (arm C) for 5 days (n=93). Mean (S.D.) log10 viral load reduction was 2.9 (1.6) in arm C, 2.5 (2.2) in arm B and 2.0 (2.1) in arm A, (P = 0.099 and 0.122 for C vs. A and B vs. A, respectively). High dose ivermectin was safe but did not show efficacy to reduce SARS-CoV-2 viral load.

1.14.2. Prophylaxis against COVID-19 Bartoszko, Siemieniuk, Kum, et al, 2021: A living systematic review and network meta-analysis evaluating the effects of prophylactic treatments on SARS-CoV-2 infection and COVID-19, which reported that the effects of ivermectin alone and in combination with iota-carrageenan as a prophylactic treatment against COVID-19 remains very uncertain with 50 and 52 fewer COVID-19 infections per 1000 people respectively compared to placebo. The meta-analysis reported serious risk of bias and very serious imprecision, leading to low certainty of evidence regarding the effectiveness of ivermectin alone and combined with iota-carrageenan on laboratory confirmed COVID-19.

1.14.3. Inpatients with COVID-19 at risk of severe disease Lim et al 2022 (ITech Study): A multicentre, open-label, randomised clinical trial conducted at 20 government hospitals and a COVID-19 quarantine centre in Malaysia between May 31 and October 25, 2021 to evaluate the effects of oral ivermectin (0.4 mg/kg/day for five days) plus standard of care in patients with confirmed COVID-19 who were 50 years or older with at least 1 comorbidity and presented with mild to moderate illness within 7 days from symptom onset (n=490). Among the 490 patients, 95 (19.4%) progressed to severe disease during the study period; 52 of 241 (21.6%) received ivermectin plus standard of care, and 43 of 249 (17.3%) received standard of care alone (RR, 1.25; 95% CI, 0.87-1.80; P =0.25). There were no statistically significant differences between ivermectin and control groups for all the prespecified secondary outcomes.

1.14.4. Treatment of mild to moderate COVID-19 infection Ravikirti et al 2021: A double blind, parallel, randomised, placebo-controlled trial between August and 31 October 2020 to evaluate the effectiveness of oral ivermectin (12 mg/day administered on day 1 and 2 post enrolment) in adult patients with mild to moderate COVID-19 (n=112); On 6th day, 23.6% of patients in the intervention arm and 31.6% in the placebo arm tested negative for SARS-CoV-2 [RR: 0.8; 95%, CI: 0.4 -1.4; p=0.348]; Mechanical ventilation was required for 1.8% of

patients in the intervention arm and 8.8% of patients in the placebo arm [RR: 0.2; 95%CI: 0.0-1.7; (p=0.102)]; No patients in the intervention arm but 7% of patients (n=4) in the placebo arm died [RR: 1.1; 95% CI; 1.0-1.2; p=0.045)].

1.15. The Advisory Group considered that the strength and quality of evidence supporting the use of ivermectin in the treatment COVID-19 was very low based on available publications. The Group noted that overall, the studies evaluating the effectiveness of ivermectin in the treatment of COVID-19 were small and did not consider factors such as vaccination, social isolation and mask wearing. In addition, many of the studies had been undertaken in less developed countries where social distancing has not been implemented. As a result of these factors the Group considered that many of the studies evaluating the effectiveness of ivermectin in the treatment of COVID-19 were at risk of bias. The Group noted there was no evidence for the effectiveness of ivermectin in the treatment of the Omicron variant of SARS-CoV-2 and its various subvariants, and the Group considered there would be no benefit from the use of ivermectin for the current treatment of COVID-19.

1.16. The Advisory Group noted that it was aware that a small number of people may be using ivermectin for the treatment of COVID-19 in New Zealand. Members raised concerns that if ivermectin were to be funded for the treatment of COVID-19 in New Zealand there was a risk that sufficient supply may not be available for currently funded indications for which there is clinical evidence of benefit.

1.17. The Advisory Group noted that internationally ivermectin has not been approved for use or funded for the treatment of COVID-19. This included jurisdictions with comparable assessment and regulatory environments to New Zealand including Australia, Canada, the European Union and the United States of America. In addition, the Group noted the public statement from Merk Sharpe & Dome, the manufacturer of ivermectin, that it does not support the use of ivermectin for the Treatment of COVID-19, noting there is no scientific basis for a potential therapeutic effect against COVID-19 from pre-clinical studies and there is no meaningful evidence for clinical activity or clinical efficacy in patients with COVID-19 disease.

