Record of the immunisation Subcommittee meeting held at PHARMAC on 15 October 2019

Immunisation Subcommittee meeting 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 record relating to Immunisation Subcommittee discussions about an application or PHARMAC staff proposal that contains 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.

This Subcommittee meeting record was reviewed by PTAC at its meeting of 20-21 February 2020, the record of which will be available in due course.

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Present from the Immunisation Subcommittee:

Sean Hanna
Ayesha Verrall
Edwin Reynolds
Elizabeth Wilson
Lance Jennings
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:

- Both PTAC Subcommittees and PTAC are statutory advisory committees established by the PHARMAC Board (external to and separate from PHARMAC staff). Both provide objective advice to PHARMAC on community and hospital pharmaceuticals and their benefits, using the PHARMAC Factors for Consideration. PTAC Subcommittees complement and are separate from PTAC; they are not subordinate.

- PTAC Subcommittees provide objective advice within specific therapeutic areas. PTAC Subcommittees are appointed to reflect specialist knowledge and expertise in health needs and treatments within their own therapeutic groups/areas of clinical practice, including the applicability of evidence to clinical funding settings in New Zealand. The Immunisation Subcommittee provides advice in the therapeutic area of immunisation and vaccines for communicable diseases.

- PTAC Subcommittees make recommendations, including providing a priority, within their therapeutic groups of interest. The Immunisation Subcommittee recommends with priority within the context of immunisation and vaccines for communicable diseases, as within that area of health need and clinical practice.

- PTAC considers Applications or PHARMAC staff proposals across all therapeutic groups in the Pharmaceutical Schedule. It has an overview view of Applications and other items referred to it for clinical advice. PTAC provides and promotes critical appraisal of strength and quality of evidence, applied rigorously, systematically and consistently across all therapeutic groups.

- PTAC Subcommittees and PTAC therefore provide separate and different, if complementary, perspectives and advice to PHARMAC. PTAC examines the same evidence with a different perspective from specialist expert PTAC Subcommittees, as do Subcommittees between them.

The Immunisation Subcommittee and other PTAC Subcommittees may therefore, at times, make recommendations for immunisation and vaccines for communicable diseases that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for immunisation and vaccines for communicable diseases that differ from PTAC Subcommittees', 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 immunisation and vaccines for communicable diseases.

PHARMAC considers the recommendations provided by both PTAC and PTAC Subcommittees when assessing applications.

2. Record of Subcommittee meeting held Friday, March 8, 2019

2.1. The Committee reviewed the record of the Immunisation Subcommittee meeting held on 8 March, 2019 and agreed that the record be accepted.

3. Therapeutic group review

Human papillomavirus vaccine (Gardasil 9)

3.1. The Subcommittee noted that supply issues during 2017 and 2018 had an impact on the distribution patterns of the HPV vaccine. It was noted that supply to school-based programmes was prioritised over that period. No further supply disruptions occurred in 2019.

3.2. The Subcommittee noted that from 1 August 2019 funding was approved for widened access to HPV vaccine with bevacizumab for recurrent respiratory papillomatosis. This is a small group and is not expected to have a significant impact on HPV vaccine usage.

Adult diphtheria and tetanus vaccine

3.3. The Subcommittee noted that ADT Booster will be delisted from 1 October 2020 and the eligibility criteria will be added to those for Boostrix.

Hepatitis B recombinant vaccine

3.4. The Subcommittee noted that there has been an ongoing supply issue for HBvaxPRO and following advice from the Subcommittee, Engerix B has been used in its place. HBvaxPRO will be delisted from 1 October 2020 and Engerix B will have sole supply status.

Measles, mumps and rubella vaccine

3.5. The Subcommittee noted that there was a spike in MMR vaccine usage in March 2019 as a result of the Canterbury measles outbreak. While the Canterbury response used approximately 30,000 doses in March, there was also a large increase in vaccine usage across the country. The Subcommittee noted that an additional supply of 40,000 doses of MMRII brand vaccine was sourced but not used for the Canterbury outbreak. It was instead used between June and September 2019 for the Auckland measles outbreak.

