Record of the Immunisation Subcommittee of PTAC Meeting held on 10 August 2021

Immunisation Subcommittee records are published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2016.

Note that this document is not necessarily a complete record of the Immunisation Subcommittee meeting; only the relevant portions of the meeting record relating to Immunisation Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Immunisation Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;

(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.

PTAC Subcommittees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Subcommittee meeting will be reviewed by PTAC at its February 2022 meeting.

PTAC Subcommittees and PTAC may differ in the advice they provide to PHARMAC, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

PHARMAC is not bound to follow the recommendations made below. Applications are prioritised by PHARMAC against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or PTAC Subcommittees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

TABLE OF CONTENTS

Attendance 3
1. The role of PTAC Subcommittees and records of meetings 3
2. Record of previous meeting held 2 December 2020 3
3. Therapeutic Group and NPPA Review 3
Human papillomavirus vaccine (Gardasil 9) 4
Adult diphtheria and tetanus vaccine 4
Hepatitis B recombinant vaccine 4
Diphtheria, tetanus, pertussis and polio vaccine 4
Haemophilus influenzae type b vaccine 4
Measles, mumps and rubella vaccine 4
Meningococcal conjugate vaccines 5
Pneumococcal conjugate vaccine 5
Pneumococcal polysaccharide vaccine 6
Diphtheria, tetanus and pertussis vaccine 6
Bacillus Calmette-Guerin vaccine 6
Diphtheria, tetanus, pertussis, polio, hepatitis B and Haemophilus influenzae type b vaccine 6
Poliomyelitis vaccine 6
Hepatitis A vaccines 6
Varicella vaccine 6
Rotavirus oral vaccine 7
Influenza vaccine 7
4. MoH pre-pandemic influenza H5N1 vaccine in the National Reserve Supply 7
5. MoH varicella report 8
6. Influenza vaccine for people with serious mental health conditions or addiction 9
7. Pneumococcal threshold monitoring 12
8. Pneumococcal polysaccharide vaccine for people over 65 years of age 15

Attendance

Present

Sean Hanna (Chair)
Edwin Reynolds
Elizabeth Wilson
Giles Newton-Howes
Karen Hoare
Lance Jennings
Michael Tatley
Nikki Turner (via zoom)
Osman Mansoor
Stephen Munn
Stuart Dalziel
Tony Walls

1. The role of PTAC Subcommittees and records of meetings

1.1. This meeting record of the Immunisation Subcommittee of PTAC is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2016, available on the PHARMAC website at https://www.pharmac.govt.nz/assets/ptac-terms-of-reference.pdf.

1.2. The Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of PTAC Subcommittees and PTAC.

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

1.4. The Immunisation Subcommittee is a Subcommittee of PTAC. The Immunisation Subcommittee and PTAC and other PTAC Subcommittees have complementary roles, expertise, experience, and perspectives. The Immunisation Subcommittee and other PTAC Subcommittees may therefore, at times, make recommendations for vaccines and immunisation that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for vaccines and immunisation that differ from the Immunisation Subcommittee's, or PTAC Subcommittees may make recommendations that differ from other PTAC Subcommittees'.

PHARMAC considers the recommendations provided by both the Immunisation Subcommittee and PTAC and any other relevant PTAC Subcommittees when assessing applications for vaccines and immunisation.

2. Record of previous meeting held 2 December 2020

2.1. The Subcommittee reviewed the record of its previous meeting held on 2 September 2020 and agreed that the minutes be accepted.

3. Therapeutic Group and NPPA Review

Therapeutic group usage data and expenditure summary

3.1. The Subcommittee noted the vaccine distribution summary data and expenditure summary for all vaccines.

Human papillomavirus vaccine (Gardasil 9)

3.2. The Subcommittee noted that the 2020 nationwide COVID-19 Alert Level 4 and 3 lockdown interrupted the school-based programme so an extra spike in usage occurred in June 2020. Overall usage was less in 2020 than 2019, and usage in the first half of 2021 remains slightly lower than the previous two years.

3.3. The Subcommittee noted that public health nurses have a high workload due to COVID-19 related work. The Subcommittee considered this is highly likely to adversely impact the HPV school based programme. The Subcommittee noted that GPs have carried on offering HPV vaccination during lockdown, but outreach services are overwhelmed. Members considered that failure of the HPV school based programme may contravene the United Nations Convention on the Rights of the Child.

Adult diphtheria and tetanus vaccine

3.4. The Subcommittee noted that ADT Booster was delisted from 1 October 2020 and the eligibility criteria were added to those for Boostrix. The increase in distribution of Boostrix in 2020 reflects the transition of usage from ADT Booster to Boostrix.

Hepatitis B recombinant vaccine

3.5. The Subcommittee noted that there had been an extensive supply issue for HBvaxPRO, it was be delisted from 1 October 2020 and Engerix B was listed with sole supply status. The Subcommittee noted that following its advice to Pharmac that a smaller injection volume presentation would be preferred for infants, Engerix B 10 mcg was listed from November 2020.

