PHARMAC
Pharmaceutical Management Agency

PHARMACEUTICAL SCHEDULE APPLICATION

From: Medical Director

Date: April 2018

Meningococcal B vaccine (Bexsero) for prevention of invasive meningococcal group B disease

SUMMARY OF PHARMACEUTICAL			
Brand Name	Bexsero	**Chemical Name**	Multicomponent meningococcal group B vaccine (recombinant, adsorbed) (4CMenB)
Indications	Immunisation against invasive disease caused by *N. meningitidis* group B strains in infants from 2 months of age and older	**Presentation**	0.5 mL suspension for injection in a prefilled syringe
Therapeutic Group	National Immunisation Schedule	**Dosage**	3+1 dosing schedule with primary doses at 6 weeks, 3 and 5 months of age and a booster dose at 12 months OR 2+1 dosing schedule with primary doses at 6 weeks and 3 months of age and a booster dose at 12 months
Supplier	GlaxoSmithKline New Zealand Limited	**Application Date**	January 2018
MOH Restrictions	Prescription medicine Currently not approved	**Proposal type**	New listing
Current Subsidy	$ Nil		
Proposed Subsidy	$ [redacted] per dose	**Manufacturer's Surcharge**	Nil
Proposed Restriction	Universal infant vaccination		
Original Pack	No	**Section F**	No

Market Data	YE 30 June 2021	YE 30 June 2022	YE 30 June 2023
Number of Patients	48,758	55,947	60,987
3+1 schedule			
Subsidy (gross)	section 9(2)	section 9(2)	section 9(2)
Net Cost to Schedule	section 9(2)	section 9(2)	section 9(2)
Net Cost to DHBs	section 9(2)	section 9(2)	section 9(2)
Net Cost to DHBs (NPV)	section 9(2)		
2+1 schedule			
Subsidy (gross)	section 9(2)	section	section 9(2)
Net Cost to Schedule	section	section 9(2)	section 9(2)
Net Cost to DHBs	section	section 9(2)	section 9(2)
Net Cost to DHBs (NPV)	section 9(2)		

Notes: NPV = Net present value, 8%; OP = Original pack

QUESTIONS TO IMMUNISATION SUBCOMMITTEE

Note to Subcommittee members: These questions have been identified by PHARMAC staff as being particularly relevant to the application. Please feel free to provide additional information as appropriate.

Health benefit

1. Which patient population would benefit most from 4CMenB (Bexsero)?
2. What is the strength and quality of evidence, including its relevance to NZ, for health benefits that may be gained from 4CMenB (Bexsero)?
3. Would 4CMenB (Bexsero) produce a health benefit for family, whānau or wider society, additional to the health benefits for people with invasive meningococcal B disease? If so how, and what is the strength and quality of evidence for this benefit?
4. Should 4CMenB (Bexsero) be funded, are there any consequences to the health system that have not been noted in the application?

Need

5. Does the draft Health Need Statement accurately describe the Health Need associated with invasive meningococcal disease?
6. What is the strength and quality of evidence in relation to health need due to invasive meningococcal disease?
7. Should the assessment of 4CMenB (Bexsero) include the possibility of a future epidemic, and if so, what is the likelihood of one occurring in the next ten years?
8. Should the assessment of 4CMenB (Bexsero) include the health need and potential health benefits arising from cross-strain protection?

9. Is it reasonable to apply the data for all strains of *N meningitidis* to Meningococcal Group B infections, and if not, which statistics would be different for the strains targeted by the 4CMenB (Bexsero) vaccine?

Suitability

10. Are there any non-clinical features of the 4CMenB (Bexsero) that may impact on use, either by the patient, by family, or by healthcare workers, that have not been considered in the application?

Costs and savings

11. Would the use of 4CMenB (Bexsero) create any significant changes in health-sector expenditure other than for direct treatment costs (e.g. diagnostic testing, nursing costs or treatment of side-effects)?

    Note that costs outside of the health sector, such as education costs, are outside of PHARMAC's statutory objective and Factors for Consideration.

    Note that some of the claimed benefits, such as economic productivity gains and reduction in bereavements, are outside of the Factors for Consideration.

12. Are the applicant's assumptions reasonable that there will be uptake of 75% in year one, 85% in year two and 92% in year three?

13. Will a catch up programme be required?

General

14. Is there any data or information missing from the application, in particular clinical trial data and commentary?

Recommendations

15. Should Bexsero be listed in the Pharmaceutical Schedule for universal childhood immunisation?

    - Name the Factors for Consideration particularly relevant to a positive or negative recommendation and explain why each is relevant.

