5.09 MENINGOCOCCAL POLYSACCHARIDE SEROGROUPS A, C, W-135 AND Y CONJUGATE VACCINE Injection 0.5 mL, MenQuadfi®, Sanofi-Aventis Australia Pty Ltd

1 Purpose of submission

1.1 The submission requested listing on the *National Health (Immunisation Program – Designated Vaccines) Determination 2014 (No.1)* (the Determination) for the prevention of invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* serogroups A, C, W135, and Y (MenA, MenC, MenW135 and MenY, respectively).

1.2 The submission requested listing meningococcal serogroup A, C, W-135 and Y Polysaccharide Tetanus Toxoid Conjugate (MenACWY-TT) vaccine (referred to herein by the brand name MenQuadfi®) on the Determination as an alternative MenACWY vaccine to the NIP-listed MenACWY-TT vaccine (referred to herein by the brand name Nimenrix®) for the prevention of meningococcal disease in the same populations (excluding children <12 months of age with specific medical risk conditions). The PBAC had not previously considered MenQuadfi.

1.3 The submission requested a listing based on a cost-minimisation analysis versus Nimenrix. The key components of the submission are presented in Table 1.

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	a) Children who are 12 months old; or b) Adolescents who are at least 14 years old but less than 20 years of age; or Specific medically at-risk subjects ≥12 months of age, including those: c) With congenital or acquired asplenia (e.g. splenectomy or hyposplenia); or d) With complement deficiency; or e) Who are undergoing eculizumab treatment.
Intervention	• Children and adolescents: A single dose of MenQuadfi administered for subjects in populations a) or b) • Medically at-risk subjects (aged 12 months or older): Two doses of primary course MenQuadfi plus booster doses for subjects in population c), d) or e).
Comparator	• Children and adolescents: A single dose of Nimenrix administered per current NIP arrangements. • Medically at-risk individuals: Two doses of Nimenrix plus booster doses as per current NIP criteria[1].
Outcomes	• Immunogenicity: proportion of subjects achieving post-vaccination SBA titres above established thresholds, proportion of patients who were responders, ratio of post vaccination GMTs. • Co-administration: immune responses to other concomitantly administered vaccines • Safety: proportion of subjects with solicited/unsolicited adverse events by severity and potential relationship to vaccination.
Clinical claim	• In children aged approximately 12 months, a single dose of MenQuadfi will deliver non-inferior comparative effectiveness and safety to a single dose of the main comparator Nimenrix; • In adolescents aged 14-19 years a single dose of MenQuadfi will deliver non-inferior comparative effectiveness and safety to a single dose of Menveo and by reasonable extrapolation can be assumed to provide comparable effectiveness and safety to a single dose of Nimenrix; • In specified medically at risk subjects aged ≥12 months there are scarce data available regarding the comparative effectiveness and safety of the ATAGI-recommended 2 x primary + booster dose regimens of MenQuadfi and Nimenrix, but no evidence or clinical expectation that the therapeutic relativity would differ from that of a single dose regimen in other populations.

GMT=geometric mean titres; NIP=National Immunisation Program; SBA=serum bactericidal antibody; ATAGI=Australian Technical Advisory Group on Immunisation

Source: Table 1.1 of the submission.

1. The recommended dose for Nimenrix is 2 to 4 in medically at-risk individuals. Children under 12 months of age receive 3 or 4 doses which does not apply to MenQuadfi.

2 Background

Registration status

2.1 MenQuadfi was registered by the Therapeutic Goods Administration (TGA) on 29 October 2020 for the following indication:

'MenQuadfi is indicated for active immunisation for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, W and Y. The use of MenQuadfi should be in accordance with official recommendations.'

2.2 The approved dose of MenQuadfi is as follows:

- Primary Vaccination
  - Individuals 12 months of age and older receive a single dose.
- Booster Vaccination

- MenQuadfi may be given as a single booster dose to adolescents and adults who have previously been primed with meningococcal vaccine at least 4 years prior.

2.3 The PBAC noted that MenQuadfi is TGA approved for use for individuals from 12 months of age, whereas Nimenrix is approved for use for individuals from 6 weeks of age. The PBAC noted the sponsor is intending to seek approval for use in infants ≥ 6 weeks of age once the data is available.

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

3.1 The proposed listing was consistent with ATAGI advice and the proposed product information (PI) provided with the submission. The requested listing is summarised in Table 2, noting the Nationally Negotiated Price (NNP) below is a proxy figure in lieu of the actual NNP being made available to the sponsor in the event the vaccine is recommended.

Table 2: Essential elements of the requested listing

Name, restriction, manner of administration, form	Nationally negotiated price	Proprietary name and manufacturer
Meningococcal (Groups A,C,Y,W) Polysaccharide Tetanus Toxoid Conjugate Vaccine, 1 x 0.5 mL syringe	$[redacted]*	MenQuadfi, Sanofi-Aventis Australia Pty Ltd
National Immunisation Program a) A child who is 12 months old; or b) A person who is at least 14 years old but less than 20 years of age; or c) A person ≥ 12 months old who has congenital or acquired asplenia (e.g. splenectomy or hyposplenia); or d) A person ≥ 12 months old who has complement deficiency; or e) A person ≥ 12 months old undergoing eculizumab treatment. • Listing is requested as a single dose for subjects in populations (a) and (b) or a two-dose primary course for subjects in circumstances (c), (d), or (e). It is further proposed that Item 7 (1A) of the Determination, describing the approved MenACWY booster schedule for medically at risk subjects, be amended to accommodate the new listing of MenQuadfi.		