Meningococcal conjugate vaccines

3.6. 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.

3.7. The Subcommittee noted that PHARMAC has consulted on a proposal to widen access to MenACWY vaccine for people in close-living situations and is actively considering proposals to fund other groups.

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

3.9. The Subcommittee considered that the notes to the meningococcal ACWY eligibility criteria in the Pharmaceutical Schedule could be updated to refer clinicians to the Immunisation Handbook for more details about the timing of doses in children under nine months of age.

3.10. The Subcommittee considered that it should review up to date New Zealand meningococcal epidemiology data at each meeting to monitor developments.

Pneumococcal conjugate vaccine

3.11. The Subcommittee noted that the Immunisation Advisory Centre pneumococcal antigen review considered that if New Zealand moved from a 3+1 to a 2+1 pneumococcal dose schedule, infant born before 35 weeks gestation may be at increased risk from pneumococcal disease. The Subcommittee considered that it could be assumed that there would be no maternal antibody protection for infants born before 28 weeks, but it is not clear if there is a difference in maternal antibody protection for infants born between 28 and 35 weeks. The Subcommittee considered that there was only a small additional health need which there was no need to address, given their indirect protection.

Diphtheria, tetanus and pertussis vaccine

3.12. 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.

Influenza vaccine

3.13. The Subcommittee noted that funded influenza vaccine distribution was slowly increasing year on year since 2017, but private influenza vaccine distribution had increased notably year on year since 2017. Total influenza vaccine distribution for 2019 had already exceeded the 2018 total by May. The Subcommittee noted the funded influenza vaccine coverage in 2019 to date was low for children aged 0-4 years and pregnant women (4% and 25% respectively).

4. Influenza vaccine application

Application

4.1. The Subcommittee reviewed a funding application from the Pharmaceutical Society for pharmacist vaccinators to be able to administer influenza vaccine to patients with serious mental health conditions or addiction.

Recommendation

4.2. The Subcommittee **recommended** that application for pharmacist influenza vaccination of people with serious mental health conditions or addiction be declined. The Subcommittee considered that there was insufficient evidence demonstrating that this group is at increased risk of influenza and that there was insufficient evidence that this group would be more likely to be vaccinated in a pharmacy than general practice.

Discussion

4.3. The Subcommittee noted that it has considered a number of applications for different types of influenza vaccines at several meetings over the last two years. The Subcommittee noted that this application did not extensively define "serious mental health conditions" but used a proxy of people who are prescribed clozapine. The Subcommittee noted that people with serious mental health conditions or addiction are not currently eligible for funded influenza vaccination in the community, although patients in long-stay inpatient mental health care units or who are compulsorily detained long-term in a forensic unit within a DHB hospital are eligible due to increased risk of infection.

4.4. The Subcommittee noted that only about 28% percent of the total population receives influenza vaccine annually. Current coverage for eligible people under 65 years of age with comorbidities is less than 50% and funded coverage for people over 65 years of age is 57%. The Subcommittee noted that pregnant women and people over 65 years of age can currently receive funded influenza vaccine in a community pharmacy. The Subcommittee considered that coverage of both target groups and the general population is low and that vaccinations given by occupational health nurses, which may not be recorded in the National Immunisation Register, is unlikely to account for much more coverage of the under 65 age group with comorbidities.

4.5. The Subcommittee noted that community opioid treatment services (OTS) are provided through community alcohol and drug services (CADS). Typically patients would have daily to weekly pharmacist contact. CADS generally encourage GP shared care with 3 monthly visits. Engagement with GPs varies across the country, with estimates of 40% shared care in Auckland and 20% in Wellington.