16. If listing is recommended, does the Subcommittee recommend a 3+1 or 2+1 dosing schedule?

17. If listing for universal childhood vaccination is recommended, what priority rating would you give to this proposal? **[low / medium / high / only if cost-neutral]**?

18. Are there any special groups outside the childhood immunisation schedule that should be included in the access criteria, such as high risk groups or close contacts?

19. Should Bexsero be listed in the Pharmaceutical Schedule for using during declared epidemics?

20. If listing for epidemics is recommended, which groups should be included in the access criteria?

21. If listing for use during declared epidemics is recommended, what priority rating would you give to this proposal? **[low / medium / high / only if cost-neutral]**?

22. Should Bexsero be listed in the Pharmaceutical Schedule for outbreak situations?

23. If listing for outbreak situations is recommended, which groups should be included in the access criteria?

24. If listing is recommended for outbreak situations, what priority rating would you give to this proposal? **[low / medium / high / only if cost-neutral]**?

25. Should Bexsero be listed in the Pharmaceutical Schedule for high risk groups and close contacts?

26. If listing is recommended for high risk groups and close contacts, what priority rating would you give to this proposal? **[low / medium / high / only if cost-neutral]**?

27. Does the Subcommittee have any recommendations additional to the application?

PURPOSE OF THIS PAPER

PHARMAC seeks the advice of the Immunisation Subcommittee about the application to list a meningococcal B vaccine, Bexsero, for universal childhood vaccination on the National Immunisation Schedule. The application proposes two possible dosing schedules:

- a 3+1 dosing schedule, with the primary doses administered at 6 weeks, 3 and 5 months of age and a booster dose at 12 months; or
- a 2+1 dosing schedule, with the primary doses administered at 6 weeks and 3 months of age and a booster dose at 12 months

The application also proposes listing for high risk groups and close contacts, the same groups currently eligible for MenC and MenACWY vaccines.

DISCUSSION

Background

Sub-committee consideration of meningococcal immunisations

Meningococcal B vaccines have previously been considered by the Immunisation Subcommittee in 2015 in regard to management of a future epidemic of Meningococcal B disease. This is the first supplier application for a Meningococcal B vaccine for universal vaccination to be considered by the Subcommittee or PTAC. In February 2018, at the recommendation of the Ministry of Health Communicable Diseases Team, PHARMAC purchased 100 doses of Bexsero as emergency stock that could be used in the event of a meningococcal B outbreak in a multi-occupancy residential setting such as university halls of ***residence.***

RFP

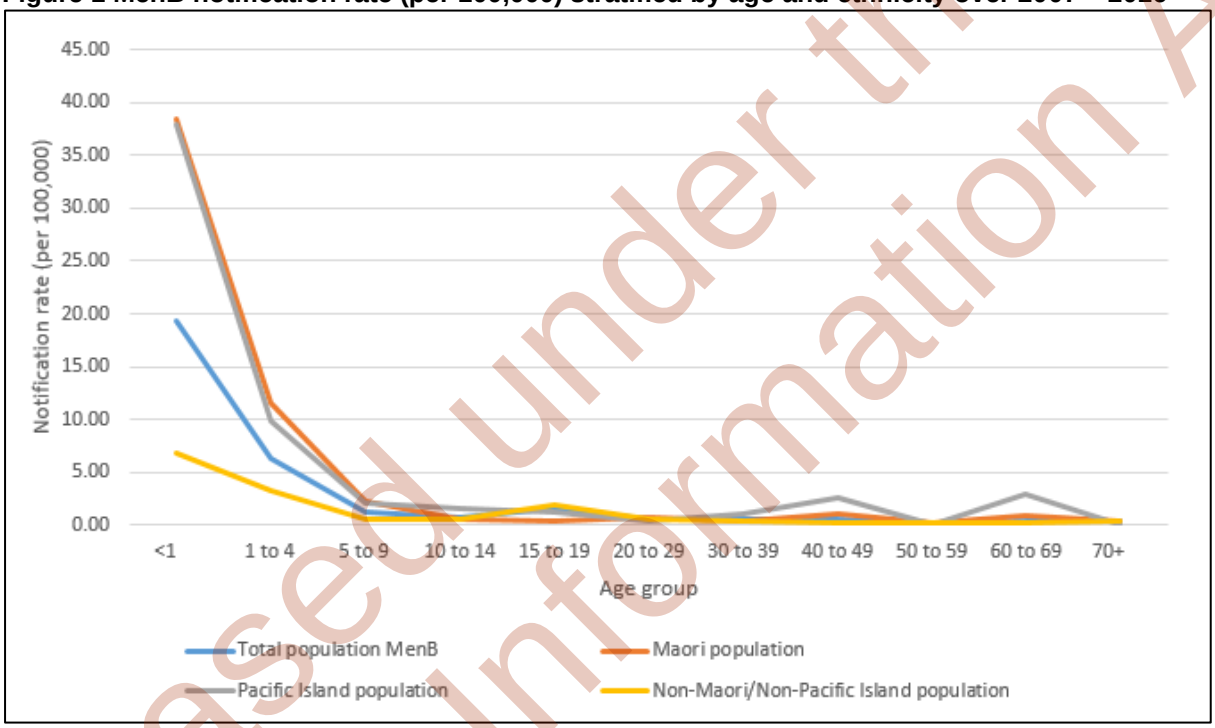
PHARMAC intends to issue an RFP for various vaccines in late 2018. Bexsero is not yet approved by Medsafe, with the file being submitted to Medsafe for priority assessment in December 2017. In order for meningococcal B vaccine to potentially be included in the RFP, PHARMAC requires clinical advice as to whether or not this vaccine should be listed, so seeks the Subcommittee's advice on this application. The application can be referred to PTAC later in 2018 once the vaccine has been approved by Medsafe.

