Record of the COVID Treatments Advisory Group Meeting held on 13 June 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 Duffy
Dr Gillian Hood
Dr Graham Mills
Dr Justin Travers
Dr Kerry Benson-Cooper
Associate Professor Marius Rademaker
Dr Nigel Raymond
Dr Robyn Manuel
Professor Stephen Munn

Apologies
Dr Jessica Keepa
Dr Tim Cutfield

1. Antiviral Treatments Update

Application

1.1. The Advisory Group reviewed the additional information for Omicron BA.2 sotrovimab and casirivimab with imdevimab efficacy.

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

Recommendation

1.3. The Advisory Group **recommended** that the antiviral access criteria be amended as follows (deletions in strikethrough, additions in bold):

Access criteria – from any relevant practitioner.

Approvals are valid for patients where the prescribing clinician confirms the patient meets the following criteria and has endorsed the prescription accordingly:
All of the following:

1. Patient has confirmed (or probable) symptomatic COVID-19, or has symptoms consistent with COVID-19 and is a household contact of a positive case; and
2. Patient's symptoms started within the last 5 days (if considering nirmatrelvir with ritonavir or molnupiravir) or within the last 7 days (if considering remdesivir); and
3. Patient does not require supplemental oxygen[#]; and
4. Either:
   - 4.1. The patient meets one of the following:
     - 4.1.1. Patient is immunocompromised* and not expected to reliably mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection, regardless of vaccination status; or
     - 4.1.2. Patient has Down syndrome; or
     - 4.1.3. Patient has sickle cell disease; or
   - 4.2. Patient has at least FIVE of the following factors:
     - 4.2.1. Any combination of high risk medical conditions for severe illness from COVID-19 identified by the Ministry of Health** (with each individual condition counting as one factor)
     - 4.2.2. Māori or any Pacific ethnicity (counts as one factor)

4.2.3. Patient is aged 65 years and over (counts as two factors, or three if patient has not completed a full course of vaccination), or is 50 years and over (counts as one factor)
4.2.4. Patient has not completed a ~~full course~~ **2 doses** of vaccination~~***~~(counts as one factor); and

5. Not to be used in conjunction with other COVID-19 antiviral treatments.

Notes:
Consider molnupiravir or remdesivir if nirmatrelvir with ritonavir is unsuitable or unavailable.
* As per Ministry of Health criteria of 'severe immunocompromise' for third primary dose
** People with high risk medical conditions identified by the Ministry of Health
~~*** 'Fully Vaccinated' defined as per the Ministry of Health definition.~~
Supplemental oxygen to maintain oxygen saturation >93% or at or above baseline for patients with chronic resting hypoxia

1.4. The Advisory Group recommended this change in response to the update to Manatū Hauora – Ministry of Health's definition of "up-to-date vaccination" and considered that specifying the doses required was the most concise and clear way to describe those most at risk.

1.5. The Advisory Group did not recommend changes to the criteria regarding rurality because there is not clear evidence for inequitable outcomes from COVID-19 within rural communities and that increasing access to these medicines was not able to be addressed by changing the funded access criteria. The Group considered that rural access would be improved by changes in the delivery of the treatments and people's awareness of the availability of treatment.

1.6. The Advisory Group considered the reference to Manatū Hauora's list of high-risk factors should be removed and replaced with a list produced in collaboration with the Manatū Hauora and Pharmac. The Group deferred a recommendation until a suggested list was able to be assessed by them.

Discussion

Acknowledgement

1.7. The Advisory Group acknowledged again 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.

Māori impact

1.8. The Advisory Group considered the overall dispensing rates for Māori and Pacific peoples appeared to be in line relative to other ethnicities in New Zealand but noted that there were known areas where dispensing rates were lower than expected, particularly, isolated rural communities such as the rural East Coast of the North Island. The Group noted that anecdotally eligible people are not requesting antivirals from their GP and so uptake is not as high as expected. The Group noted particularly in the East Coast, the impact of road closures on the ability for supplies of treatment to reach the furthest communities and people's ability to get to the hospital if higher level care is needed. The Group considered that there is not clear evidence for inequitable outcomes from COVID-19 within rural communities and that increasing access to these medicines was unlikely to be addressed by changing the access criteria. The Group considered rural access is

likely to be improved by changes in the delivery of the treatments and people's awareness of the availability of treatment.

