Immunisation Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC)

Meeting held on 26 July 2017

(minutes for web publishing)

Immunisation Subcommittee minutes 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 minutes 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.

These Subcommittee minutes will be reviewed by PTAC at its meeting on 8 & 9 February 2018, the record of which will be available in due course.

Record of the Immunisation Subcommittee of the Pharmacology and Therapeutics Committee (PTAC) meeting held at PHARMAC on 26 July 2017

1 Record of previous subcommittee meeting

1.1 The Subcommittee noted the minutes from the previous meeting held on 18 November 2016. There were no comments on the previous meeting minutes and the Subcommittee accepted them as a true account of the meeting.

1.2 The Subcommittee noted there were several action points from the November 2016 meeting that should be transferred to the current action points list for future reference:

i. PHARMAC should contact Dr Joan Ingram, who developed the adult HIV special immunisation NZ guideline, and request her to apply for funding of diphtheria, tetanus and pertussis (Tdap) vaccine for patients living with HIV, rather than simply Td vaccine.

ii. Criteria for funding hepatitis B and meningococcal vaccines for patients undergoing more than 28 days of immunosuppression should be changed to allow use pre-immunosuppression for more than 28 days.

2 Therapeutic Group Review

Therapeutic Group Usage Data and Expenditure Summary

2.1 The Subcommittee noted the distribution data for each vaccine and expenditure summary of the Therapeutic Group Review. Members noted this data does not reflect the number of vaccines administered to patients, rather the number of vaccines that are delivered to funded vaccinators.

Human papillomavirus vaccines (HPV)

2.2 The Subcommittee noted the early usage data of the HPV – 9 valent vaccine since its introduction in January 2017 when access to the funded vaccine had widened to include males up to the age of 26 years. The Subcommittee noted that the actual numbers of uptake of the vaccine were higher than that predicted and this was difficult to interpret due to the change from a three-dose regime to a 9-valent two dose vaccine for children 14 years and under, and the mass implementation of the school-based HPV immunisation programmes for 11-12 year olds. Members noted PHARMAC staff would continue to monitor uptake closely.

Diphtheria, tetanus and pertussis vaccine

2.3 The Subcommittee noted the distribution of the diphtheria, tetanus and pertussis vaccine. The Subcommittee noted the higher numbers of vaccine were distributed in the first half of the calendar year and that further investigation would be required to understand the reason of the distribution pattern.

Hepatitis A vaccines

2.4 The Subcommittee noted an increased distribution of funded hepatitis A vaccines between 1 July 2014 and 30 June 2017. The Subcommittee noted the two outbreaks of hepatitis A in 2016 that may have contributed to the increased uptake.

Previous recommendations/ Action point summary

2.5 The Subcommittee noted action points made at its previous meetings, particularly in May 2016 and October 2016, and the current status of these action points.

2.6 Members noted there were a number of action points that were still to be progressed and these would be prioritised by PHARMAC staff relevant to other vaccine therapeutic group work.

Meningococcal conjugate vaccine

2.7 The Subcommittee noted its deferred recommendation in February 2014 to widen access to meningococcal C vaccinations for consideration for universal use, and requested PHARMAC staff assess funding the vaccine for people in close living situations, universal vaccination for infants and teenagers as well as a catch-up programme. The Subcommittee noted that the analysis, when completed by PHARMAC, would be provided to the Subcommittee for review at their next meeting.

Ranked proposals

2.8 The Subcommittee noted that applications for zoster vaccine, widening access to influenza vaccine, and widening access to pertussis vaccine were ranked and would be progressed pending available funding.

To be discussed at this meeting

2.9 The Subcommittee noted that its recommendation made in October 2016 that PHARMAC request an application from renal disease specialists and discuss immunisation at the upcoming Nephrology meeting was on the agenda of this meeting (agenda item 7 – matters arising and correspondence).

NPPA applications

2.10 The Subcommittee noted that since 2015, PHARMAC had received a small number of NPPA applications for HPV, DTaP, and pneumococcal vaccines but did not consider that any of these indications for immunisations should be considered for listing in the Schedule at this stage.

Looking forward

2.11 The Subcommittee noted that countries that have introduced varicella vaccine have often moved to a two-dose regimen and the Subcommittee had previously indicated this should be considered in the future. Members noted the availability of a combined varicella with measles, mumps, rubella vaccine.