Meningococcal disease

Invasive meningococcal disease (IMD) rates are higher in New Zealand than in other comparable countries such as Australia, US, Canada and England. The applicant notes that most cases of meningococcal disease in New Zealand are caused by meningococcal group B (57.4% (523/911) over the period 2007 – 2016). In 2016, 70% of meningococcal cases that could be typed were serogroup B. In the same period, the proportion of serogroup B cases in the under 5 years of age was higher, at 82%. In 2017, 68 out 112 (60%) of notified meningococcal cases were serogroup B.

People of all ages and ethnicities are at risk of developing meningococcal (MenB) disease, although it disproportionately affects infants <1 year of age and Maori and Pacific Island populations (Figure 1).

Figure 1 MenB notification rate (per 100,000) stratified by age and ethnicity over 2007 – 2016



Source: ESR and Stats NZ; Supplier application attachment 01

MenB notification rate (per 100,000) by age and ethnicity from 2014 - 2016

	Age	2014	2015	2016
Māori	<1	18.28	48.60	18.01
	1 to 4	8.98	4.54	3.05
	5 to 9	0.00	0.00	1.20
Pacific	<1	13.04	12.84	25.29
	1 to 4	3.26	6.42	9.48
	5 to 9	0.00	2.82	2.77
Total Population	<1	6.82	18.58	10.02
	1 to 4	4.40	4.87	4.49
	5 to 9	0.00	0.32	1.24

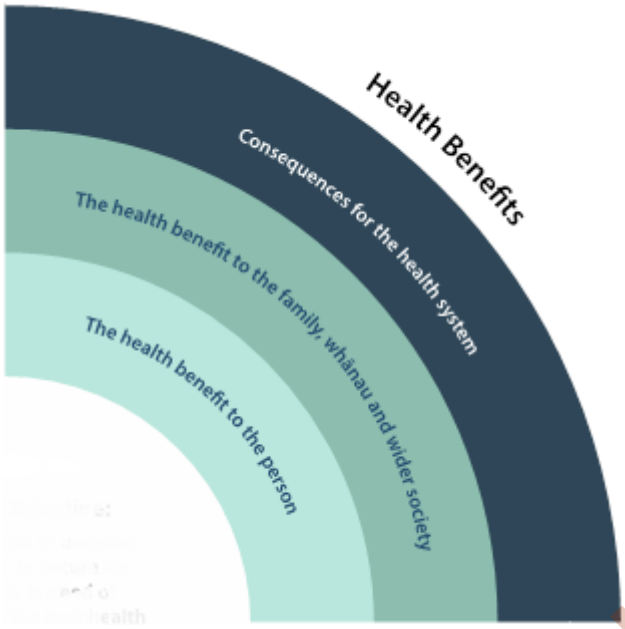
Source: ESR and Stats NZ; Supplier application attachment 01

NZ MenB epidemic

From 1991 – 2007 New Zealand experienced a prolonged epidemic of MenB, driven by a single group B subtype (B: P1.7-2,4), resulting in 6,128 cases and 252 deaths. The MeNZB vaccine was introduced from 2004 – 2008 to manage the epidemic and the number of disease notifications declined dramatically. The immune response to the vaccine was short-lived and it is not expected that anyone previously vaccinated would still have existing immunity to B disease.