Uptake of oral antiviral treatments

1.9. The Advisory Group noted the results of a Royal College of General Practitioners (RNZGP) survey about the prescribing of oral antiviral treatments for COVID-19 which suggested that the main barriers to patients receiving treatments were time and resource constraints, and the workforce capacity feeding into general practice. The Group noted the difficulty for some communities, particularly rural communities, to see a GP and the negative impact this would have on their ability to access treatment. The Group also considered there may be a general social shift in attitude to COVID-19 within the community, where it is becoming accepted and therefore there is less urgency to receive these medicines.

1.10. The Advisory Group noted that those that are eligible for oral antiviral treatment are potentially not accessing them due to a lack of awareness of the availability of these medicines. The Group considered that if those that are eligible are not being prescribed an oral antiviral and as a result the rates of dispensing are low then further widening of the access criteria will not help target this group any more than current criteria. The Group considered that increasing awareness within eligible groups, namely Māori and Pacific peoples and those with higher-risk co-morbidities, would be a more effective way to target the treatments and encourage uptake. The Group noted Manatū Hauora's campaigns to date including communications with the disability sector, Down Syndrome Association, Māori and Pacific providers, and direct communications with those that have had 3 primary doses of the COVID-19 vaccine and information is also available on Manatū Hauora's website and the Unite Against Covid website. The Group considered this contrasted with the messaging for antibiotic use in the community where people are encouraged not to use or request antibiotics to reduce antibiotic resistance and was potentially confusing for the public.

1.11. The Advisory Group considered the effort for people to continue to get tested, as societally we move into an endemic phase where COVID-19 in the community is more accepted. The Group noted that the dispensing rate reported was dependent on the number of people reporting a positive test to Manatū Hauora and that there is an unknown group of people that may have had COVID-19 but not tested or reported. The Group also noted the impact of accessibility of Rapid Antigen Tests (RATs) on people's ability to report a positive test where those unable to access RATs are not able to test and therefore may face additional difficulties receiving an antiviral treatment.

1.12. The Advisory Group considered the proportion of people with COVID-19 in the Intensive Care Unit (ICU) currently, to be less than those with influenza. The Group considered the estimate of those in ICU because of COVID-19 would be 8-10 people with the peak being around 33-40 people nationwide. The Group noted that in pregnant people Omicron variants are 14 times less severe than the Delta variant. The Group noted that data from ICUs is not yet available to understand the clinical significance of those with COVID-19 and their use of funded COVID-19 treatments prior to admission to hospital or the ICU.

1.13. The Advisory Group considered the potential upcoming wave of COVID-19 cases is likely to affect mostly those over 50 years old. The Group considered that the available stock of oral antivirals was sufficient to allow for greater uptake and noted the possibility to obtain more stock in the future.

New definition of vaccination

1.14. The Advisory Group noted that on 24 May 2022 the Ministry of Health made the decision to replace its previous definition for 'Fully Vaccinated' with a new definition for being 'up-to-date' with your vaccinations. The Group noted that applying this change in definition to the access criteria would mean that people who have not received booster vaccinations despite being eligible would be considered to have incomplete vaccination against COVID-19. This is a factor for access to antiviral COVID-19 treatments and therefore would be expected to increase uptake.

1.15. The Advisory Group noted that the cumulative hospitalisation rates from August 2021 to present comparing those with differing vaccination status reported hospitalisation rates in those cases that were not vaccinated compared to those cases that were vaccinated with 2 doses and those that were boosted, and considered that the most significant difference was between the unvaccinated and the vaccinated with two doses groups. The Group estimated the number needed to treat (NNT) to prevent one hospitalisation for unvaccinated people to be 42 people compared to vaccinated with at least two doses. The Group considered that the NNT would be estimated as 500 people to prevent one hospitalisation if those who only received two doses of the vaccine were included in the definition of "unvaccinated" in the access criteria. The Group noted that during the time this data was collected that the variant environment has changed from Delta to Omicron variant dominance and that the hospitalisation rate across all vaccination statuses has likely fallen with this shift. The Group considered that this was a good reason not to change the definition of vaccination to include booster and additional doses of COVID-19 vaccine, as the NNT with antivirals would be significantly increased with very little benefit.

1.16. The Advisory Group considered that, in general, it is preferred to have a single definition of 'Vaccination' that applies across the sector. The Group noted the Manatū Hauora updated definition would change the meaning of "fully vaccinated' within the current access criteria.

1.17. The Advisory Group noted that if this change was adopted all people who had received a primary course of vaccination against COVID-19 (two doses) but had not received a booster, or additional doses of COVID-19 vaccination would not necessarily be eligible as they would require other co-morbidities for funding. The Group considered this group could be estimated as 12,000 people per week but could not estimate the total number of people that would potentially be eligible within this group. The Group considered the potential impact of adopting the Manatū Hauora definition of being 'up to date' on vaccinations on stock levels and the risk of people at significantly higher risk of severe illness following SARS-CoV-2 infection being unable to access treatment.