3.6. The Subcommittee considered that lower usage of Engerix B may be as a result of reduced immigration and consequently fewer eligible people.

Diphtheria, tetanus, pertussis and polio vaccine

3.7. The Subcommittee noted the distribution of diphtheria, tetanus, pertussis and polio vaccine was lower during the COVID-19 lockdown than with previous years and continues to track lower than previous years up to June 2021.

Haemophilus influenzae type b vaccine

3.8. The Subcommittee noted the distribution of Haemophilus influenzae type b vaccine continued to track consistently with previous years, although was reduced during the COVID-19 lockdown period.

Measles, mumps and rubella vaccine

3.9. The Subcommittee considered that the 15-30 year old campaign is not going well, and many DHBs have delayed the programme until October 2021 as resources have been more directed to the COVID-19 vaccination programme. The Subcommittee noted that the MMR vaccine was not able to promoted at COVID-19 vaccination events, which was a missed opportunity. The Subcommittee considered that the equity gap has not been closed, and as it is likely that there will be future measles outbreaks, there is an urgent need to close the equity gap.

3.10. The Subcommittee noted that a few measles cases have been reported in South East Asia in 2021. Global rates are generally low, but it is expected that rates will rise as countries open their borders and international travel resumes.

3.11. The Subcommittee noted that the South Auckland measles outbreak mainly affected pre-school children. The Subcommittee considered it is highly likley that there will be future measles outbreaks and expressed concern that available resources are not being utilised to reach at-risk children.

3.12. The Subcommittee noted that the COVID TAG is considering the question of giving MMR vaccine at the same time as the COVID-19 vaccine. Members noted that there is not yet data available on concomitant administration. Members considered that from first principles the two could be administered together, but there is no data to inform this approach. Members considered that there could be an opportunity for COVID-19 vaccination appointments to be used for MMR screening.

Meningococcal conjugate vaccines

3.13. The Subcommittee noted that while usage of MenACWY vaccine is typically between 100 and 150 doses per month, there was a spike in distribution in December 2018 for the Northland MenW outbreak response.

3.14. The Subcommittee noted that since access to MenACWY vaccine was widened for people in close-living situations there is a smaller spike in January and February each year, likely due to secondary or tertiary students entering halls of residence or boarding hostels at the start of the academic year. The Subcommittee noted that Pharmac is actively considering proposals to fund a number of other groups.

3.15. The Subcommittee noted that proposals to fund MenB vaccine for a number of groups are also under active consideration for funding by Pharmac.

3.16. The Subcommittee considered that the number of meningococcal cases in 2020 was affected by COVID-19 public health measures and was lower than might otherwise have been expected. The Subcommittee considered that Pharmac should not use the 2020 usage figures as a basis for forecasting future vaccine usage or estimating health need, but should use the 2016-2019 years for these purposes. The Subcommittee considered that Pharmac should use 10 year average case data for meningococcal modelling purposes.

3.17. The Subcommittee noted that the proportion of group W meningococcal cases had been increasing until 2018, but from 2019 the proportion of group B cases had started to rise again. The Subcommittee considered that internationally there was a resurgence in group W cases, rather than the resurgence in group B cases seen in New Zealand. The Subcommittee considered that the prevalence of group B cases is high in Māori and Pacific peoples.

Pneumococcal conjugate vaccine

3.18. The Subcommittee noted the distribution and expenditure patterns for pneumococcal conjugate vaccines. The Subcommittee noted that usage of pneumococcal conjugate vaccines had reduced by a third since July 2020, which coincided with the change from a 3+1 to 2+1 dose schedule for PCV10.

Pneumococcal polysaccharide vaccine

3.19. The Subcommittee noted the distribution of pneumococcal polysaccharide vaccine (PPV23) increased significantly in March 2020, due to heightened public interest in pneumococcal vaccines.

Diphtheria, tetanus and pertussis vaccine

3.20. The Subcommittee noted that from 1 July 2019 access was widened for pertussis vaccine to include pregnant women from the second trimester of pregnancy, and parents or primary care givers of infants admitted to a Neonatal Intensive Care Unit or Specialist Care Baby Unit for more than three days.

3.21. The Subcommittee noted that usage had increased since July 2020, in line with the expected additional usage from the delisting of ADT Booster and subsequent usage of Boostrix for the 45 and 65 year old tetanus boosters. The Subcommittee noted that, to reflect current immunisation practice, the Boostrix eligibility criteria have been amended to state that the tetanus booster may be given for patients “from 45 years old” or “from 65 years old”. The Subcommittee considered that even though the previous eligibility criteria stated that patients were eligible in their 45th or 65th year, it was common practice to offer the boosters at some time after those ages.