GlaxoSmithKline New Zealand Limited (GSKNZ) is seeking funding on the National Immunisation Schedule (NIS) for 4CMenB (Bexsero), a multicomponent vaccine consisting of four highly immunogenic components that help protect against a broad range of disease-causing group B strains.

Health Benefits



Details of the pharmaceutical under consideration

The health benefits to the person, family, whānau and wider society

The applicant notes that 4CMenB is a highly immunogenic, multicomponent vaccine that has the potential to protect against a broad range of disease-causing group B strains.

Meningococcal infection is transmitted from person to person through aerosol droplets, respiratory secretions and saliva, so active immunisation against *N. meningitidis* group B strains may prevent MenB infection and subsequent transmission to family or whānau members. The applicant considers vaccination with 4CMenB will help protect against future outbreaks, reducing the likelihood of requiring chemoprophylactic antibiotics. Immunisation with 4CMenB may reduce the likelihood of another MenB outbreak, preventing the associated burden and cost to the family, whānau and wider society.

The applicant has provided three randomised, multicentre phase IIb/III clinical trials comparing the immunogenicity and safety of 4CMenB and non-interference with routine vaccinations in infants and toddlers:

Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunisation schedules
Gossger et al. JAMA 2012;307(6):573-82. (Appendix 1)

A phase IIb, multicentre, open-label, parallel group, randomised controlled study of 1,885 infants enrolled at age 2 months. Participants were randomised into one of three groups to receive 4CMenB in combination with routine vaccines in varying schedules or to receive routine vaccines alone.

The main outcome measure was the percentage of participants with human complement serum bactericidal activity (hSBA) titre of 1:5 or greater against 3 MenB strains specific for vaccine antigens (NZ98/254, 44/76-SL and 5/99).

After three 4CMenB vaccinations, 99% or more of infants developed hSBA titres of 1:5 or greater against strains 44/76-SL and 5/99. For strain NZ98/254, this proportion varied and was 79%, 86.1% or 81.7% respectively for each dosing schedule.

The authors concluded that 4CMenB vaccine is immunogenic against reference strains when administered with routine vaccines at 2, 4 and 6 or at 2, 3 and 4 months of age, producing minimal interference with the response to routine infant vaccinations.

Immunogenicity and safety of an investigational multicomponent, recombinant, meningococcal serogroup B vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomised trials
Vesikari et al. Lancet 2013;381:825-35.

A phase III, partially-blinded, randomised, multicentre, controlled study to evaluate immunogenicity, safety and lot to lot consistency of 4CMenB vaccine when administered with routine infant vaccinations to healthy infants.

2,627 infants were enrolled in the open-label phase, 1003 in the observer-blind phase and 1,555 in the booster study. Lot-to-lot consistency was demonstrated for the three 4CMenB lots. Of 1,181 infants tested 1 month after three 4CMenB doses, 100% had hSBA titres of 5 or more for against strains selective for factor H binding protein and neisserial adhesin A, and 84% for New Zealand outer membrane vesicle.

Immune responses to routine vaccines were much the same with or without concomitant 4CMenB, but concomitant vaccination was associated with increased reactogenicity. 77% of infants had fever of 38.5 ºC or higher after any 4CMenB dose, compared with 45% after routine vaccines alone and 47% with MenC. Two febrile seizures were deemed probably related to 4CMenB.

The authors concluded that 4CMenB is immunogenic in infants and children aged 12 months with no clinically relevant interference with routine vaccines, but increases reactogenicity when administered concomitantly with routine vaccines.

Reduced schedules of 4CMenB vaccine in infants and catch-up series in children: Immunogenicity and safety results from a randomised open-label phase IIIb trial
Martinon-Torres et al. Vaccine 2017;35:3548-57.

A phase IIIb, open-label, multicentre study to evaluate the safety, tolerability and immunogenicity of 4CMenB when administered alone to healthy infants according to different immunisation schedules and to healthy children aged 2 to 10 years.

754 infants and 404 children were enrolled in this study. Sufficiency of immune responses was reported after two doses in 98-100% of infants receiving 2+1 schedules. Similarly, 95-99% of children demonstrated sufficiency of immune response following 2 catch-up doses.

A total of 45 serious adverse reactions were reported, of which 3 were considered related to vaccination.

International comparison

A ‘2+1’ 4CMenB schedule was funded in the UK national immunisation programme in September 2015, based on the 2012 rates of MenB notifications for infants and children aged 1-4 years in the UK and Ireland (UK 22 and 7.6 per 100,000 respectively, Ireland 23

and 6.8 per 100,000 respectively). These rates are similar to those observed in New Zealand in 2007-2016 for infants (19.38 per 100,000) but lower than the same age group in Maori and Pacific Island populations (38.40 and 37.88 per 100,000 respectively).