*The submission estimated a proxy NNP cost of $[redacted] for Nimenrix based on a recent published Australian cost effectiveness analysis of the MenACWY vaccine in Australian adolescents.
Source: compiled during the evaluation based on section 1.4 and section 3 of the submission.

3.2 The submission proposed to list MenQuadfi on the Determination for similar populations to Nimenrix, which at the time of submission was the only NIP-listed quadrivalent meningococcal (serogroups ACWY) conjugate vaccine. The proposed NIP vaccination schedule for MenQuadfi is summarised in Section 8.

3.3 According to the MenQuadfi approved PI, a single dose of MenQuadfi should be administrated to children and adolescents. The ATAGI proposed 'a 2 dose schedule with an interval of 8 weeks between doses for those with a specified medical condition associated with an increased risk of IMD' for the primary vaccination schedule.

3.4 The submission assumed a proxy NNP of MenQuadfi of $[redacted], which was the estimated price of Nimenrix. The Pre-Subcommittee Response (PSCR) clarified that the

sponsor would match the revealed NNP for Nimenrix and the tender price for MenQuadfi will be negotiated in accordance with standard processes in response to a request for tender.

3.5 The proposed listing for children and adolescents was consistent with the clinical trials and the draft PI provided with the submission. However, the clinical trials and the PI do not include medically at-risk individuals. The ESC noted that the PBAC previously recommended MenACWY for medically at-risk individuals.

For more detail on PBAC's view, see section 7 PBAC outcome.

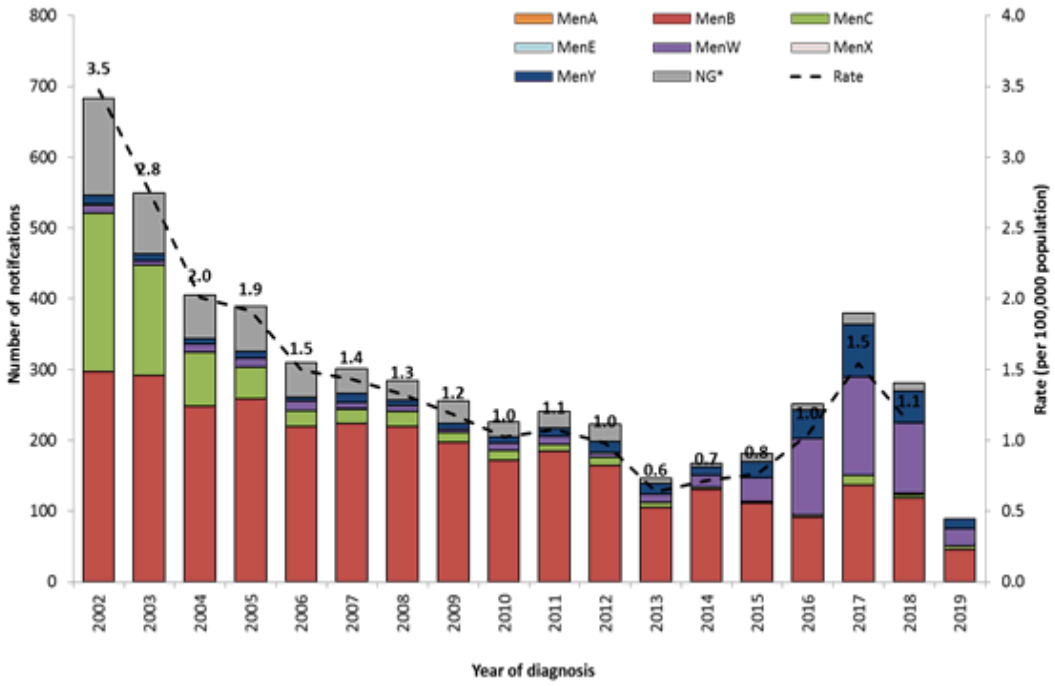
4 Population and disease

4.1 IMD is a rare disease caused by the bacterium *Neisseria meningitidis*. The sole ecological niche of the bacterium is the mucosa of the oropharynx of humans. Acquisition demands person-to-person transmission via direct contact or through dispersion of respiratory droplets from an infected to a susceptible individual. IMD can cause meningitis and septicaemia. Meningococcal disease can progress rapidly to a serious disease and have a high mortality rate (5-10%), despite appropriate antibiotic therapy. Ten to thirty percent of children and adolescents who survive the acute disease phase develop debilitating permanent sequelae, such as limb deformity, scarring, deafness and neurologic deficits. The case fatality rate for all cases of IMD was around 5.7% in 2018, however may be higher for MenW135[1].