Bacillus Calmette-Guerin vaccine

3.22. The Subcommittee noted that there was a long-standing shortage of BCG vaccine from June 2015 to June 2018. There have been no further supply issues.

Diphtheria, tetanus, pertussis, polio, hepatitis B and Haemophilus influenzae type b vaccine

3.23. The Subcommittee noted the distribution pattern of the hexavalent vaccine has been tracking consistently with previous years, apart from a reduction in usage during the 2020 COVID-19 lockdown.

Poliomyelitis vaccine

3.24. The Subcommittee noted that usage of poliomyelitis vaccine had increase from January-December 2019. Members considered that this may be related to increased vaccination rates in recent immigrants, particularly from countries where oral polio vaccine is used. The Subcommittee noted that usage has subsequently returned to normal levels.

Hepatitis A vaccines

3.25. The Subcommittee note the distribution for hepatitis A vaccines showed occasional peaks in distribution for both paediatric and adult vaccines, which were related to localised outbreaks.

Varicella vaccine

3.26. The Subcommittee noted that following the 2018 Vaccines RFP, a brand change from Varilrix to Varivax was implemented from 1 July 2020. Usage was reduced during the 2020 COVID-19 lockdown, and has been lower than usual up to June 2021.

Rotavirus oral vaccine

3.27. The Subcommittee noted that distribution of rotavirus oral vaccine remained steady over the last 12 months.

Influenza vaccine

3.28. The Subcommittee noted that for the 2021 influenza season, quadrivalent and adjuvanted quadrivalent vaccines are funded. Adjuvanted quadrivalent vaccine was funded to address manufacturing delays with quadrivalent vaccine. The Subcommittee noted that Pharmac is open to funding adjuvanted quadrivalent vaccine in future years, if it was offered on a cost neutral basis to quadrivalent vaccine, in line with the Subcommittee recommendation.

3.29. The Subcommittee noted that immunisation claims for funded influenza vaccine reached an all time high of 900,000 doses in 2020, but it is expected that claims for 2021 would be a similar level to previous years, in the range of 600,000-700,000 doses.

3.30. The Subcommittee noted that in 2020, influenza vaccine distribution reached an all time high of 1.7 million doses. The Subcommittee considered that this high uptake was driven by health sector messaging to prevent influenza to stay out of hospital and protect the health system for COVID-19 patients. The Subcommittee noted that due to significant ongoing uncertainty about the impact of COVID-19, the supplier agreed to obtain 2.4 million doses for 2021. However, based on distribution to July 2021, usage is expected to only reach 1.4 million doses for 2021.

3.31. The Subcommittee noted that funded influenza coverage rates for people over 65 years were: 62.5% for non-Māori, non-Pacific people, 45.8% for Māori and 55.8% for Pacific people. The Subcommittee considered that a significant equity gap still exists for Māori and Pacific people.

3.32.

NPPA applications

3.33. The Subcommittee noted that since September 2019, PHARMAC had received a small number of NPPA applications. These were for meningococcal B vaccine and HPV vaccine.

4. MoH pre-pandemic influenza H5N1 vaccine in the National Reserve Supply

Application

4.1. The Subcommittee considered a paper from the Ministry of Health seeking advice on the continued rationale for keeping pre-pandemic H5N1 influenza vaccine in the National Reserve Supply and whether there are additional influenza antigens that should be covered by a pre-pandemic influenza vaccine.

Discussion

4.2. The Subcommittee noted that New Zealand has maintained a Strategic National Reserve Supply (NRS) of critical items since 2007. This includes items which are held centrally by the Ministry of Health, including pre-pandemic H5N1 influenza vaccine.

4.3. The Subcommittee considered that influenza A viruses continue to circulate globally and have the potential to cause pandemics in some years, so holding a national reserve supply of influenza vaccine is still an important strategy to mitigate the risks of an influenza pandemic.

4.4. The Subcommittee considered that the H5 virus remains the highest risk antigen to protect against, although human-to-human transmission is rare. The Subcommittee considered that the H7N9 virus also has some pandemic risk, but the vaccination of poultry has reduced the number of human infections, so H5N1 would be the main virus of interest to protect against.

4.5. The Subcommittee considered that vaccine technology is changing, with some manufacturers investigating universal influenza vaccines to cover both major groups of influenza virus. The Subcommittee considered that the Ministry should continue to horizon scan for new vaccine developments as these could provide a more flexible pre-pandemic vaccine supply than the current strategy of maintaining reserves of the main strain of concern.

4.6. The Subcommittee considered it important to maintain a pandemic plan. The Subcommittee considered that recent experience from the COVID-19 pandemic should be used to refine the plan further. Factors that could be addressed in the plan include the risks that international travellers pose for spreading influenza, the use of dedicated managed isolation and quarantine facilities, and prioritising groups to receive vaccines first.