In the first 10 months of the programme, cases of MenB disease halved in vaccine eligible infants. Similar results were observed after adjustment for disease trends in the 4 years before vaccine introduction and in non-vaccine eligible children (Parikh et al. Lancet 2016; 388(10061): 2775-82).

Consequences for the health system

Dosing schedule

The applicant has proposed two dosing schedule options, 3+1 and 2+1. The 3+1 dosing schedule has the primary administrations at 6 weeks, 3 and 5 months and a booster at 12 months. The 2+1 dosing schedule has the primary administrations at 6 weeks and 3 months and a booster at 12 months. With both dosing schedule proposals, the primary doses are aligned with the current National Immunisation Schedule (NIS), but the 12-month booster would be an additional visit which would result in additional work for vaccinators and increased vaccination claim costs for the Ministry of Health. The booster vaccination could be given at 15 months to align with the NIS, but this would mean five injections would be given at the 15 months visit under the current schedule.

Paracetamol administration

The applicant recommends that prophylactic administration of paracetamol with every dose of 4CMenB to manage the known reactogenicity of the vaccine. Paracetamol is currently not recommended to be administered for childhood vaccinations, so this would represent an additional cost and increase in vaccinator workload to manage this. Vaccinators would need to be provided with training around the recommendation for prophylactic paracetamol. We seek the advice of the Sub-committee regarding use of paracetamol in this setting.

Burden

The applicant considers that including 4CMenB in the NIS would reduce the burden on the healthcare system from the consequences of meningococcal infection, including reduced requirement for emergency transport to Starship ICU and reduced requirements for therapy associated with long term sequelae.

This proposal relates to the Increased Immunisations Government health system priority through improved disease prevention.

Need[1]

1 Please note PHARMAC's Factors For Consideration schematic currently does not explicitly refer to the health needs of family, whānau and wider society, but this factor should be considered alongside those depicted in the schematic.

Description of the disease

Health need

PHARMAC and PTAC have recently introduced standardised Health Need Statements to describe the health need associated with a health condition. We seek your comment on the content of the draft Health Need Statement in Appendix 2.

The applicant has focused on the health need created by the current 'baseline' rates of IMD, outside of outbreaks and epidemics (i.e., a typical or 'steady state' rate of IMD over a specified period of time e.g. a year). The health economic assessment provided by the applicant is based on a vaccination programme that reduces this baseline incidence of cases. We seek your views on whether it would also be appropriate to assign a probability of epidemic, and whether to consider that in both the Health Need Statement and in the Health Benefits attributable to a vaccination programme.

Sequelae of disease

The applicant has supplied a literature review identifying long-term sequelae of IMD. We seek your critical appraisal of the applicant's literature review.

Sub-types

Most of the statistics quoted by GSK and published by ESR are for all sub-types of *N meningitidis*. We seek your views on whether it is reasonable to extrapolate general data such as severity, transmission dynamics, and case-fatality from all sub-types to just the strains targeted by the Bexsero vaccine. For example, case-fatality rates range from 3% in GSK's modelling, to "5-10%" in the quoted references, to "approximately 10%" in the applicant's synopsis.

The applicant does not claim any potential benefits arising from cross-strain protection, including to gonorrhoea infections. In your view, are such health benefits significant enough that PHARMAC should consider them and the corresponding health needs?

Health need outside scope

We note also the applicant has identified 'health needs' that are outside the usual scope of PHARMAC's assessment (see Table 94 of submission). The applicant's cost-effectiveness analysis includes a "bereavement quality of life loss" and "productivity loss" that is explicitly excluded by PHARMAC's guidelines for pharmacoeconomic analysis (the PFPA). The applicant also applies a "Quality adjustment factor" of 3 to the health benefits gained by the vaccination programme. While Quality Adjustment is the methodology recently used by the UK JCVI, PHARMAC's approach is to clearly identify the health need (severity) separately from health benefits, and then to consider each Factor separately when ranking competing proposals for pharmaceutical funding.