2.12 The Subcommittee noted that a respiratory syncytial virus (RSV) vaccine was in development and this would be of interest to the Subcommittee if it became available in New Zealand.

2.13 The Subcommittee noted that there were new influenza vaccines on the horizon to improve efficacy in the elderly and intranasal live-attenuated vaccines (LAIVs) appropriate for use in children.

3 Correspondence and Matters Arising

Matters Arising

Vaccines for patients with renal disease

3.1 The Subcommittee noted the recommendation it made on the needs of patients at various stages of kidney disease at its 2016 meeting to request that PHARMAC seek advice from renal disease specialists at the next Nephrology Subcommittee meeting.

3.2 The Subcommittee noted the minutes from the December 2016 Nephrology Subcommittee meeting The Subcommittee noted in particular the following from the Nephrology Subcommittee minutes:

i. that chronic kidney disease (CKD) was the terminology considered appropriate when describing patients with renal disease and the stages of CKD (paragraph 5.2)
ii. that patients with CKD and renal transplant recipients were well covered with the current eligibility of funded vaccines (paragraph 5.4), and noted there were some small gaps
iii. that the Immunisation Advisory Centre had worked with a paediatric nephrologist to defined transplant patients for the purpose of immunisations.

3.3 The Subcommittee agreed with the recommendation by the Nephrology Subcommittee and requested that evidence for pneumococcal vaccine, zoster vaccine and hepatitis B vaccination for transplant patients and patients with CKD grades 4 and 5 be reviewed by the Immunisation Subcommittee at its next meeting.

Vaccine supply issues

Hepatitis B vaccine, adult presentation

3.4 The Subcommittee noted that the supplier, Merck Sharp & Dohme (MSD) had notified PHARMAC of an out of stock situation for the supply of the HBvaxPRO adult hepatitis B vaccine Inj 10 mcg per 1 mL vial until June/July 2018. This was the result of a global stock shortage due to a manufacturing issue. There were no stock concerns for the paediatric and hospital presentations (Inj 40 mcg per 1 mL vial, used for dialysis and transplant patients) at this time.

3.5 The Subcommittee noted that the immediate situation could be managed with stock on hand until August 2017, and that PHARMAC was working with the supplier towards securing appropriate vaccine for August 2017 until June 2018.

3.6 The Subcommittee noted that MSD had sourced prefilled syringes of its adult formulation and that registration with Medsafe was currently underway, which would provide sufficient stock for August – December 2017. The Subcommittee also noted that GSK, who currently supplied the private market, had agreed to supply their adult hepatitis B vaccine, Engerix-B (20 mcg in 1 mL vial), to mid-2018 when resupply of the MSD product was expected.

3.7 The Subcommittee noted that once supply alternatives were confirmed, PHARMAC would work with the Ministry of Health immunisation team to provide relevant information to vaccinators about the alternative products.

Correspondence

Widened access to funded influenza vaccine

3.8 The Subcommittee noted that since its last meeting PHARMAC had received and funded two requests for influenza vaccine for children affected by natural disasters. The Subcommittee noted that widened access to the influenza vaccine for children affected by the Kaikoura earthquake had been funded since 1 May 2017, and access for children affected by the Edgecumbe floods was funded since 1 July 2017.

3.9 The Subcommittee noted that PHARMAC had funded influenza vaccines for children affected by natural disasters based on a previous funding decision for influenza vaccine for individuals affected by the Christchurch earthquake (which were in place from 2011 to 2016).

3.10 The Subcommittee noted in both requests for funded influenza vaccine for children affected by the Kaikoura earthquake and the Edgecumbe floods, DHBs advised that families would be at greater risk of contracting influenza due to families living in either damaged houses or in overcrowded living conditions.

3.11 The Subcommittee noted there was no data to support use of influenza vaccine in the setting of a natural disaster. Members considered there were wider equity issues to take in account. The Subcommittee considered it was appropriate for PHARMAC to consider such requests on a case by case basis.

Pneumococcal vaccines for high risk adult groups

3.12 The Subcommittee noted a request that high-risk adult groups that may benefit from funded pneumococcal vaccination (PCV13 followed by PPV23) be reviewed. The following evidence was provided to support the request:

i. Weycker et al. Rates and costs of invasive pneumococcal disease and pneumonia in persons with underlying medical conditions. BMC Health Serv Res. 2016;16:182.