1.18. The Advisory Group estimated the number needed to harm (NNH) from these medicines (adverse effects including gastrointestinal upset) to be 50 (ie a 2% absolute excess

incidence of adverse effects) and considered that the NNT should at least match this, otherwise the treatments could be causing more harm than benefit.

1.19. The Advisory Group considered that references to 'fully vaccinated' within the access criteria be interpreted as those people who have received 2 or more doses of a COVID-19 vaccine, and did not recommend changes to the access criteria for antiviral treatments to reflect Manatū Hauora's definition for being 'up to date' with COVID-19 vaccination.

Inequities in access

1.20. The Advisory Group noted that ensuring comprehensive, quality services for people living in rural areas is a priority for the Government. The Group noted that Pharmac had received requests from stakeholders, including Manatū Hauora, to consider including rurality as a factor for access to antiviral treatments for COVID-19. The Group noted that some rural locations are likely to mean that a person does not have easy access to a Te Whatu Ora Hospital or other healthcare services that may be available in urban centres.

1.21. The Advisory Group noted the dispensing rate (courses dispensed over notified cases) was stable. The Group noted that the dispensing rate increases with age as expected. The Group noted that although this rate was stable it was likely lower than expected. The Group noted that this information did not include dispensing in hospital or on a PSO or standing order which may be more likely to occur outside urban settings. The Group noted the overall dispensing rates for Māori and Pacific peoples appeared to be in line with dispensing rates to people of other ethnicities in New Zealand but noted that there were known areas where rates were lower than expected, particularly, isolated rural communities such as the rural East Coast of the North Island.

1.22. The Advisory Group noted those in rural areas were accessing oral antivirals at a lower rate than urban areas. The Group noted that there was a correlation with lower rural dispensing rates and areas with significant rural Māori populations, particularly the East Coast of the North Island. The Group considered the provided heat maps describing travel time to GP clinics, pharmacies, and local schools where medicines could be kept, noting that even very rural areas had a GP clinic within 30-60 minutes however, the availability of appointments at these clinics was not described. The Group considered that an increase in the time to arrival at medical facilities could result in otherwise eligible people being unable to receive treatment (because they may exceed the time window for receiving treatment) which would likely increase the risk of death, hospitalisation or complication from COVID-19.

1.23. The Advisory Group considered the possibility of education about the availability of the oral antivirals in combination with widening access for rural people to improve uptake within these communities. The Group noted that anecdotally people are not requesting antivirals from their GP and so uptake is not as high as expected. The Group noted that particularly in the East Coast, the impact of road closures on the ability for supply to reach the furthest communities and their ability to get to the hospital if higher level care is needed.

1.24. The Advisory Group considered the likelihood of the availability of other healthcare professionals including Pharmacists and Nurse Practitioners in rural areas and the benefit to access for rural people if they were able to prescribe and dispense the

treatments to people to reduce the barrier of two centres involved in the prescription and dispensing of treatment. The Group noted that pharmacy could be well placed to provide single point access for RATs and treatment following a positive test. The Group considered that other community hubs (supported by healthcare professionals) could be used as single point access clinics in a similar way. The Group considered the ability of pharmacists to certify or confirm comorbidities for those requiring treatment to be dependent on the person's ability to self-identify their co-morbidities or access this information on behalf of the person via their medical records. The Group noted that nationwide pharmacist access to medical records (to certify comorbidities) differs, but majority of the country has some access through different systems depending on the region. The Group considered there would be increased coverage over weekends if pharmacists were able to prescribe and dispense oral antivirals that would be beneficial given the time-restricted nature of the treatments. The Group noted that prescribing and dispensing by pharmacists had successfully been implemented in Quebec, Canada.

1.25. The Advisory Group noted that Manatū Hauora had received feedback from rural communities requesting widened access criteria to include people living rurally. The Advisory Group noted that none of its members were rural health experts, however it had been asked by Pharmac to consider this. The Group considered that based on the evidence it had available there was no clear evidence for inequitable outcomes from COVID-19 within rural communities and changing the access criteria would not be expected to improve people's ability to access these medicines. The Group considered it was likely rural access would, be improved by changes in the delivery of the treatments and people's awareness of the availability of treatment.