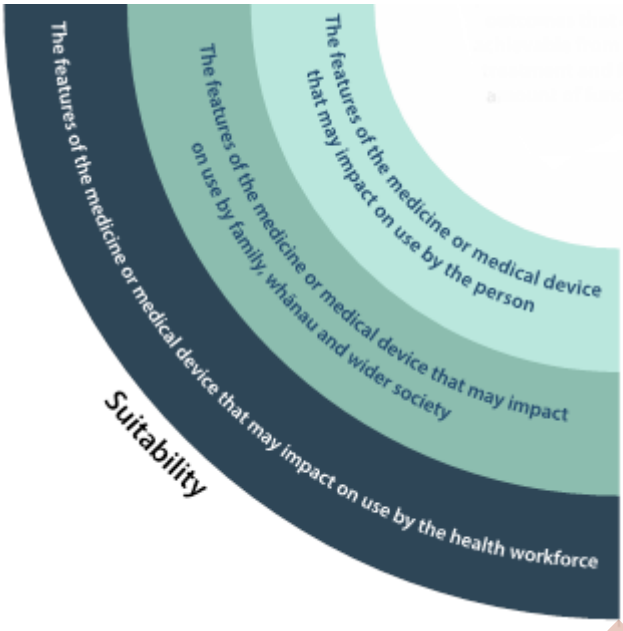
Health disparities

Invasive meningococcal disease disproportionately affects those of Māori and Pacific descent with these populations exhibiting four times higher rates of MenB across all age groups compared to the non-Māori/non-Pacific population from 2007–2016 children. Māori and Pacific infants <1 year of age had a six times higher rate of MenB disease from 2007–2016 compared to non-Māori/non-Pacific Island children. The disproportionate distribution of IMD among Māori may be attributed to their low socioeconomic status and household crowding.

Other groups experiencing disparities

Rates are highest in Pacific peoples. The disproportionate distribution of IMD among Pacific peoples may be attributed to their low socioeconomic status and household crowding.

Suitability



The features of the medicine or medical device that impact on use

Pre-filled syringes

Bexsero is supplied as a 0.5 mL suspension in a pre-filled syringe (Type I glass) with a plunger stopper (Type I bromobutyl rubber) and with a protective tip cap (Type II rubber). Internationally available pack sizes are one syringe with or without needles, or ten syringes without needles. Not all pack sizes may be distributed in New Zealand.

One dose (0.5 mL) contains:

Recombinant *Neisseria meningitidis* group B fHbp fusion protein	50 mcg
Recombinant *Neisseria meningitidis* group B NadA protein	50 mcg
Recombinant *Neisseria meningitidis* group B NHBA fusion protein	50 mcg
OMV from *Neisseria meningitidis* group B strain NZ98/254 measured as amount of total protein containing the Porin A (PorA P1.4)	25 mcg

Medsafe

Bexsero does not yet have Medsafe consent for distribution but is undergoing a priority evaluation.

GSKNZ have applied for the indication of active immunisation against invasive disease caused by *N. meningitidis* group B strains, in individuals from 2 months of age and older.

The Medsafe application is for approval of a 3+1 dosing schedule, as an abbreviated submission based on the Australian TGA approval. GSKNZ notes it intends to submit an update for a 2+1 dosing schedule immediately following approval by the TGA.

Costs and Savings

Health-related costs and savings to the person, their family, whānau and wider society

Costs and savings to pharmaceutical expenditure

Cost per patient

GSKNZ is proposing a price of section per dose. With a 3+1 dosing schedule the annual cost per infant would be section , but with a 2+1 schedule the cost would be section 9(2) per infant. If the vaccine is administered at the same time as other infant vaccinations, there not be additional vaccination claim costs the Ministry of Health. If any doses are administered as a stand-alone vaccination, there would be a vaccination claim of $20 payable.

To accommodate a 2+1 schedule, the Ministry of Health has proposed some possible changes to the National Immunisation Schedule which would add the primary doses to the 6 week and 3 month visits, and introduce a new 12 month visit where meningococcal B booster would be administered at the same time as pneumococcal and MMR vaccines. If the proposed National Immunisation Schedule changes were adopted, the additional vaccination claim of $20 for the estimated 65,010 children in the first year would total $1.3 million.

Estimated Incremental Total Cost of Listing

3+1 Schedule	2020	2021	2022	2023	2024
Total number of infants aged 0 years	65,010	65,820	66,290	66,570	66,710

Estimated number of infants to be vaccinated	48,758	55,947	60,987	61,244	61,373
Number of doses					
Primary doses	146,273	167,841	182,960	183,733	184,120
Booster doses	0	48,758	55,947	60,987	61,244
Total number of doses	146,273	216,599	238,907	244,720	245,364
Total cost of vaccinations	section 9(2)(b)(ii), 9(2)	section 9(2)(b)(ii), 9(2)(ba(i)	section 9(2)(b)(ii), 9(2)(ba(i)	section 9(2)(b)(ii), 9(2)(ba(i)	section 9(2) s