4.7. The Subcommittee considered that the 150,000 doses of vaccine held in the national reserve is a relatively small quantity. The Subcommittee considered that the Ministry should reconsider the quantity required, taking into account learnings from the COVID-19 response, including the priority groups to vaccinate. The Subcommittee considered that 150,000 doses would not be enough to cover all front-line health care professionals and border workers. The Subcommittee considered that there should be sufficient vaccine to cover essential workers.

5. MoH varicella report

Application

5.1. The Subcommittee considered a report from the Ministry of Health on the effect of vaccination on the epidemiology of varicella and zoster hospitalisations in New Zealand.

Discussion

1.1. The Subcommittee noted that varicella vaccines have been available in New Zealand since 1999. Since July 2017, a single dose of varicella vaccine has been publicly funded for:

1.1.1. Varicella (chickenpox)

- children at age 15 months
- previously unvaccinated children turning 11 years old on or after 1 July 2017 (who have not previously had a varicella infection)
- certain special groups and their household contacts if they are not immune to varicella.

1.1.2. Zoster (shingles)

- individuals at age 65 years
- catch-up of individuals aged 66-80 years, inclusive (the catch-up programme ceases on 31 December 2021).

5.2. The Subcommittee noted that varicella and zoster are not notifiable diseases, so the report used hospitalisations to describe the epidemiology. The Subcommittee considered that there are limitations to data based on hospital coding, so it is likely that not all relevant hospital admissions have been captured. The Subcommittee requested that the Ministry investigate the possibility of obtaining updated data on the burden of varicella and zoster in primary care, to brought to a future Subcommittee meeting.

5.3. The Subcommittee noted that varicella-related hospitalisations have halved for Māori and non-Māori in the period from 2016/17 to 2019/20. The Subcommittee considered that, while it is early days for the programme, the trends are looking promising with an overall decrease in hospitalisation burden.

5.4. The Subcommittee considered that use of a combined measles, mumps, rubella and varicella (MMRV) vaccine as a second dose given at 15 months of age would be a useful addition to the immunisation programme. The Subcommittee considered that there is an increased risk of febrile convulsions with MMRV compared to MMR and varicella given separately, but this risk can be lowered by giving MMRV as the second dose.

5.5. The Subcommittee considered that it would like Pharmac to again include an option for MMRV as a second varicella dose in its next competitive process for vaccines.

5.6. The Subcommittee noted that an additional shingles vaccine (Shingrix) has been approved by Medsafe. The Subcommittee noted that Shingrix is a recombinant vaccine, so has more favourable safety profile in the elderly, and particularly for the immunocompromised, than a live attenuated zoster vaccine. The Subcommittee considered that if Shingrix was listed on the Pharmaceutical Schedule in the future, one dose of Shingrix would be required for people previously immunised with Zostavax.

6. Influenza vaccine for people with serious mental health conditions or addiction

Application

6.1. The Subcommittee reviewed a funding application from the Pharmaceutical Society for influenza vaccine for people with serious mental health conditions or addiction.

Recommendation

1.2. The Subcommittee recommended that influenza vaccine for people with serious mental health conditions or addiction be listed with a medium priority within the context of vaccines and immunisation, subject to the following Special Authority criteria:

1.3. INFLUENZA VACCINE - people under 65 years of age who:
i) have any of the following serious mental health conditions:
a) schizophrenia, or
b) major depressive disorder, or
c) bipolar disorder, or

d) schizoaffective disorder, or
ii) are currently accessing secondary or tertiary mental health and addiction services.

6.2. In making this recommendation, the Subcommittee noted the significant health need of people with serious mental health conditions or addiction. The Subcommittee considered that although there was not strong empirical evidence for health benefit in this group, there was good biological and psychosocial plausibility for benefit. The Subcommittee considered that the group with mental health conditions that would benefit most from influenza vaccination was the same as that eligible for COVID-19 vaccination under the Group 3 criteria.

Discussion

6.3. The Subcommittee noted that at its October 2019 meeting it reviewed an application for the funding of influenza vaccine administered by pharmacists to people with serious mental health conditions or addiction. The Subcommittee recommended the application be declined as it considered there was insufficient evidence provided to demonstrate that people with serious mental health conditions or addiction were at increased risk of influenza, or that this group would be more likely to present for vaccination in pharmacy rather than general practice.

6.4. The Subcommittee noted that the Pharmaceutical Society of New Zealand (PSNZ) had submitted some New Zealand health data and recently published evidence to support a further review of the application. The Subcommittee noted that PSNZ had consulted widely with a number of professional bodies and revised its application to remove the request for vaccination only by pharmacists. Letters of support from a number of professional bodies were included with the application update.

6.5. The Subcommittee considered the SHIVERS (Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance) study (Influenza Other Respir Viruses. 2015; 9(4):179-90). The Subcommittee noted that influenza infection rates were highest in children: 26.1% of influenza infections reported were in children under 5 years of age; 30.6% of infections were in school aged children from 5-19 years of age.