1.18. The Group noted that in New Zealand the Ministry of Health and Medsafe have strongly recommended that, on the basis of the evidence available, ivermectin should not be used in the prevention or treatment of COVID-19.

2. Fluvoxamine for the Treatment of COVID-19

Application

2.1. The Advisory Group reviewed material provided by Pharmac staff regarding the use of fluvoxamine for the treatment of COVID-19.

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

Recommendation

2.3. The Advisory Group noted that no application has been submitted to Pharmac for the funding of fluvoxamine for the treatment of people infected with COVID-19.

2.4. The Advisory Group recommended that fluvoxamine not be funded for the treatment of COVID-19 at this time, on the basis of the low certainty of evidence available for fluvoxamine in this setting.

2.5. The Advisory Group acknowledged the importance of securing a portfolio of treatments for COVID-19 for New Zealand and noted it would welcome any additional information regarding the effectiveness of fluvoxamine in the treatment of COVID-19.

Discussion

2.6. The Advisory Group noted that no priority ranking (within the context of treatments for COVID-19) was sought by Pharmac, reflecting the rapidly evolving evidence for treatments in COVID-19 and separate funding outside the Combined Pharmaceutical Budget, and therefore did not need to discuss a priority ranking.

2.7. The Advisory Group reiterated this was an area of rapidly evolving evidence and knowledge and specified that its recommendation may need to be considered in the future, noting this was based on currently available data from published studies and could be subject to change should new data become available, warranting further review.

2.8. The Advisory Group noted that fluvoxamine is oral selective serotonin reuptake inhibitor (SSRI) used (historically in NZ until 2016) for depression, anxiety and obsessive-compulsive disorders.

2.9. The Advisory Group noted that the mechanism of action for fluvoxamine against COVID-19 is currently unknown but that there were potential therapeutic mechanisms under investigation including anti-inflammatory action via the sigma-1 receptor or direct antiviral action against SARS-CoV-2.

2.10. The Advisory Group noted that fluvoxamine is not currently available in New Zealand but it is expected supply could be secured at relatively short notice.

2.11. The Advisory Group noted that the dosing of fluvoxamine in clinical trials for the treatment of COVID-19 is variable and was approximately 100 mg twice daily for ten to fifteen days for the treatment paradigm of early mild-moderate COVID-19 cases to prevent progression to severe COVID-19 disease.

2.12. The Advisory Group noted that routine treatment side effects from fluvoxamine are relatively uncommon and that there is an extensive body of clinical evidence around the adverse effect profile of the medicine.

2.13. The Advisory Group considered clinical evidence for fluvoxamine for the treatment of COVID-19:

2.14. The Advisory Group noted Reis et al. Effect of early treatment with fluvoxamine on risk of emergency care and hospitalisation among patients with COVID-19; October 2021.

2.14.1. The TOGETHER trial was a phase III double-blind, placebo controlled randomised controlled trial (RCT) with an adaptive platform study conducted January to August 2021 in Brazil. Patients were required to be aged 50+ years or 18+ years with one high risk condition and be unvaccinated against COVID-19. Patients received titrated 100 mg twice daily fluvoxamine or placebo.

2.14.2. The trial had a composite primary endpoint of emergency setting observation for >6 hours or hospitalisation due to progression of COVID-19 within 28 days after randomisation. The trial was halted due to meeting its stopping criteria of 97.6% superiority with 1497 patients enrolled. Of the patients treated 11% (79/741) in fluvoxamine arm met the primary endpoint vs. 16% (119/756) in placebo arm (relative risk 0.68; 95% CI, 0.52–0.88).

2.14.3. The Advisory Group noted that the risk factors of the population studied may not represent an equivalent population in New Zealand and that there were concerns about the non-standard endpoints of the trial that made it difficult to interpret any benefit from fluvoxamine.

2.14.4. The Advisory Group further noted the January-August 2021 time period of the study and that the predominant SARS-COV-2 variant at the time in Brazil was the Gamma SARS-CoV-2 variant of concern (VoC) as opposed to the Delta and Omicron variants which were the primary VoC present in New Zealand at this time.

2.15. The Advisory Group noted Lenze et al. Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19. JAMA 2020 (STOP-COVID Trial)

2.15.1. The STOP-COVID Trial was a phase II double-blind randomised controlled trial (RCT) of fluvoxamine in non-hospitalised patients with COVID-19 in the United States. It enrolled 152 patients across treatment and placebo arms. Patients received titrated 100 mg twice daily fluvoxamine or placebo. The primary endpoint was clinical deterioration measured by presence of dyspnoea and/or hospitalisation for shortness of breath or pneumonia, or decrease in SpO_2 saturation (<92% on room air) and/or supplemental oxygen requirement to keep SpO_2 saturation ≥92%).