3.13 The Subcommittee noted that the Weycker et al. study analysed surveillance data for around 20 diseases or risk factors and calculated broad age-specific relative risks

for either invasive pneumococcal disease or all-cause pneumonia. However, there was insufficient data in the publication to inform any specific recommendations according to univariate disease-specific overall (all-age) risk or discrete (mutually exclusive) multivariate models, particularly if it was assumed some correlation/interdependence between some diseases (thus diluting or exacerbating true effects from isolated conditions).

3.14 The Subcommittee considered that further analysis would be necessary to help inform recommendations such as a multivariate analysis of discrete (mutually exclusive) disease-specific outcomes that adjusted for age and other variables including interdependent disease/risk correlations.

3.15 The Subcommittee noted the Weycker et al. analysis and relative risks related to the United States, and considered that New Zealand data and epidemiology was required.

3.16 The Subcommittee requested that in the meantime, pending further analysis including the use of New Zealand data, PHARMAC staff initiate an application, with support from the Subcommittee, to consider funded access of the pneumococcal vaccine to adults at risk of pneumococcal infection due to lung disease, liver disease and Down syndrome. The Subcommittee also considered that New Zealand data would be helpful to support the international data, as other underlying medical condition groups might be identified at risk in the New Zealand setting.

Meningococcal conjugate vaccine for infected patients

3.17 The Subcommittee noted that PHARMAC had received feedback from The Royal Australasian College of Physicians and The Paediatric Society of New Zealand regarding access to meningococcal conjugate vaccine, following the changes to the immunisation consultation that was circulated on 9 December 2016. The Subcommittee noted that feedback received identified that meningococcal (Groups A, C, Y and W-135) conjugate vaccine was funded for close contacts of meningococcal cases but not to the patient themselves and requested that patients themselves be funded for the vaccine.

3.18 The Subcommittee considered that someone who had previously been infected with meningococcal bacteria had a higher risk of contracting another meningococcal infection of different serotype. The Subcommittee estimated there would be about 40 patients per year that would be eligible for vaccination under the amended criteria. The Subcommittee recommended that funded access to the meningococcal (Groups A, C, Y and W-135) conjugate vaccine should be extended to include patients who have been infected with meningococcal bacteria.

Varicella vaccine for children with severe chronic skin conditions

3.19 The Subcommittee noted that PHARMAC had received a request from Wellington Regional Public Health to widen the funding of varicella vaccine following the changes to the immunisation consultation that was circulated on 9 December 2016. The Subcommittee noted that the concern raised by Wellington Regional Public Health was that children aged between 15 months and 11 years who had chronic skin conditions, such as eczema requiring specialist care, who had not received a

varicella vaccine were particularly prone to severe infection with bacterial superinfection.

3.20 The Subcommittee noted Starship Children's Hospital guidelines to consider varicella vaccination to those unprotected children seen through Starship's specialist eczema outpatient clinics, but considered that this specialist care was not required for everyone and it would be difficult to restrict to patients with severe skin conditions.

3.21 The Subcommittee noted international evidence that indicated that children with eczema did not experience worse varicella disease, although noted that data was lacking. The Subcommittee did not consider it necessary to extend the funding of varicella vaccine to children with chronic skin conditions.

3.22 The Subcommittee considered that high risk patients with skin conditions were those receiving immunosuppressant therapies, and these patients would be covered under other inclusion criteria.

4 Pneumococcal vaccine for neuromuscular conditions

4.1 The Subcommittee reviewed an application received from the Muscular Dystrophy Association of New Zealand for the funding of pneumococcal vaccines for patients with neuromuscular disorders.

4.2 The Subcommittee noted that neuromuscular diseases comprised a range of neuromuscular conditions for which pneumococcal vaccine was requested and would estimate the patient numbers to be at least 6,000 patients. These conditions include patients with:

i. Multiple sclerosis
ii. Spinal muscular atrophy
iii. Congenital myopathies
iv. Myasthenia gravis
v. Limb-girdle muscular dystrophies
vi. Polymyositis
vii. Dermatomyositis
viii. Less common muscular dystrophies.

4.3 The Subcommittee noted the high-risk group within the list of neuromuscular disease included people on glucocorticosteroids or patients on mechanical ventilation.