2+1 Schedule	**2020**	**2021**	**2022**	**2023**	**2024**
Total number of infants aged 0 years	65,010	65,820	66,290	66,570	66,710
Estimated number of infants to be vaccinated	48,758	55,947	60,987	61,244	61,373
Number of doses					
Primary doses	67,515	111,894	121,974	122,489	122,746
Booster doses	0	48,758	55,947	60,987	61,244
Total number of doses	97,515	160,652	177,921	193,476	183,991
Total cost of vaccinations	section 9(2)(b)(ii), 9(2)(ba(i)	section 9(2)(b)(ii), 9(2)	section 9(2)(b)(ii), 9(2)(ba(i)	section 9(2)(b)(ii), 9(2)(ba(i)	section 9(2) s

The supplier assumes an uptake of 75% in year one, 85% in year two and 92% in year three.

Costs and savings to the rest of the health system

The supplier provided the following estimates for cost savings to the health system expected to result in the first year from the introduction of 4CMenB, with 5-year non-discounted savings of approximately $1.76m for both schedules.

Cost	3+1 schedule	2+1 schedule
Acute care cost saved	$139,679	$133,789
Direct medical cost long-term sequelae saved	$18,061	$17,299
Long-term caregiving cost saved	$9,489	$9,089
Public health management and outbreak cost saved	$3,789	$3,629
Total direct cost due to disease saved	$171,019	$163,808

Other costs and savings

Under costs, the applicant includes costs to the education sector for special needs education, which is outside of Vote: Health and hence not considered in PHARMAC's budget allocation decisions.

Cost Effectiveness (combining the Health Benefits and Costs quadrants)

Applicant's Economic Evaluation

The applicant submitted an economic evaluation as part of the application. The applicant has focused on the health need created by the current 'baseline' rates of IMD, outside of outbreaks and epidemics (i.e., a typical or 'steady state' rate of IMD). The health economic assessment provided by the applicant is based on a vaccination programme that reduces this baseline incidence of cases.

The application assesses cost-effectiveness on the basis of three scopes:

1. The '**current guidelines'** scenario follows PHARMAC pharmacoeconomic guidelines for the health economic evaluation of the impact of 4CMenB on IMD in New Zealand. This approach considers impact on cost and effects falling directly within the health care system.
2. An **'update'** scenario reflecting cross-protection against serogroup W and the impact of the disease on the quality of life of the family network and long-term caregivers due to short-term and long-term impact of the disease and a bereavement factor. Consideration of these additional factors currently falls 'out of scope' according to PHARMAC pharmacoeconomic guidelines.
3. Additionally, the **societal perspective,** including the parameters of the 'update' scenario plus the impact of costs associated with special education needs of patients, productivity loss due to acute care for both patients and parents in the case of children having IMD, productivity loss due to long-term sequelae disability in the patient, and the productivity loss of one parent staying at home to care for the child with severe long-term sequelae until the end of their school age

The results of the '**current guidelines'** cost-effectiveness analysis was section QALYs per $1 million invested. For the 2+1 schedule the result is se QALYs per $m.

The '**update**' scenario saw section QALYs per $1 million and section QALYs per $1 million for the 3+1 and 2+1 schedule respectively.

Incorporating the **societal perspective**: the result improves to section QALYs per $1 million in the 3+1 scenario and to section QALYs per $1 million in the 2+1 scenario.

These indicate section 9(2)(b)(ii), cost-effectiveness under current evaluation guidelines. Key results of the analyses are the following:

- Over a 100-year time horizon 2,007 vaccine-preventable IMD cases were prevented through the introduction of a 4CMenB vaccination program with a 3+1 schedule in the 'current guidelines' scenario.
- Within the first five years of the 4CMenB vaccination programme, at least 63 vaccine preventable IMD cases were prevented, including a reduction of more than 58% of vaccine preventable IMD cases among the vulnerable population of infants (age <1 year).
- The 'update' scenario, captures additional aspects of MenB disease (e.g., severity of disease, impact of disease and burden beyond the patient) and the 4CMenB vaccine (cross-protection W), resulting in section QALYS per $1 million for the 3+1 schedule and section QALYS per $1 million for the 2+1 schedule.

UK JVCI Consideration

Of note should be deliberations in the UK, in particular the JCVI position statement on use of Bexsero® meningococcal B vaccine in the UK (March 2014) (Appendix 1). In particular it noted: "*the cost-effectiveness of the vaccine was very sensitive to a number of inputs that had potential to vary the results around the cost-effectiveness threshold…..The Committee therefore published an interim statement for consultation in July 2013, which indicated that the vaccine was highly unlikely to demonstrate cost-effectiveness at any vaccine price*".