2.15.2. The Advisory Group noted the dropout rate of enrolled patients in the STOP-COVID Trial was nearly 20% and that 8.3% of patients (6/72) in the placebo arm met the criteria for clinical deterioration compared with none (0/80) in the treatment arm.

2.15.3. The Advisory Group considered the STOP-COVID trial supported further investigation of fluvoxamine as a treatment for COVID-19 but that it was of insufficient size and power to be independently conclusive.

2.16. The Advisory Group noted Lenze et al. Fluvoxamine for Early Treatment of Covid-19. (STOP-COVID 2 Trial)

2.16.1. The Advisory Group noted that STOP-COVID-2 was unpublished but that summary results from the trial were available for analysis.

2.16.2. The Advisory Group noted STOP-COVID 2 was a phase III RCT from the same trialists as for the STOP-COVID trial and the dosing, patient group and study criteria were the same. The study ran from December 2020 to September 2021 before being stopped for futility, having only recruited 551 of 880 patients.

2.16.3. The Advisory Group noted the halt of the trial was due to the low COVID-19 case rate and severity leading to inability to generate statistically significant data from the trial. The Advisory Group considered the likely reason for this was low overall case numbers at the time and the COVID-19 vaccination rollout across the United States which began at approximately the same time as the trial.

2.16.4. The Advisory Group noted that the COVID-19 vaccination rate in New Zealand at present was significantly higher than that of the United States at the time of the STOP-COVID-2 Trial.

2.17. On balance of the evidence available at the time of its 28 February 2022 meeting, the Advisory Group considered that the strength and quality of evidence supporting the use of fluvoxamine in the treatment COVID-19 was low.

2.18. The Advisory Group noted that overall, the studies evaluating the effectiveness of fluvoxamine in the treatment of COVID-19 were of limited quality and the pivotal STOP-COVID 2 trial was halted due to futility, as further participants were unable to be recruited. The Advisory Group further noted there was no evidence for the effectiveness of fluvoxamine in the treatment of the Omicron variant of SARS-CoV-2 and its various subvariants.

2.19. On balance of the evidence available the Advisory Group recommended against the use of fluvoxamine to treat COVID-19 at this time.

3. Oral antivirals (nirmatrelvir with ritonavir and molnupiravir) access criteria.

Discussion

Acknowledgement

3.1. The Advisory Group acknowledged the particular impact of COVID-19 on Māori and Pacific people, older people, people who are immunocompromised, people with premorbid conditions (eg. lung disease, diabetes, heart disease, etc), and/or disabled people.

Background

3.2. The Advisory Group discussed early consultation feedback on the proposed access criteria for the use of Pfizer's oral protease inhibitor (nirmatrelvir with ritonavir) and Merck's oral antiviral (molnupiravir) for the treatment of mild to moderate COVID-19.

3.3. The Advisory Group noted that it reviewed the available evidence regarding the use of Pfizer's oral protease inhibitor (nirmatrelvir with ritonavir) for the treatment of mild to moderate COVID-19 at its meeting 13 December 2021 and had recommended access criteria. The criteria that Pharmac has consulted on (released 16 February 2022 and closing 2 March) were based on the advice at the time. The Group noted that since then,

clinical evidence and the New Zealand experience of COVID-19 cases, with a growing Omicron outbreak, had changed.

3.4. The Advisory Group considered that it is likely that criteria would need to be targeted further, in light of much higher case numbers associated with the Omicron variant of SARS-CoV-2, limited antiviral stock available and further confounding factors such as the lower potency of the Omicron variant compared to earlier ancestral, Alpha and Delta variants.

3.5. The Advisory Group also noted that Pharmac had temporarily widened access to remdesivir (from 28 February 2022) to enable clinicians to use it earlier in the disease course for people with COVID-19 at risk of developing severe disease. The Group noted that the oral antivirals Pharmac has secured for treating COVID-19 were still some weeks away from availability in New Zealand and remdesivir was the only antiviral treatment currently available for use in COVID-19.

Oral antiviral access criteria

3.6. The Advisory Group recommended that nirmatrelvir with ritonavir be funded subject to access criteria. The Group recommended that unvaccinated people be funded with at least 3 risk factors and vaccinated people be eligible for those with at least 5 risk factors (age, ethnicity and comorbidities as previously discussed).