Further consideration of the funding criteria for oral antivirals

1.26. The Advisory Group noted the reference to the Manatū Hauora website for the high-risk conditions within the oral antiviral criteria. The Group noted that the intention of this was to have a single source of information for prescribers to refer to, and it aligns with Manatū Hauora without needing to update the criteria every time Manatū Hauora updates its list. The Group considered that the Manatū Hauora list on their website lacked clear clinical governance and was intended for people to check if they were considered high risk, not as clinical guidance. The Group considered that a list of high-risk conditions should be included in the criteria. The Group considered a collaborative list would be a useful way to meet both Manatū Hauora and Pharmac's needs.

1.27. The Advisory Group considered the implementation 'tick-box' tool could be useful to help with clarity and interpretation of the of the criteria and for prescribers to understand whether their patient is eligible. The Group noted that there is an existing tool available on the Pharmac.

1.28. The Advisory Group noted the inclusion of specific conditions, specifically Down syndrome and sickle cell anaemia within the criteria, as people with conditions are at significantly higher risk of severe COVID-19 than others. The Group noted that this meant they are included twice, once within the Ministry list and additionally in the Pharmac criteria to increase the ability of people with high-risk conditions to access treatment.

Remdesivir update

1.29. The Advisory Group noted that the use of remdesivir had decreased since oral antiviral treatments had become available. The Group noted that remdesivir was being used as an alternative to nirmatrelvir plus ritonavir and in people who are hospitalised and are expected to progress to severe illness.

1.30. The Advisory Group noted that the hospital access criteria for remdesivir were proposed to be widened to reduce the barrier for use in moderate disease. The Group considered the proposed criteria to be appropriate noting specifically people eligible to receive remdesivir should not be on or be expected to require mechanical ventilation within the next 24 hours. The Group considered that people receiving non-invasive ventilation should be eligible to receive remdesivir if required and it is unlikely to cause harm in this context. The Group considered that the differentiation should be made clear within national guidelines.

1.31. The Advisory Group noted that the wider criteria for remdesivir was only applied in hospital settings. The Group considered the availability of remdesivir to people who are hospitalised in the home and considered that they would already be covered by the hospital criteria. The Group considered that the broad definition of hospitalisation could include people that are being given outpatient therapy (eg outpatient infusion services) in addition to these people being covered by the community criteria.

2. Omicron BA.2 sotrovimab and casirivimab with imdevimab efficacy

Application

2.1. The Advisory Group reviewed the application for Omicron BA.2 sotrovimab and casirivimab with imdevimab efficacy 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 **recommended** that consideration for change of the proposed Access Criteria for sotrovimab and current Access Criteria for casirivimab with imdevimab be deferred until there is more data to support the efficacy and safety of these medicines in Omicron BA.2.

Discussion

Sotrovimab background

2.4. Sotrovimab in the treatment of COVID-19 was considered by the Advisory Group at its April 2022 meeting. The Group noted growing evidence that sotrovimab may not be effective against BA.2 Omicron subvariants. At the time of the meeting (3 June 2022), Omicron BA.2 was the dominant subvariant in New Zealand making up 99% of the sequenced community cases in the past 2 weeks. Sotrovimab compared to other monoclonal antibodies demonstrated retained efficacy against the BA.1 Omicron subvariant of SARS-CoV-2. Early results reported for the use of sotrovimab in the

treatment of the BA.2 Omicron subvariant of SARS-CoV-2 suggested reduced efficacy. In response to these reports and data shared with it by the suppler, the FDA announced on 4 May 2022 that sotrovimab is no longer authorised to treat COVID-19 in any U.S. region because the authorised dose of sotrovimab (500 mg) is unlikely to be effective against the BA.2 subvariant, which had since become the dominant variant of SARS-CoV-2 in the USA. The FDA also concluded that additional clinical safety data, in the authorised population (treatment of mild to moderate COVID-19), would be required to support increasing the dose of sotrovimab for use in treating patients with the Omicron B.1.1.529/BA.2 subvariants.

Casirivimab with imdevimab background

2.5. The Advisory Group noted that there are a number of studies reporting a reduction of *in vitro* efficacy of casirivimab with imdevimab against the Omicron BA.1 variant of SARS-CoV-2 (Takashita et al. 2022; Iketani et al. 2022; Bruel et al. 2022). Considering these reports, the FDA made the decision to limit the use of casirivimab with imdevimab to only when a patient has been infected with a susceptible variant. In response to the BA.2 subvariant of Omicron becoming dominant the FDA requested Roche provide information regarding whether higher doses may neutralise the BA.2 subvariant of Omicron. The Advisory Group noted Roche had prepared two papers and a presentation detailing these findings. In summary, the mean fold reduction in neutralisation activity of casirivimab with imdevimab against BA.1 was >1,460-fold compared to reference virus. In comparison the mean fold reduction in neutralisation activity of casirivimab with imdevimab against BA.2 was >315-fold when evaluated in serum and *in vitro*.