4.4 The Subcommittee noted that the proposal was for a single dose of 13-valent pneumococcal conjugate vaccine (PCV13) followed by a three-dose regime of 23-valent pneumococcal polysaccharide vaccine (PPV23) at 8 weeks, 5 years later and at 65 years of age.

4.5 The Subcommittee considered there is weak evidence to support the use of pneumococcal vaccine in neuromuscular conditions. Members noted there was some discussion regarding risk factors relevant to neuromuscular conditions such as impaired cough, mucus production and respiratory failure in the Weycker et al. study (discussed in matters arising) with regards to surveillance data for diseases

or risk factors and calculated age-specific relative risks for either invasive pneumococcal disease or all-cause pneumonia.

4.6 The Subcommittee noted a prospective, randomised, placebo controlled, double blind study by Maruyama et al (BMJ 2010;340:c1004) of PCV23 efficacy in 1,006 rest home residents in Japan. The Subcommittee noted there was some reduction in pneumonia, pneumococcal pneumonia and death from pneumococcal pneumonia in the PCV23 group, but noted there was not a reduction in overall death.

4.7 The Subcommittee noted previous recommendations made by PTAC at the August 2015 meeting to decline funding of PPV23 and PCV13 for individuals over the age of 65.

4.8 The Subcommittee considered that there was a lack of epidemiological and efficacy data and no good quality evidence to support health benefits of pneumococcal vaccination for patients with neuromuscular disease and for their family, whanau or wider society.

4.9 The Subcommittee considered the applicant estimate of 1,500 prevalent patients seemed low and agreed with the PHARMAC staff estimate of approximately 6,000 patients in New Zealand with neuromuscular conditions that may be eligible under the proposed criteria. Members noted further analysis on patient numbers would be required for this group.

4.10 The Subcommittee **recommended** that the funding application for pneumococcal vaccination for individuals with neuromuscular conditions be declined due to the lack of efficacy data.

5 GSK Schedule options submission

5.1 The Subcommittee noted the GSK Ltd discussion paper regarding potential future scheduling scenarios and GSK Ltd manufactured vaccines.

5.2 The Subcommittee noted the vaccine timing schedules in Australia, Canada, the United Kingdom, the United States and Sweden and the differences compared to the current New Zealand National Immunisation Schedule.

Pneumococcal vaccine

5.3 The Subcommittee considered that a 2 + 1 schedule for PCV10 might be an option to consider in the future and noted that there was emerging good quality data regarding this dose schedule.

Pertussis vaccine

5.4 The Subcommittee considered that the pertussis strategy was about the prevention of severe pertussis in very young infants and not the elimination of pertussis because there is no strong evidence for herd immunity. The Subcommittee noted that protection against infection with *Bordetella pertussis* following vaccination was effective for only a few years.

5.5 The Subcommittee noted that New Zealand, unlike most Western countries, including Australia (recently reintroduced), Canada, and the United States, did not have a toddler dose of the pertussis vaccine.

5.6 The Subcommittee noted that many of the European countries had a pertussis schedule of 2 + 1 (two doses which occurred under 12 months of age and a booster dose from one year of age).

5.7 The Subcommittee considered that young infants remained at risk of pertussis infection, in part because of low maternal coverage with the pregnancy dose of pertussis vaccine. Members also noted that preterm infants born before 28 weeks of age have a greater risk and are not well covered with the current third trimester strategy. The Subcommittee discussed whether maternal coverage could be improved by widening the window for pertussis vaccination to women in their 2nd trimester (alluding to recent changed recommendations and data elsewhere), but considered evaluation was needed to whether maternal antibody interference would lead to lower vaccine induced serum antibody titres in infants, which could potentially result in a higher incidence of *B. pertussis* infection and/or pertussis in toddlers. Members considered that, given the potential for health gains but also the lead times necessary for any national roll-out of access changes, widening access to pertussis vaccination in pregnancy to include the second trimester was a high priority for early assessment.

5.8 The Subcommittee noted New Zealand starts the pertussis primary course in infants earlier than other countries at 6 weeks rather than 2 months or later. Members discussed the pros and cons for a 6-week dose versus a 2-month dose and the intent to vaccinate those most at risk. The Subcommittee noted there were a number of factors to consider regarding changing the timing of visits, and considered that maternal immunisation rates would need to be improved before moving the 6-week dose to a 2-month dose.