4.6. The Subcommittee noted that clozapine is prescribed for treatment-resistant schizophrenia. Patients taking clozapine should be monitored for symptoms and signs of cardiac toxicity, neutropenia and constipation. Regular blood tests are mandatory to detect blood dyscrasias and for continued supply of the medicine. Pharmacists have a role in this monitoring, ensuring that the blood test has been had within three days of the medicine being dispensed. In this way, patients are very engaged with community pharmacy, but less likely to be engaged with their GP as they would typically be managed by secondary services. The Subcommittee noted that there were approximately 4,300 patients prescribed clozapine in 2016. Approximately 600 pharmacies are approved to administer influenza vaccine, but only approximately 400 of these are actively administering influenza vaccine each season.

4.7. The Subcommittee noted a number of studies and papers provided with the application, including:

- Khieu et al. Vaccine 2015;33:4087-92

- Khieu et al. J Infect 2017;75:225-33
- He-Ara-Oranga: Report of the Government Inquiry into Mental Health and Addiction (Nov 2018) (Appendix 2)
- Lorenz et al. Int J Psychiatry Med 2013;46:1-3
- Happell et al. Arch Psychiatr Nurs 2012;26:192-201
- Cunningham et al. NZMJ 2014;127:31-41

4.8. The Subcommittee considered that the evidence provided by the applicant did not show that there is an increased rate of influenza cases in people with schizophrenia or addiction, or that people with serious mental health disorders or addiction have reduced interactions with primary care. However, they are more likely to have increase co-morbidities such as COPD, respiratory disease and ischaemic heart disease. The Subcommittee considered that people with low socioeconomic status have increased rates of influenza and a higher burden of disease.

4.9. The Subcommittee noted that pharmacists can currently vaccinate people over 65 years of age and pregnant women. There may be a gain in equity of access if pharmacists were able to administer influenza vaccine to people under 65 years of age with comorbidities. The Subcommittee considered that there would be a number of potential implementation issues to address if pharmacists were to vaccinate people under 65 years of age with comorbidities, as pharmacists do not have access to patient healthcare records and will not easily be able to confirm the patient's eligibility.

4.10. The Subcommittee noted that the influenza vaccine applications it had previously considered included earlier access before 65 years of age for Māori and Pacific People, and universal childhood vaccination.

4.11. The Subcommittee considered that the funded groups for influenza vaccine differ across countries. The Subcommittee considered that it should review the currently funded groups for influenza vaccine and consider options for widened access at a future meeting.

4.12. The Subcommittee considered that the evidence provided by the applicant did not demonstrate a health benefit from administering influenza vaccine in pharmacy for people with serious mental health disorders or opioid addiction. The Subcommittee considered that it should discuss pharmacy vaccination for people under 65 years of age with chronic health conditions at a future meeting.

5. Pneumococcal polysaccharide vaccine for CLL/SLL patients application

Application

5.1. The Subcommittee considered a clinician funding application to widen access to PPV23 vaccine for patients with untreated chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL).

Recommendation

5.2. The Subcommittee **recommended** that the application to widen access to PPV23 vaccine for patients with untreated chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) be declined. The Subcommittee considered that there is no

evidence for a benefit from vaccination with PPV23 in addition to PCV13 in untreated CLL/SLL.

Discussion

5.3. The Subcommittee noted that Pneumococcal Conjugate Vaccine (PCV13) and Pneumococcal Polysaccharide Vaccine (PPV23) are currently listed in the Pharmaceutical Schedule for children up to the age of 59 months as well as for high risk individuals. PCV13 is funded for pre- or post-haematopoietic stem cell transplant (HSCT) or chemotherapy, but PPV23 is only currently funded post-HSCT or chemotherapy. The Subcommittee considered that current funding criteria for PCV13 would mean that all CLL/SLL patients would be eligible for PCV13.

5.4. The Subcommittee considered a randomised controlled trial by the Swedish CLL Group (Svensson et al. Vaccine 2018;36:3701-7). The Subcommittee noted that the study was intended to determine if patients with untreated CLL would generate a greater immune response from vaccination with PCV13 compared with PPV23, for most serotypes common to both vaccines. The trial demonstrated a better immune response to PCV13 than PPV23 in 10/12 serotypes one month after vaccination and in 5/12 serotypes six months after vaccination. The authors proposed that PCV13 should be administered as early as possible during the course of the disease, with PPV23 eight weeks later.