Discussion

2.6. The Advisory Group considered why resistance to monoclonal antibodies is increasing over time. It was assumed that vaccine pressure was causing a general decrease in efficacy in monoclonal antibodies that target the spike protein of the virus. It was considered that the susceptibility of future variants was unpredictable and therefore the ongoing use of these treatments would be unknown.

2.7. The Advisory Group considered that these treatments would likely be used in the severely immunocompromised patient group for those with mild to moderate COVID-19. The Group considered that there was a potential gap in the availability of treatments for patients that initially presented with mild to moderate illness but had not yet progressed to persistent infection. It was noted that these patients are usually under specialist care and if there are concerns that serological testing for COVID-19 antibodies is used.

2.8. The Advisory Group considered that sotrovimab should not be excluded from use in double therapy (convalescent plasma or antivirals plus a monoclonal antibody) in treatment of severely immunocompromised patients. At the time of the meeting the Advisory Group noted that these patients are being treated with convalescent plasma only.

2.9. The Advisory Group considered the following changes to the access criteria:

2.9.1. The Advisory Group noted that the criteria for casirivimab with imdevimab and proposed criteria for sotrovimab contained dosing criteria. The Group considered

that this could be changed on the receipt and assessment of the above information requested by the FDA in relation to these treatments and Medsafe approval.

2.9.2. The Advisory Group considered simplifying the criteria so only to include the profoundly immunocompromised that have likely to have not responded or have serological confirmation of lack of adequate response and are under care of appropriate specialists.

The Advisory Group considered that due to the lack of current data for sotrovimab and casirivimab with imdevimab efficacy in Omicron BA.1 and BA.2 subvariants that no recommendation to change the access criteria could be made. The Group considered that more safety and efficacy data was needed.

3. Pharmac draft consultation: access criteria for tixagevimab with cilgavimab and sotrovimab and for treatment of persistent infection

Application

3.1. The Advisory Group reviewed the draft consultation containing the access criteria for tixagevimab and cilgavimab for the pre-exposure prophylaxis of COVID-19.

3.2. The Advisory Group reviewed the draft consultation containing the access criteria for sotrovimab for COVID-19 in the treatment of high-risk immunocompromised patients.

3.3. The Advisory Group reviewed the draft consultation containing the access criteria for nirmatrelvir with ritonavir, molnupiravir, remdesivir, casirivimab with imdevimab, sotrovimab, and tixagevimab and cilgavimab for the treatment of persistent SARS-CoV-2 infection.

Recommendation

3.4. The Advisory Group recommended that tixagevimab and cilgavimab be funded for the prophylactic treatment of COVID-19, subject to the following access criteria:

Indication – Pre-exposure prophylaxis

Access criteria - Any relevant practitioner. Approvals are valid for patients where the prescribing clinician confirms the patient meets the following criteria and has endorsed the prescription accordingly:

All of the following:

1. Patient does not currently have COVID-19 infection
   AND
2. Either
   - 2.1. Patient is severely immunocompromised and considered to be at risk of inadequate immune response to COVID-19 vaccination or infection due to one of the following clinical situations:
     - B-cell or T-cell depleting therapy (eg rituximab, obinutuzumab, ocrelizumab) within the previous 12 months or planned to receive within two weeks of tixagevimab and cilgavimab administration
     - Receiving Bruton tyrosine kinase inhibitors
     - Chimeric antigen receptor T cell recipient
     - Haematopoietic stem cell transplant recipient within last 12 months, or who has chronic graft versus host disease or who requires significant ongoing immunosuppression for another reasons
     - Haematologic malignancy and is on active therapy
     - Lung transplant recipient (any time frame)

- Solid-organ transplant recipient within last 12 months
- Combined primary immunodeficiency syndromes (including Severe combined immunodeficiency (SCID))
- Common variable immunodeficiency (CVID) with additional T-cell defects, past opportunistic infection or requiring immunosuppressive therapy
- Newly diagnosed humoral immunodeficiency with baseline IgG < 3g/L
- HIV with a CD4 T lymphocyte cell count <200 cells/mm3
- Sphingosine 1- phosphate receptor modulator therapy (eg fingolimod) within previous 12 months
- High dose cyclophosphamide (>1g/m2) within previous 6 months.

OR

2.2 Patient is not able to be vaccinated against COVID-19 due to a medical reason (for example a history of severe adverse reaction to a COVID-19 vaccine or components) and is considered at high risk of severe illness from COVID-19 infection.