5.9 The Subcommittee discussed a 12-month pertussis scheduling programme with vaccinations at 2, 4 and 12 months of age

Hepatitis B

5.10 The Subcommittee noted the WHO recommends a birth dose of hepatitis B vaccine. Members considered this should only be considered in New Zealand if there is a need for it and that it would be helpful to look at the NZ data to evaluate rates of maternal hepatitis B more regularly.

5.11 The Subcommittee noted that currently there is not strong evidence for a birth dose of Hepatitis B vaccine, based on what appears to be an effective maternal screening programme and noted that the United Kingdom does not include a birth dose of hepatitis B vaccine in its schedule.

Varicella vaccine

5.12 The Subcommittee noted that it had previously indicated that a second dose of varicella vaccine should be considered for the New Zealand schedule at a later

stage and this may pose some challenges regarding timing of a second dose with other vaccines.

5.13 The Subcommittee noted that Australia had a novel approach to its scheduling of varicella and MMR vaccines. The Subcommittee noted that varicella and MMR were independently administered during the same visit at the age of one year, which then permitted later vaccination with the combined MMRV product also in the second year of life. The Subcommittee considered that it may be possible for New Zealand to use a similar approach with combination vaccines to accommodate a two-dose varicella vaccine regime in the future.

Influenza vaccine

5.14 The Subcommittee noted the theoretical bases for the effectiveness of live attenuated influenza vaccines in different childhood populations. The Subcommittee noted that the apparent ineffectiveness of live attenuated influenza vaccines in children in the United States might be due to previous vaccinations interfering with the live attenuated immune response.

5.15 The Subcommittee noted that England had introduced universal influenza vaccine in school aged children. Members noted that Professor Andy Pollard was visiting New Zealand later in the year to present at the Paediatric Society Conference and could provide some insights into this programme.

5.16 The Subcommittee considered increasing access of the funded vaccine for universal vaccination or to targeted groups as well as groups to support 'ring fence protection' should be reviewed at the next Subcommittee meeting. The Subcommittee requested that IMAC put together a funding application for consideration.

Tetanus, diphtheria and pertussis vaccine

5.17 The Subcommittee considered the tetanus vaccine funded for adults at 45 years and 65 years of age should be reviewed as there may be little benefit to providing this. Members considered if it was retained, then it may be worth considering the Tdap vaccine for this age group because it could provide additional protection against pertussis.

New vaccines

Zoster vaccine

5.18 The Subcommittee noted that the GSK zoster vaccine, Shingrix, demonstrated high efficacy in the elderly and noted that the vaccine is a 2-dose regime at 0 and 6 months.

Meningococcal B vaccine

5.19 The Subcommittee noted that the New Zealand notification rate of meningococcal B disease was relatively low at 1.4/100,000.

5.20 The Subcommittee noted that the proposed scheduling of GSK's meningococcal B vaccine, Bexsero, was 2+ 1 or 3+1.

5.21 The Subcommittee noted that there would be challenges to fit the meningococcal B vaccine into the current childhood immunisation schedule.

Meningococcal C vaccine

5.22 The Subcommittee discussed strategies for the introduction of a universal meningococcal C vaccine.

5.23 The Subcommittee noted that the United Kingdom had introduced an infant vaccination programme followed by a catch-up programme, whereas the Netherlands began with a catch-up programme followed by an infant programme then expanding to a teenage years' vaccination programme.

5.24 The Subcommittee considered that a universal vaccination campaign to establish herd immunity followed by an infant programme may be a potential strategy to consider for the meningococcal C vaccine.

6 Other business

Influenza vaccine funding criteria

6.1 The Subcommittee discussed whether it was appropriate to widen funded access of the influenza vaccine to older Māori by lowering the eligible age to 50 years. The Subcommittee considered that Māori that would be at increased risk of complications due to influenza would likely have co-morbidities that would already make them eligible for the funded influenza vaccine. The Subcommittee discussed whether aged-based cut-offs for vaccines were appropriate and considered that in the absence of a marker for the ability of individuals to respond to vaccination, age is the most accurate predictor of immune status.

Pertussis vaccine funding

6.2 The Subcommittee noted that the diphtheria, tetanus and pertussis vaccine is funded for pregnant women between 28-38 weeks gestation and that there was evidence that pregnant women should be recommended for pertussis vaccination earlier, in their second trimester. The Subcommittee suggested that it soon review the evidence and consider whether vaccination for pertussis should be available for women earlier in their pregnancy.