5.5. The Subcommittee considered a review of infectious complications in patients with CLL (Morrison VA. Clin Lymphoma Myeloma 2009;9:365-70). The review noted that CLL/SLL patients have an elevated risk of pneumococcal disease. A number of immunisations have been examined in patients with CLL but they have shown suboptimal responses because of impaired antibody production and defects in antigen presentation. The review noted that conjugated vaccines would be more likely to give better responses than polysaccharide vaccines.

5.6. The Subcommittee considered a clinical practice guideline from the British Committee for Standards in Haematology (Oscier et al. Br. J. Haematol 2012;159:541-64). The Subcommittee noted that the guideline discusses immunisation and recommendations for immunisations for people with CLL. It notes that there are no randomised studies showing that vaccination of any type alters infection rates of outcomes from acquired infections in CLL. The guidelines note that some patients respond particularly if vaccinated early in the disease and if conjugate vaccines for *S, pneumoniae* are used (PCV13).

5.7. The Subcommittee considered a review article addressing the pathogenesis of infections due to CLL or therapy-related immunosuppression (Tadmor et al. Expert Rev Hematol. 2018;11:57-70). The Subcommittee noted that the majority of patients with CLL suffer from infections during their disease and these account for approximately 60% of deaths in CLL. Patients are predisposed to infection both as a consequence of CLL and as a result of therapy. The review noted that in the absence of agreed international guidelines, several national bodies have recommended infection prophylaxis in specific circumstances. The Subcommittee noted that this would include offering up to three doses of PPV23 for patients who have already received one dose of PCV13.

5.8. The Subcommittee considered a clinical practice guideline from the European Society for Medical Oncology (ESMO) Guidelines Committee (Eichhorst et al. Ann Onc 2015;26 Suppl 5:v78-84). The Subcommittee noted that the guideline considers that infections are a common complication in CLL patients following treatment with immunosuppressive agents. The guideline recommended pneumococcal

vaccination in early-stage CLL, but did not specify the vaccine type or pneumococcal serotypes covered.

5.9. The Subcommittee considered that the evidence for benefit from vaccination with PCV13 followed by PPV23 was of poor quality and low strength, consisting of small observational studies and international guideline recommendations. The Subcommittee considered that the above Svensson et al. 2018 trial demonstrated a good immune response to PCV13, but did not provide evidence of additional benefit for subsequent vaccination with PPV23. The Subcommittee considered that there is a theoretical benefit to broadening immune response to more serotypes with PPV23, but this is not supported by the evidence at this time. The Subcommittee considered that the evidence did not support amending the eligibility criteria for PPV23 with respect to immunosuppression to be aligned with those for PCV13.

6. Additional 15 month pertussis dose for childhood schedule

Application

6.1. The Subcommittee considered a Ministry of Health review of the evidence regarding the addition of a pertussis-containing vaccine in the second year of life to the Pharmaceutical Schedule.

Recommendation

6.2. The Subcommittee **recommended** that the Ministry of Health should prioritise improving maternal pertussis vaccination coverage over the possible introduction of an additional pertussis-containing dose in the second year of life.

Discussion

6.3. The Subcommittee noted that it had considered childhood pertussis schedules at a number of previous meetings (July 2917, September 2018, March 2019) and at a Ministry of Health Immunisation Schedule Review Meeting in November 2017.

6.4. The Subcommittee considered a review of the evidence for an additional pertussis-containing vaccine in the second year of life.