3.5. In making this recommendation, the Advisory Group considered:

- The consultation should include the reasons for not including serology testing in the criteria to identify eligible people, and specific questions regarding the equitable use of serology
- Patient group size estimated at 10,000 to 20,000 people
- Changes to criteria as follows:
    - Inclusion of Bruton tyrosine kinase inhibitors,
    - B-cell and T-cell depleting therapy criteria combined (pre and post treatment),
    - Immuno-deficiency group specified as combined primary immunodeficiency, common variable immunodeficiency, with additional T-cell defects, past opportunistic infection or requiring immunosuppressive therapy,
    - CD4 T lymphocyte cell count in HIV group increased to <200 cells/mm^3, and
    - Hypogammaglobulinemia included as 'Newly diagnosed humoral immunodeficiency with baseline IgG <3g/L'

3.6. The Advisory Group **recommended** that sotrovimab be funded for the treatment of COVID-19 for high-risk immunocompromised patients, subject to the following access criteria:

Indication – Treatment of COVID-19 for high-risk immunocompromised patients
Access criteria – Any relevant practitioner
Approvals are valid for patients where the prescribing clinician confirms the patient meets the following criteria and has endorsed the prescription accordingly
All of the following:

1. Patient has confirmed (or probable) symptomatic COVID-19 or has symptoms consistent with COVID-19 and is a household contact of a positive case; and
2. COVID-19 is confirmed or very likely due to a sotrovimab-susceptible SARS-CoV-2 variant; and
3. Patient's symptoms started within the last 7 days; and
4. Patient does not require supplemental oxygen[#]; and
5. Treatment with a funded COVID-19 antiviral is not clinically appropriate; and
6. Patient is immunocompromised* AND is not expected to mount an adequate immune response to COVID-19 vaccination or COVID-19 infection, regardless of vaccination status

Notes:
* As per Ministry of Health criteria (external link) of 'severe immunocompromise' for third primary dose
# Supplemental oxygen to maintain oxygen saturation >93% or at or above baseline for patients with chronic resting hypoxia

3.7. In making this recommendation, the Advisory Group considered:

- Current evidence supporting good efficacy against the Omicron BA.2 variant of SARS-CoV-2 is limited, but considered that this will be used to treat those who are very vulnerable and in combination with other treatments
- Until there is more data on efficacy and patient group size, the criteria should remain in line with the trial eligibility criteria and could be reviewed pending more information
- The consultation should include the reasons for not including serology testing in the criteria to identify eligible people, and include specific questions regarding the equitable use of serology

3.8. The Advisory Group **recommended** that nirmatrelvir with ritonavir, molnupiravir, remdesivir, casirivimab with imdevimab, sotrovimab and tixagevimab with cilgavimab be funded for the treatment of persistent COVID-19, subject to the following access criteria:

Initial Application – Treatment of persistent COVID-19 infection*
Access criteria – Any relevant practitioner
Approvals are valid for patients where the prescribing clinician confirms the patient meets the following criteria and has endorsed the prescription accordingly
All of the following:
1. Patient has laboratory confirmed diagnosis of persistent COVID-19 infection (≥20 days); and
2. Patient is immunocompromised; and
3. A multidisciplinary team (including an infectious disease physician) considers the treatment plan to be appropriate.

Note: Indications marked with * are unapproved indications.

3.9. In making this recommendation, the Advisory Group considered:

- Baricitinib and tocilizumab should be excluded from funding for this indication
- This will likely be a small group that requires timely treatment and specialist inpatient treatment
- To avoid inclusion of people treated with Paxlovid asymptomatic but infectious rebound after 5 days without immunosuppression, the ‘patient is immunocompromised’ criterion should remain
- Criteria changes include removal of the criterion that specifies that a patient is not expected to mount an immune response to COVID-19 infection, as this is already implied by the indication

Discussion

Māori impact

3.10. The Advisory Group considered the impact on Māori and Pacific people in making the discussed changes. The Group considered there was no specific data for the persistent infection group and the number of Māori who would be included in this group. The Group considered that that it is likely that Māori will experience greater severe disease than non-Māori. The Group considered the impact on whanau of people with persistent infection. The Group considered that Māori whanau may be more directly affected by the extended isolation period required for these people. The Group noted that changes that impacted rural communities will have a greater effect on Māori within those communities.

Background of consult

3.11. We are seeking feedback on proposed access criteria for tixagevimab with cilgavimab (Evusheld) for the pre-exposure prophylaxis of COVID-19 in severely immunocompromised people at risk of COVID-19 infection, sotrovimab (Xevudy) for the treatment of mild to moderate COVID-19 infection in people at high risk of progression to severe disease, and treatment of persistent COVID-19 infection with any relevant currently funded treatment for COVID-19.