6.6. The Subcommittee noted that while infection rates are highest in children, the highest proportion of influenza infections resulting in hospitalisation and death is seen in adults aged over 65 years. (Immunisation Advisory Centre (IMAC) 2017 Influenza Antigen Review). The Subcommittee considered that this was consistent with New Zealand hospitalisation modelling data from Khieu et al. Vaccine 2015;33:4087-92 and mortality modelling data from Khieu et al. J Infect 2017;75:225-33.

6.7. The Subcommittee noted that Khieu et al. (2015) modelled all cause hospitalisation rates per 100,000 for the period 1994-2008. The modelling gave rates of 149.9 for people aged 65-79 years; 80.0 for Māori of all ages; and 83.3 for Pacific People of all ages. The Subcommittee noted that Khieu et al. (2017) modelled influenza mortality, estimating the average mortality rate and identifying differences in risk by age, sex, ethnicity and socioeconomic position. The modelling estimated a crude influenza mortality rate of 13.5 per 100,000 for all causes, and a rate of 90.3 per 100,000 for influenza-attributable deaths in people aged 65 years and older. The Subcommittee considered that this modelling data was consistent with national general practice and virological surveillance, indicating that the annual burden from influenza is high in New Zealand and highest in older adults.

6.8. The Subcommittee noted that Khieu et al. (2017) found a large disparity of influenza attributable mortality among ethnic groups. Māori and Pacific People had higher mortality rates compared to European/Others, but also accounted for only 3% of the

total population of people aged 80 years and over. Age-standardised mortality rates showed that the risk of influenza deaths was higher for Māori (2.7 times) and Pacific People (1.5 times) than that for European and Others.

6.9. The Subcommittee considered that there are inequities in access to influenza vaccine for Māori and Pacific Peoples. Influenza vaccination coverage measured through general practice claims submitted to the Ministry of Health suggest that up to 25 June 2021, 46% of Māori and 56% of Pacific People aged 65 years and over had been vaccinated, compared to 62.5% of the overall population aged 65 years and over.

6.10. The Subcommittee considered Ministry of Health cohort data for the five-year period 2015-2019. The data was for people who had at least one dispensing of clozapine and who had attended at least one in-scope mental health and addiction activity in the same year. It included demographics, immunisation events, PHO enrolments and publicly funded hospital discharges where the primary diagnosis is in Chapter 10 Diseases of the respiratory system (ICD 10 version 8 codes J00-J99). The Subcommittee noted that, as supplied by the applicant, the data required further analysis to remove patient duplication and remove patients from ICD codes other than the relevant respiratory ICD codes J00-J99. The Subcommittee noted that, on average, 42% of patients receiving clozapine were either of Māori or Pacific ethnicity, and 42.7% of hospitalisations were for Māori or Pacific patients. The Subcommittee noted that, on average, 14% of the cohort was vaccinated.

6.11. The Subcommittee considered an observational study of potentially preventable hospitalisations (PPH) in New South Wales mental health service users (Sara et al. Epidemiology and Psychiatric Services. 2021;30:1-10). The Subcommittee noted that:

6.11.1. mental health service users had higher rates of PPH admission (AIRR[1] 3.6 (CI 3.5-3.6)) and a larger number of hospital days (AIRR 5.2 (CI 5.2-5.3)) than other NSW residents.

6.11.2. potentially preventable hospitalisations were substantially increased in people with mental health conditions.

6.11.3. vaccine preventable hospitalisations increased sharply in mental health service users from 35 years of age onwards.

6.11.4. increased rates of PPH in mental health service users were not accounted for by socioeconomic disadvantage.

6.12. The Subcommittee considered that the evidence supporting influenza vaccination for people with serious mental health conditions or addiction is of low quality, but considered from first principles that there is good biological and psychosocial plausibility. The Subcommittee considered that there is stronger evidence supporting COVID-19 vaccination for people with serious mental health conditions or addiction, but noted a lot of resource has been applied to studying COVID-19 vaccination in the context of the global pandemic, in contrast to the lack of ongoing research into influenza vaccination.

6.13. The Subcommittee considered that estimates of the eligible group size based on the number of people using clozapine and opioid substitution treatment likely

[1] *AIRR: adjusted incident rate ratio*

underestimated the size of the group that would benefit from influenza vaccination. The Subcommittee considered that the group most likely to benefit from influenza vaccination was the same as the mental health group defined for COVID-19 vaccine eligibility in Group 3 (patients with a serious mental health condition (schizophrenia, major depressive disorder, bipolar disorder or schizoaffective disorder) and people currently accessing secondary and tertiary mental health and addiction services).