6.5. The Subcommittee considered the EPIC study reporting pertussis vaccine effectiveness (VE) for New Zealand. The Subcommittee noted that VE against pertussis hospitalisation was 93% (95% CI 87-96) following three doses in infants aged 5-11 months who receive three doses compared to zero doses. The protection was sustained through the children's fourth birthdays (VE ≥ 91%). VE against non-hospitalised pertussis was also sustained after three doses, from 86% (95% CI 80-90) among 5-11 month olds to 84% (95% CI 80-88) among 3 year olds. (Radke et al. Vaccine 2017;35:177-83).

6.6. The Subcommittee noted that a WHO position paper reported that a number of countries have experienced a resurgence in pertussis while using an aP vaccine (Australia, Portugal, USA and UK), although New Zealand has not experienced the same resurgence.
(WHO position paper. https://www.who.int/wer/2015/wer9035.pdf).

6.7. The Subcommittee considered the epidemiology for pertussis notifications and hospitalisations since 1998. The Subcommittee considered that while notifications show a regular pattern of pertussis epidemics every four to five years, hospitalisations of children under 1 year of age are relatively consistent. The

Subcommittee considered that the notification patterns showed some evidence of protection with the dose at four years of age. The Subcommittee considered that there was no evidence of waning of pertussis vaccine effectiveness by four years of age in New Zealand.

6.8. The Subcommittee considered that there was no evidence for a clear health benefit from introduction of a pertussis booster in the second year of life, although it may help to simplify the infant immunisation schedule.

6.9. The Subcommittee considered a systematic review of 40 studies examining possible blunting of the infant's immune response to vaccination caused by maternal vaccination during pregnancy. The Subcommittee noted that although there was some documentation of blunting of immune responses to some antigens in neonates born to women vaccinated during pregnancy, there was no apparent effect on vaccine efficacy. (Switzer et al. Infect Dis Ther. 2019;8:499-541). The Subcommittee considered that although maternal blunting of the neonate antibodies may occur, it has not been shown to be of clinical significance. The Subcommittee noted that a New Zealand study is underway to investigate the clinical relevance of maternal blunting. The Subcommittee considered that it should review the maternal blunting data when it becomes available.

6.10. The Subcommittee noted that coverage for maternal pertussis vaccination in pregnancy is still low at approximately 25%, compared with the UK which has coverage of approximately 70%. The Subcommittee considered that contributing factors to the lower coverage in New Zealand could include less promotion to pregnant women and the lack of funding for any pregnancy visits in primary care after 12 weeks gestation.

6.11. The Subcommittee considered that there was a clear to priority to improve maternal pertussis coverage to protect infants under three months of age, rather than providing an additional pertussis booster dose in the second year of life.

7. Ministry of Health measles outbreak update

7.1. The Subcommittee considered an update from the Ministry of Health about the current measles outbreak.

7.2. The Subcommittee noted that there are five DHB regions with measles outbreaks: Northland, Waikato, Southern and Lakes, but the demographics for cases in each region are different. Northland has a lot of cases in the 5-29 year range, Southern and Waikato have cases mainly in the 15-29 age range, Lakes and Bay of Plenty have cases in the 15-29 age range but they are also spread across all ages under 40. Auckland has had a large number of cases in the 15-29 age range, but the overall number of cases is starting to decrease.

7.3. The Subcommittee noted that nationally, the highest rates were in the 15-29 age range, but the last serosurvey showed the lowest measles immunity in the 30-40 year group. The Subcommittee noted that the Ministry considers this may reflect the more active lifestyle and social mixing of the 15-29 year group.

7.4. The Subcommittee noted that consideration is being given to the introduction of a MMR0 dose (MMR vaccination before the scheduled 15 month dose) in the Auckland region. Members considered that it appeared that the epidemic was declining but it would not be possible to be certain for several months. The Subcommittee considered that the case for introducing MMR0 would have been stronger several months ago at the height of the outbreak, but with case numbers

reducing, the benefit was not so clear now. The Subcommittee considered that it still supported the Ministry of Health's Expert Advisory Group recommendation to introduce MMR0 in Auckland but noted that this should be reassessed in three months' time to take into account the status of the outbreak.