3.6.1. The Group recommended funding for those who are unvaccinated with at least 3 risk factors (increasing age, ethnicity, and relevant comorbidities), or

3.6.2. The Group recommended funding for those who are vaccinated with at least 5 risk factors (increasing age, ethnicity, and relevant comorbidities).

3.7. The Advisory Group considered some early feedback from the public consultation on oral antiviral access criteria and noted the high level of detail from many pieces of feedback. The Group extended its thanks to all that submitted feedback, noting that it may not be possible to address each item in this meeting but that all issues would be considered by Pharmac.

3.8. The Advisory Group noted concerns raised in the consultation feedback that the previously proposed criteria were overly broad and would allow access to younger patient groups when increasing older age was a significant factor in risk for severe COVID-19 disease.

3.9. The Advisory Group noted feedback that the age and ethnicity access criteria may create barriers to access for paediatric patients with complex medical conditions such as high-risk lung disease. The Group noted that the proposed criteria did not exclude paediatric patients from accessing nirmatrelvir with ritonavir and molnupiravir. However, paediatric patients have not been considered explicitly in the development of the criteria due to a lack of clinical data on safety and efficacy. The Group noted that COVID-19 is generally less severe in children.

3.10. The Advisory Group considered the ethnicity components of the access criteria. The Group noted the equity issues faced by many Māori and Pacific peoples in accessing healthcare as well as the differing health profiles of Māori and Pacific peoples within

Aotearoa New Zealand, alongside their higher COVID-19 case-morbidity (Steyn et al. N Z Med J. 2021;134:28-43), and concluded that including ethnicity-based criteria was both appropriate and proportionate. The Group considered that the criteria for Māori and Pacific peoples should be in addition to the diagnosed comorbidities listed in the criteria, as many Māori and Pacific peoples have greater rates of both diagnosed and undiagnosed comorbidities and have less access to appropriate healthcare. The Group considered that the proposed tightening of access criteria by risk factors would address the concerns raised in the consultation process around age-based access for different patient groups.

3.11. The Advisory Group considered feedback requesting access to nirmatrelvir with ritonavir and molnupiravir for people with rare disorders. The Group noted that there are potentially a large number of rare disorders and noted that in many cases a rare disorder is not necessarily a risk factor for poorer outcomes or progression to severe COVID-19. The Group considered that further consideration of the impact on rare disorders was appropriate and that some may need to be included in the list of risk factors. Members noted evidence is limited in this space and considered that determining which rare disorders would put people at most at risk would be challenging. The Group noted feedback on haematology risk factors and sickle cell disease in COVID-19 patients. The Group noted that for some groups one antiviral would be more appropriate, due to the mechanism of action or potential drug interactions with ritonavir, and that detailed and clear guidance will be needed for prescribers.

3.12. The Advisory Group considered feedback on the inclusion of vaccination status in the access criteria. The Group noted that two doses of vaccination against COVID-19 remained highly effective against severe disease and that booster doses further increased the level of protection. The Group noted the greatly increased vulnerability of people who were unvaccinated or did not respond to a primary course of vaccination to severe COVID-19 disease, as well as the limited supply of both oral antivirals. The Group considered that inclusion of vaccination status in the access criteria was clinically appropriate given these peoples increased risk.

3.13. The Advisory Group considered the potential for weighting different co-morbidities and factors for treatment with oral antivirals. The Group noted that at this stage of the Omicron variant outbreak definitive Aotearoa New Zealand COVID-19 hospital and ICU admissions data is not available and considered that without such data to inform risk criteria it would be difficult to appropriately weight different risk factors.

3.14. The Advisory Group considered the recent WHO Guidelines for treatment with molnupiravir and noted the WHO's proposed threshold of recommending treatment of people with a greater than 10% chance of requiring hospitalisation for COVID-19.

3.15. The Advisory Group concluded that the criteria for both nirmatrelvir with ritonavir and molnupiravir should be harmonised and that detailed and clear guidance should be developed for prescribers to be able to correctly select the appropriate treatment.

3.16. The Advisory Group concluded that the current proposed criteria for oral antiviral access were too broad, given the likely supply constraints and potential issues around access.

3.17. The Advisory Group noted that no priority ranking (within the context of treatments for COVID-19) was sought by Pharmac, reflecting the rapidly evolving evidence for treatments in COVID-19 and separate funding outside the Combined Pharmaceutical Budget, and therefore did not need to discuss a priority ranking.