6.14. The Subcommittee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for influenza vaccine if it were to be funded in New Zealand for serious mental health or addiction patients meeting the proposed eligibility criteria. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Subcommittee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Patients with a serious mental health condition (schizophrenia, major depressive disorder, bipolar disorder or schizoaffective disorder) and people currently accessing secondary or tertiary mental health and addiction services
Intervention	Annual, single dose of Influenza Vaccine
Comparator(s) (NZ context)	No treatment
Outcome(s)	Reduced hospitalisations, reduced GP service utilisation

Table definitions:

Population: The target population for the pharmaceutical, including any population defining characteristics (eg. line of therapy, disease subgroup)

Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).

Comparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).

Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.

7. Pneumococcal threshold monitoring

Application

7.1. The Subcommittee considered surveillance data on the rising incidence of invasive pneumococcal disease (IPD) serotype 19A in the context of overall decline of IPD.

Recommendation

7.2. The Subcommittee recommended that PCV13 vaccine be listed in the Pharmaceutical Schedule with a 2+1 dosing schedule for children under 5 years of age, with a high priority within the context of vaccines and immunisation.

7.3. The Subcommittee considered that recent published data, suggests that PCV10 cross protection against serotype 19A is not as strong as initially thought. The Subcommittee considered that PCV13 would give better protection against 19A than PCV10. The Subcommittee considered that a 2+1 dosing schedule would be appropriate until any evidence might emerge to show a difference in effectiveness between 2+1 and 3+1 schedules.

Discussion

7.4. The Subcommittee noted that in July 2021 the Institute of Environmental Science and Research (ESR) provided a report to the Ministry of Health and Pharmac, detailing recent trends in IPD, particularly noting the recent increase in serotype 19A notifications.

7.5. The Subcommittee noted that three conjugated pneumococcal vaccines have been listed in the National Immunisation Schedule at different times since 2008:

Vaccine	Funded Period	Vaccine Serotypes
PCV7 (Prevenar)	July 2028 - June 2011	4, 6B, 9V, 14, 18C, 19F, 23F
PCV10 (Synflorix)	July 2011 - June 2014	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F
PCV13 (Prevenar13)	July 2104 - June 2017	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
PCV10 (Synflorix)	July 2017 - present	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F

7.6. The Subcommittee noted that there was a transition period of approximately three months for each brand change to allow use of existing vaccine supplies.

7.7. The Subcommittee noted that although PCV10 does not include serotypes 6A or 19A, it does have some cross-reactivity against these serotypes. The Subcommittee noted that at its September 2018 meeting, it reviewed the evidence relating to the use of PCV10 vs PCV13 to protect against IPD, and also clinical data relating to a move from the 3+1 dosing schedule to the current 2+1 dosing schedule. The Subcommittee noted that it had recommended that it would be a suitable option for New Zealand to move to a 2+1 schedule and this was subsequently implemented from July 2020.

7.8. The Subcommittee noted that following the reintroduction of PCV10 in July 2017, ESR established a threshold for monitoring changes in serotype distribution in children under two years of age. The threshold was established at 9.1 cases per 100,000 children under two years of age. In its report to the Ministry, ESR reported that for the 12 months ending December 2019, the rate of 19A was 4.1 and remained steady until the 12 months ending December 2020, when it increased to 7.4. In the 12 months ending June 2021 the rate for 19A reached 13.1, exceeding the threshold of 9.1 for the first time since monitoring began. The Subcommittee noted that the purpose for establishing the threshold for serotypes of interest was to trigger further analysis if the threshold was exceeded.

7.9. The Subcommittee noted that from 2011 to 2020, the overall rate per 100,000 population of IPD has continued to decline, and the rate in children under 2 years of age has continued decline, apart from a slight increase in 2018. The Subcommittee noted that from 2018 to 2020, the rate per 100,000 population of IPD due to serotype 19A has increased more than threefold in children under 2 years of age, while over the same period, the rate for people 65 years or older has decreased.

7.10. The Subcommittee considered that Māori and Pacific peoples were over-represented in the 19A cases occurring in 2020 in children under 5 years of age, with 39% and 28% of cases, respectively.

7.11. The Subcommittee considered ESR provisional 2021 IPD data to 30 June 2021 and noted that all 11 cases with vaccine preventable serotypes (PCV10) amongst children under 5 years of age were 19A. The Subcommittee considered that serotype replacement had been a theoretical concern since pneumococcal vaccines were introduced, and variable replacement has been documented, but the benefits of pneumococcal vaccination have not been eroded due to serotype replacement.

7.12. The Subcommittee considered a study looking at serotype replacement trends following the introduction of pneumococcal conjugate vaccines in Europe, North America and Australia (Løchen et al. Sci Rep 2020;10:18977). The Subcommittee noted that although IPD incidence due to vaccine preventable serotypes had decreased in countries, partial replacement by non-vaccine preventable serotypes was observed following widespread vaccine uptake. While vaccine effectiveness against vaccine preventable serotypes was observed in infants, there was wide variation in overall IPD rates across countries due to serotype replacement.