Changes requested by the Committee to the evaluation were generally, but not exclusively positive towards the impact of the vaccine, the Committee considered it important these were modelled to ensure the robustness of the model. The changes made were:

- Revision of quality of life losses to include additional quality of life losses associated with the short-term phase of IMD
- Inclusion in the base case model of a quality of life adjustment factor agreed by the JCVI in June 2013 (as opposed to this being accounted for in an additional analysis as had been done previously)
- An increased incidence of disease, considered by the Committee more representative of average incidence over a longer period
- Inclusion of new data on the rate of minor and severe sequelae following IMD • Inclusion of a proportion of litigation costs associated with meningococcal disease in the NHS
- Inclusion of quality of life losses to family members.

For an ***infant programme*** JCVI subsequently agreed that the most plausible scenario included the parameters of 95% efficacy, 88% strain coverage, 18 and 36 month duration of protection after primary and booster doses, and 30% vaccine efficacy against acquisition of carriage.

For both 2, 3, 4, 12 month and 2, 4, 12 month schedules, a cost-effective price for the vaccine existed for an infant programme. However, whilst a positive vaccine price existed, indicating cost-effectiveness, the vaccine price was significantly lower than the list price for Bexsero®.

For an ***adolescent programme*** the Committee agreed the most plausible scenario included parameter estimates of 95% efficacy, 88% strain coverage, 120 month duration of protection and 30% protection against acquisition of carriage, and using these parameters, agreed that a positive cost-effective price for the vaccine existed for a two dose adolescent programme. The price was again much lower than the list price for Bexsero®. However the Committee agreed there was considerable uncertainty pertaining to these parameters.

Key Modelling Issues

The technical development of an assessment of the cost-effectiveness of treatments for transmitted, vaccine preventable diseases is an extremely complex process which requires careful consideration of numerous assumptions regarding the 'disease pathway' including:

- **economic evaluation scenario frame:** the disease scenario(s) being considered: i.e., 'baseline' rates of disease versus outbreak/epidemic levels
- **epidemiology:** subsequent estimates of 'baseline' and epidemic rates of MenB in New Zealand (i.e., health need);
- **vaccine-specific assumptions**: vaccine efficacy, vaccine uptake, strain 'matching' or coverage, duration/survival of protection, protection against acquisition of carriage, etc. This includes consideration by age and dosing regimen.
- **other specific input parameters**: including sequalae outcomes and their probabilities and associated quality of life, transmission rates, contact matrices and case fatality ratios (CFRs), quality of life with specific emphasis on ensuring New Zealand applicability.

For all of these, particular attention must be given to levels of uncertainty and sensitivity scenarios.

We seek the Sub-committee views in particular on the following:

- whether it would also be appropriate to assign a probability of epidemic in order to determine the health need and subsequent cost-effectiveness outcome in this scenario;
- whether it is reasonable to extrapolate general data such as severity, transmission dynamics, and case-fatality from all sub-types to just the strains targeted by the Bexsero vaccine. For example, case-fatality rates range from 3% in GSK's modelling, to "5-10%" in the quoted references, to "approximately 10%" in the applicant's synopsis. Also, are all these inputs applicable to the New Zealand context.
- The supplier assumes an uptake of 75% in year one, 85% in year two and 92% in year three. Are these realistic/appropriate? If New Zealand's NIS was subsequently revised by the Ministry of Health, resulting in 5 doses in 15 months, would this change uptake? Would it be impacted by the introduction of a reactogenic vaccination or would this be mitigated by parental education efforts?
- The applicant does not claim any potential benefits arising from cross-strain protection, including to gonorrhoea infections. In your view, are such health benefits significant enough that PHARMAC should consider them?

THE FACTORS FOR CONSIDERATION

Factors are presented here in the order they appear in the paper, without implying any ranking or relative importance.

NEED

- The health need of the person
- The availability and suitability of existing medicines, medical devices and treatments
- The health need of family, whānau, and wider society
- The impact on the Māori health areas of focus and Māori health outcomes
- The impact on the health outcomes of population groups experiencing health disparities
- The impact on Government health priorities

HEALTH BENEFITS

- The health benefit to the person
- The health benefit to family, whānau and wider society
- Consequences for the health system

SUITABILITY

- The features of the medicine or medical device that impact on use by the person
- The features of the medicine or medical device that impact on use by family, whānau and wider society
- The features of the medicine or medical device that impact on use by the health workforce

COSTS AND SAVINGS

- Health-related costs and savings to the person
- Health-related costs and savings to the family, whānau and wider society
- Costs and savings to pharmaceutical expenditure
- Costs and savings to the rest of the health system