3.12. Changes are proposed to be made to the Pharmaceutical Schedule from 1 July 2022 in preparation of these treatments being available in July 2022. Access criteria would be implemented if approved by Medsafe and stock is available in the country.

3.13. Tixagevimab with cilgavimab was considered by the Advisory Group at the 13 December 2021 and 14 April 2022 meetings. Sotrovimab for the treatment of COVID-19 was considered the Advisory Group at its April 2022 meeting. Nirmatrelvir with ritonavir, molnupiravir, remdesivir, casirivimab with imdevimab, sotrovimab, and tixagevimab with cilgavimab for the treatment of persistent COVID-19 infection was considered by the Advisory Group at its May 2022 meeting. Based on the recommendations in these meetings initial access criteria was developed for consultation.

Tixagevimab with cilgavimab for pre-exposure prophylaxis

3.14. The Advisory Group considered that the tixagevimab with cilgavimab criteria for pre-exposure prophylaxis should target those people at increased risk of severe disease explicitly. The Group considered that not all patient groups are at equal risk of severe disease. The Group considered that the patient groups known to be affected should be the focus of the criteria, with the perceived at-risk group being secondary to these groups. The Group considered the proposed criteria included an estimated 10,000-20,000 people. The Group considered, due to unknown risk in this patient group, that likely numbers that would come to harm if untreated would be low (<100 people) potentially due to shielding or because the actual risk is lower than currently understood.

3.15. The Advisory Group considered that those at highest risk, if not using serology, would be those with at least a 50% risk that they have not responded to vaccination or will not respond to COVID-19 infection. The Group noted this was to represent this as the first-priority group. The Group considered that the evidence for benefit is limited, and this makes targeting groups for treatment difficult.

3.16. The Advisory Group considered focusing on 5 major at-risk groups:

- people receiving B cell depleting agents,
- chimeric antigen receptor T cell recipients,
- haematopoietic stem cell transplant recipients,
- those with graft v host disease or
- solid organ transplant with acute rejection requiring treatment with B or T cell depleting agents

3.17. The Advisory Group considered the number of different jurisdictions have different lists for the pre-exposure prophylaxis target groups. The Group noted that, due to stock constraints, different jurisdictions targeted different groups of at-risk people. The Group

considered that these selections of people were likely developed during a time when the Delta variant was dominant and noted the BA.2 Omicron subvariant is currently the dominant variant in New Zealand.

3.18. The Advisory Group noted that those due to receive B-cell depleting therapy within two weeks of tixagevimab with cilgavimab administration are included in the criteria, so prophylaxis can be given prior to starting B-cell depleting therapy.

3.19. The Advisory Group considered that those on Burton tyrosine kinase inhibitors should be included in the high-risk group.

3.20. The Advisory Group considered that immune dysregulation has a wide definition and includes any patient with an immune-related issue. The Group considered that the criteria needed to be more specific to higher risk subgroups within those defined as immune dysregulation.

3.21. The Advisory Group considered that the haematological malignancies on active treatment group is a wide-ranging and this would likely include all people under the care of a haematologist.

3.22. The Advisory Group considered that there was potential cross over between those who had received a solid-organ transplant within the last 12 months and those with solid-organ transplants who had received recent treatment for acute rejection with T or B cells depleting agents. However, it was considered that one group was prior to treatment, and one was after treatment for acute rejection. The Group considered the solid organ transplant in the last 12 months would be sufficient to target the people most at risk.

3.23. The Advisory Group noted that T-cell deficiency was included in the access criteria, but not hypogammaglobulinemia. The Group considered that these individuals may receive adequate immunoglobulin passively however they should be considered in the group for funding.

3.24. The Advisory Group considered that the HIV group should include treated and untreated people. The Group considered that the CD4 <50 cells/mm^3 threshold was better set at CD4 <200 cells/mm3, as this is the threshold that AIDS symptoms would occur and thus an indicator of immunosuppression. The Group considered that this would likely be a small number of people.

3.25. At its April 2022 meeting, the Advisory Group recommended that SARS-CoV-2 antibody assay (serology testing) be used to assess those who have not responded to COVID-19 vaccination or infection as a criterion for accessing pre-exposure prophylaxis treatment. The Group considered that without serology the treatment group would be estimated around 20,000 people. The Group noted that serology testing was available, but the health system did not have the capacity to allow this group to be tested.