7.13. The Subcommittee considered a literature review reported by Htar et al. Exp Rev Vaccine 2019;12:1243-70. The Subcommittee noted that the majority of PCV10 studies included in the review did not show a reduction in serotype 19A carriage from vaccines containing serotype 19F but not 19A. However, PCV13 studies consistently showed the ability of PCV13, which contains serotype 19A, to reduce 19A carriage, regardless of study design or vaccine schedule.

7.14. The Subcommittee considered a systematic review reported by Berman-Rosa et al. Pediatrics 2020;145(4):e20190377. The Subcommittee noted that PCV13 vaccine effectiveness (VE) against serotype 19A post-primary series was significant for the 3+1 but not 2+1 schedule. PCV10 cross protection against 19A was in children 5 years of age or under with one or more doses (82,2% and 71%). The Subcommittee noted that the authors concluded that both PCV10 and PCV13 provide protection against IPD, with PCV10 protecting against 19A IPD, but this VE has not been verified in the youngest age groups.

7.15. The Subcommittee noted that the World Health Organization SAGE 2017 PRIME systematic review recommended the use of either PCV10 or PCV13 in a 3+0 or 2+1 dosing schedule, starting as early as 6 weeks. The Subcommittee noted that the authors considered that there was no evidence at the time of different net impact on overall disease burden between the two products, but also considered that PCV13 may have additional benefit in settings where disease attributable to serotypes 19A or 6A is significant.

7.16. The Subcommittee considered that recent international reviews of pneumococcal disease challenge the equivalence of PCV10 and PCV13 against serotype 19A. The Subcommittee considered that the rise in 19A cases observed in New Zealand could be due to other causes. The Subcommittee considered that there is no clear evidence to suggest that the 2+1 dosing schedule is not as effective as 3+1 for either PCV10 or PCV13. Members noted that 19A rates were increasing in New Zealand before the dose schedule was changed from 3+1 to 2+1.

7.17. The Subcommittee considered that when it recommended changing from a 3+1 to 2+1 schedule at its September 2018 meeting, the data available at the time supported the equivalence of PCV10 and PCV13 with respect to serotype 19A coverage. The Subcommittee considered data published since that time suggests

that the cross protection against 19A is not as strong as initially thought. The Subcommittee considered that PCV13 would give better protection against 19A. The Subcommittee acknowledged there could be a long lead to time to manage commercial and logistical considerations of any vaccine brand change, and did not consider that a change was urgently required. The Subcommittee considered that ESR should continue monitoring and reporting on changes in childhood pneumococcal serotypes.

8. Pneumococcal polysaccharide vaccine for people over 65 years of age

Application

8.1. The Subcommittee considered a supplier application for 23 valent pneumococcal polysaccharide vaccine (PPV23) for the immunisation of people 65 to 80 years of age who have not received vaccination within 5 years (and were not >65 years of age at the time of prior vaccination).

Recommendation

8.2. The Subcommittee recommended that the 23 valent pneumococcal polysaccharide vaccine for people over the age of 65 be declined.

8.3. In making this recommendation, the Subcommittee considered:

- the low-quality evidence and imprecise results for the efficacy of PPV23 against non-bacteraemic pneumococcal pneumonia;
- inconclusive evidence of efficacy against PPV23 serotypes and invasive pneumococcal disease (IPD);
- the lack of evidence for benefit for the Māori and Pacific populations;
- the lack of data in people over the age of 60 who had risk factors other than hospitalisation;
- that the addition of conjugate pneumococcal vaccine 13-valent (PCV13) is likely needed prior to receiving PPV23 for patients to receive any measurable benefit.

Discussion

8.4. The Subcommittee noted that PPV23 has been previously considered by both PTAC and the Immunisation Subcommittee on multiple occasions:

8.4.1. By PTAC in February 2014 where an application for people aged 65 years and over was recommended for decline;

8.4.2. By The Immunisation Subcommittee in February 2015 where no formal recommendation was given;

8.4.3. By PTAC in August 2015 where an application for people aged 65 years and over was recommended for decline.

8.5. The Subcommittee noted that the application was most recently reviewed by PTAC in March 2021, where it was again recommended for decline. The Subcommittee noted that PTAC considered the evidence for PPV23 against pneumococcal infection in those aged over 65 to be of poor quality and mixed strength, with low-moderate, inconclusive evidence of efficacy against PPV23 serotypes and invasive pneumococcal disease (IPD), and low-quality evidence and imprecise results for the

efficacy of PPV23 against non-bacteraemic pneumococcal pneumonia (NBPP). PTAC also noted that effectiveness was not demonstrated to be consistent in the general population, and that the meta-analyses reported a wide range of effectiveness estimates. The Subcommittee noted PTAC's past advice was that PPV23 is effective against IPD, and that more robust evidence is needed to show efficacy against NBPP. PTAC also considered that the evidence presented for PPV23 against NBPP is imprecise and of low quality. The Subcommittee noted that PTAC considered that although there appears to be limited benefit with PPV23, there would be no additional clinical risk to widening access, and no non-clinical features of the vaccine that would impact on its use by healthcare workers that are different to other vaccines. The Subcommittee noted and agreed with PTAC's considerations and recommendation.