3.18. The Advisory Group considered that the PICO (population, intervention, comparator, outcomes) information for nirmatrelvir with ritonavir and molnupiravir to be the same as previously considered in the December 2021 meeting.

Remdesivir access criteria

3.19. The Advisory Group noted that the remdesivir access criteria had recently been updated to align with the criteria for nirmatrelvir with ritonavir and molnupiravir proposed by the Group in February 2022. The Group considered that the access criteria for remdesivir should be updated in light of the latest feedback on nirmatrelvir with ritonavir.

4. Pharmac Update and Horizon Scanning

Discussion

4.1. The Advisory Group noted that Pharmac is working to secure a portfolio of COVID-19 treatments for New Zealand that cover all severities of illness and variants.

4.2. The Advisory Group noted that at the time of the meeting there were four treatments that were currently available and explicitly funded in New Zealand for the treatment of COVID-19 including: tocilizumab, baricitinib, remdesivir, casirivimab and imdevimab.

4.3. The Advisory Group noted that tocilizumab is currently subject to supply constraints with very limited availability. The Advisory Group noted that supply of baricitinib had been secured as an alternative to tocilizumab for the treatment of COVID-19 and was funded subject to the same access criteria in Part II Section H of the Pharmaceutical Schedule for the treatment of moderate to severe COVID-19.

4.4. The Advisory Group noted that casirivimab with imdevimab had been funded and listed on the Pharmaceutical Schedule for the treatment of COVID-19 from 1 February 2022. The Advisory Group noted that based on emerging evidence and information provided by the supplier (Roche) casirivimab with imdevimab was not expected to be effective against the Omicron variant of SARS-CoV-2.

4.5. The Advisory Group discussed that due to the evolving nature of COVID-19, recommendations and decisions to secure treatments were being made based on limited evidence. The Advisory Group acknowledged that there was a risk that not all treatments would be effective against all variants, and this was why a portfolio approach had been adopted.

4.6. The Advisory Group considered it would be important to continue to have regular meetings to review evidence for the effectiveness of available treatments for COVID-19 against emerging variants to ensure that effective treatments remain available, and the access criteria remain appropriate.

4.7. The Advisory Group noted that at the time of the meeting the Omicron variant of SARS-CoV-2 was dominant in New Zealand. The Advisory Group discussed that compared to the Delta variant Omicron appeared to result in a milder illness for the majority of people and lower rates of COVID-19 hospitalisation and ICU admission. The Advisory Group considered it would be important to consider currently circulating and emerging variants of COVID-19 when considering future treatments for COVID-19 and horizon scanning.

4.8. The Advisory Group noted that Pharmac was in the process of negotiating final agreements for 60,000 courses each of two oral antiviral treatments for COVID-19 (nirmatrelvir with ritonavir and molnupiravir) and it was expected that these treatments could be available from March-April 2022, subject to Medsafe approval and supply delivery timeframes.

4.9. The Advisory Group discussed at that the time of the meeting the PANORMIC trial, evaluating the effectiveness of molnupiravir was ongoing. The Group considered it would be important to review the results of this trial once they become available.

4.10. The Advisory Group noted that Pharmac is also in discussions with two suppliers of monoclonal antibody treatments (tixagevimab with cilgavimab and sotrovimab), which appear to be effective in the treatment of currently circulating variants of COVID-19.

4.11. The Advisory Group discussed that it could be challenging to administer monoclonal antibody treatments to eligible people within the required timeframe as administration is typically undertaken in a hospital setting. The Advisory Group discussed that for this reason oral antiviral treatments were expected to be more suitable for use in the community.

4.12. The Advisory Group noted that Pharmac had engaged with a number of suppliers of potential treatments for COVID-19 including fluvoxamine, sarilumab lenzilumab, regdanvimab and ensovibep, The Advisory Group considered that bebtelovimab, a monoclonal antibody treatment supplied by Eli Lilly and recently granted Emergency Use Authorisation (EUA) by the Food and Drug Administration (FDA) could also be added to this list.

4.13. The Advisory Group considered it would be important to continue to evaluate new and existing treatments for COVID-19 as evidence for effectiveness emerges.

4.14. The Advisory Group considered it would also be important to regularly consider the composition of New Zealand's portfolio of COVID-19 treatments and the access criteria for these as new variants of COVID-19 emerge, which may cause different severities of illness or disease progression.

4.15. The Advisory Group considered it would be important for data on the people receiving funded COVID-19 treatments to be collected and regularly reviewed to ensure the populations with the highest health needs are being targeted by access criteria and receiving treatments.