3.26. The Advisory Group also noted that outside of either no antibody or very high antibody titre there is no evidence of correlation between immune response and antibody titre in the context of Omicron. The Group noted that interpretation of these results is not currently clear, and testing is potentially inaccessible for some people. The Group considered optional serology testing to allow discretion for people that have had four

doses (three doses in a primary course and a booster) of vaccine to know they have not responded before having a 6-monthly gluteal injection.

3.27. The Advisory Group considered inequities surrounding use of serology in rural communities where there may be difficulty getting to a laboratory. The Group considered that small urban area serology services often only have single sites. The Group considered that giving people discretion to use serology may reduce inequities. The Group also considered that these inequities would include accessing services to administer the treatment, as it is given as two gluteal injections.

3.28. The Advisory Group considered that the consultation should include the discussion of serology and reasons for not including it as a requirement in the criteria. The Group considered that the consult should include specific questions regarding the use of serology and its definition.

3.29. The Advisory Group noted that tixagevimab with cilgavimab will be funded under the pre-exposure prophylaxis and persistent infection indications. The Group noted that people that have not cleared the infection in 20 days would have to delay administration of treatment until being funded under the persistent infection criteria. The Group considered this meant opportunistic prophylactic administration may be missed for hospitalised people with COVID-19. The Group considered this was a small group within the wider group considered for prophylaxis funding and there is currently limited evidence for use of tixagevimab with cilgavimab for treatment of COVID-19. The Group considered that these are distinct patient groups to be considered separately.

3.30. The Advisory Group considered that the risk of an immunocompromised patient getting re-infected within the three-week window after clearing COVID-19 before being given tixagevimab with cilgavimab for prophylaxis was low. The Group considered that if a patient is able to clear an infection, then that is evidence of some degree of immunity against severe disease and death. The Group considered that an immunocompromised patient who can clear a SARS-CoV-2 infection will potentially have better protection from other variants of SARS-CoV-2 than someone who has never been infected or is unable to mount an immune response (persistent infection). The Group considered that this is dependent on the SARS-CoV-2 variants in circulation.

3.31. The Advisory Group considered that if a person can clear a SARS-CoV-2 infection then they have a proven immune response compared to someone with no SARS-CoV-2 exposure. The Group considered that the people able to mount an immune response will likely have a lesser response and for a shorter period and that due to the changing variant environment, a previous serological response does not assure immune response to another variant.

3.32. The Advisory Group considered the length of time after recovering from COVID-19 that a patient could be offered tixagevimab with cilgavimab for prophylaxis. The Group considered that there was insufficient evidence to make a recommendation at this time.

Sotrovimab for high-risk immunocompromised patients

3.33. The Advisory Group considered the access criteria for sotrovimab. The Group noted that the proposed criteria were developed from the trial criteria. The Group noted that, as

discussed at the April 2022 meeting, there is limited evidence supporting efficacy against the Omicron BA.2 variant of SARS-CoV-2. The Group noted that the requirement for serology testing was removed in line with the advice sought.

3.34. The Advisory Group considered that this treatment would likely be used in people with persistent infection in combination with oral antivirals and convalescent plasma. The Group noted that this is a small group of patients. The Group considered until there is more data on the efficacy and patient group size that the criteria should remain in line with the trial criteria and could be reviewed on receipt of more information.

Treatment of persistent COVID-19 infection

3.35. The Advisory Group considered that the persistent infection access criteria. The Group noted that this was discussed during the April 2022 meeting. The Group noted that this patient group is exceptional but for timely administration of treatment standardised criteria would be the most practical option.

3.36. The Advisory Group noted that these criteria would apply to all COVID-19 treatments. The Group considered that tocilizumab and baricitinib should be excluded from funding under these criteria as they do not treat COVID-19 infection but its symptoms.

3.37. The Advisory Group considered that a confirmed deficiency is difficult to define and a lack of sufficient evidence of a neutralising response is more correct.

3.38. The Advisory Group considered that many people will have positive PCR tests after infection, but the target group are people with immunosuppression. The Group considered that rebound infection after treatment with Paxlovid where people are asymptomatic but infectious. The Group considered that this may not impact the patient themselves but may impact the community, they live in.

3.39. The Advisory Group noted that the criteria were HML only with the intention to restrict the treatment of persistent infection to hospital. The Group considered that the restriction for persistent infection to Section H (Hospital only) is in line with current process for these people. The Group considered the system impacts of hospitalising these people. The Group considered the small number of people in this group and that specialist monitoring and investigation in hospital would be required. The Group considered rurality of these people. The Group considered that these people would likely be known to hospital staff and would likely live close to secondary care given the nature and complexity of their conditions.