8.6. The Subcommittee noted that pneumococcal infection is a common disease that affects all age groups and has the potential to cause significant illness, sometimes leading to hospitalisation or death. The Subcommittee noted that in 2019 the rate of invasive pneumococcal disease was 25 per 100,000 population for those aged 65-80 years, and that Māori and Pacific people are overrepresented, with rates of 37.0 and 28.9 per 100,000, respectively. The Subcommittee noted that *S. pneumoniae* is the underlying pathogen in 30-50% of cases of NBPP. The Subcommittee noted 16 people aged 65 or over died in 2018 as a result of pneumococcal infection. The Subcommittee noted that any herd immunity effects from the childhood pneumococcal vaccination programme has not reduced the pneumococcal related mortality rates in the over 65-year age group.

8.7. The Subcommittee noted that the PPV23 vaccine is currently funded on the Pharmaceutical Schedule for vaccination of adults aged 18 years and older with HIV infection; who are pre- or post-HSCT or chemotherapy; who are pre- or post-splenectomy or with functional asplenia; who are pre- or post-solid organ transplant; undergoing renal dialysis; with complement deficiency (acquired or inherited); with cochlear implants; with primary immunodeficiency. The Subcommittee noted that Pharmac also funds one dose of pneumococcal conjugate vaccine (PCV13) for people with chronic conditions who are at higher risk of pneumococcal infection with a maximum of three doses of PPV23 in a lifetime for revaccination of patients, and for those between the age of 12 months and 18 years who have previously received two doses of the primary course of PCV10.

8.8. The Subcommittee noted that the PPV23 vaccine includes antigens of 23 different serotypes of *S. pneumoniae*, which are responsible for more than 90% of cases of invasive pneumococcal (WHO 2003). The Subcommittee noted that the recommended dosage of PPV23 is a single 0.5 mL dose of Pneumovax 23 subcutaneously or intramuscularly.

8.9. The Subcommittee noted the following evidence relating to the use of PPV23 in the prevention of pneumococcal disease in the 65–80-year age group:

- Kim et al. Vaccine. 2019;37:2797-804
- Suzuki et al. Lancet Infect Dis. 2017;17:313-21
- Vila-Corcoles et al. Clin Infect Dis. 2006;43:860-8
- Maruyama et al. BMJ. 2010;340:c1004
- Wiemken et al. Vaccine. 2014;32(19):2198-203

- Ochpa-Gondar et al. Clin Infect Dis. 2014;58:909-17
- Moberly et al. Cochrane Database Syst Rev 2013:CD000422
- Falkenhorst et al. PLoS One. 2017;12:e0169368
- Winje et al. Norwegian Institute of Public Health. 2019
- Berild et al. Pathogens. 2020;9:259
- Menzies et al. Med J Aust. 2014;200:112-5
- Ahn et al. Vaccine. 2015; 33:4770-4775
- Maruyama et al. BMJ. 2010;340:c1004
- Htar et al. PLoS One. 2017;12:e0177985
- Baldo et al. PLoS One. 2016;11:e0166637
- Schiffner-Rohe et al. PLoS One. 2016;11:e0146338

8.10. The Subcommittee considered that since PPVs stimulate a T-cell independent immune response, in contrast to PCVs, which stimulate T-cell memory response, PCV13 may have to be given in conjunction with PPV23 in order to achieve a benefit in the 65 year and over population.

8.11. The Subcommittee also noted and agreed with PTAC's consideration that there is a lack of evidence of effect for preventing non-bacteraemic pneumococcal pneumonia, a lack of evidence that PPV23 would reduce inequity in the Māori and Pacific population, there is insufficient data regarding the use of PPV23 in people between the ages of 60 and 65, that estimates of beneficial effect were wide and imprecise, and that the addition of conjugate pneumococcal vaccine 13-valent (PCV13) is likely needed prior to receiving PPV23 for patients to receive any measurable benefit.

8.12. The Subcommittee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for pneumococcal 23-valent vaccine if it were to be funded in New Zealand for people aged over 65 years. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Subcommittee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Adults aged 65 to 80 years old.
Intervention	Single 0.5 mL dose pneumococcal vaccine.
Comparator(s) (NZ context)	Nothing.
Outcome(s)	Lower rates of invasive pneumococcal disease (IPD) and non-bacteraemic pneumococcal pneumonia (NBPP), resulting in reduced hospitalisation and mortality.
Table definitions:	

Population: The target population for the pharmaceutical, including any population defining characteristics (eg. line of therapy, disease subgroup)

Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).

Comparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).

Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.