4.2 The number of meningococcal notifications in Australia by serogroup over time is presented in Figure 1. The rate of IMD declined since 2002, then increased from 2013 till 2017 due to an increase in MenW135 and MenY cases.

[1] Australian Government Department of Health (2018) Invasive meningococcal disease national surveillance report Quarter 4 2018.

Figure 1: Annual cases and rate of IMD, Australia, 1 January 2002 to 30 June 2019 by serogroup



Source: Figure 1.2 of the submission

4.3 In 2017-2018, temporary State and Territory-based MenACWY vaccination programs targeting adolescents were implemented. In 2018, the MenACWY vaccination program was listed on the NIP for children 12 months old. In 2019, the NIP was expanded to adolescents aged 14–19 years, replacing the temporary State and Territory program. The PBAC noted that since the introduction of the national vaccination program, the cases of IMD, particularly those caused by MenW and MenY, have declined. The ESC noted that Menveo was listed on the NIP for adolescents aged 14-19 years in 2020.

4.4 In the first half of 2019, there was a total of 89 cases of IMD in Australia, of which around 52% were MenB, 28% were MenW135, 15% were MenY, and 6% were MenC[2].

4.5 The listing of MenQuadfi on the NIP will not result in any change to the current clinical management algorithm, other than adding MenQuadfi as an additional MenACWY vaccine on the NIP for individuals ≥12 months of age.

For more detail on PBAC's view, see section 7 PBAC outcome.

[2] Australian Government Department of Health (2019) Invasive meningococcal disease national surveillance report Quarter 1 January to 30 June 2019.

5 Comparator

5.1 The submission nominated Nimenrix as the main comparator because it was the only NIP-listed MenACWY vaccine for the proposed populations at the time of submission. The ATAGI also considered Nimenrix as the main comparator. The ESC agreed with the ATAGI that this was appropriate.

5.2 At the time of submission, Nimenrix was the only NIP-listed MenACWY vaccine and it was available to three populations:

- 12 months old
- 14–16 years (school programs), with all people aged less than 20 years being eligible for free catch up vaccine
- People older than 6 weeks with: congenital or acquired asplenia (e.g. splenectomy) or hyposplenia, complement deficiency or undergoing eculizumab treatment (referred to as medically at-risk population).

5.3 The ESC noted that the proposed three populations for MenQuadfi are aligned with the three populations currently listed on the NIP, except for the medically at-risk individuals for which MenQuadfi has an age restriction of ≥12 months.

5.4 The submission nominated meningococcal serogroup A, C, W-135 and Y Oligosaccharide CRM_{197} Conjugate vaccine (referred to herein by the brand name Menveo®) as a near market comparator for the proposed adolescent population. This was because Menveo was recommended by the PBAC in July 2018 to be listed on the Determination for the proposed adolescent population on a cost minimisation basis to Nimenrix. The evaluation considered this was reasonable and further noted Menveo was listed on the Determination for the adolescent cohort in August 2020.

5.5 The submission also nominated the meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate vaccine (referred to herein by the brand name Menactra®) as a near market comparator for the adolescent population. Menactra has been registered in Australia since 2011 and has not yet been considered by the PBAC, therefore it may be a less relevant near market comparator. Additionally, the ATAGI considered Nimenrix to be superior to Menactra in the adolescent age group in terms of immunogenicity.

5.6 In adolescents, the ATAGI acknowledged a lack of direct comparative trials between MenQuadfi and Nimenrix, but noted that studies demonstrate non-inferior immunogenicity for all serogroups against other meningococcal conjugate vaccines registered in Australia (Menveo and Menactra).

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

6.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

6.3 The submission was based on two randomised controlled trials comparing MenQuadfi to Nimenrix in children aged 12-23 months (MET51, N=918; MET54, N=188), and one randomised controlled trial comparing MenQuadfi to Menveo in children and adolescents aged 10-17 years (MET50, N=1,715).

6.4 The submission also presented one supplementary trial comparing MenQuadfi in combination with other paediatric vaccines (MMR+V vaccine, TaP IPV-HB-Hib, and PCV13) (MET57, N=1,183) in children aged 12-23 months. This trial did not include another active meningococcal vaccine control group. The submission stated that 'overall, vaccination with MenQuadfi was considered to be well tolerated in this population, when administered alone or concomitantly with other licensed vaccines commonly administered to this cohort. No major safety concerns were identified with MenQuadfi. There were no important changes in the safety profiles of licensed vaccines when co-administered with MenQuadfi, and no new clinically important findings were identified in the study.'

6.5 The submission also presented two supplementary trials comparing MenQuadfi to Menactra in adolescents and adults (MET43, N=3,344; MET56, N=810). The submission stated that 'non-inferiority of the immune response was demonstrated for all serogroups and the point estimate of the proportion of MenQuadfi responders was numerically higher for all serogroups in both the overall population and the adolescent subset. Other immunogenicity outcomes were generally consistent with the primary outcome.'

6.6 The submission presented no trial data to support use in the proposed medically at-risk population. In May 2019, the PBAC recommended that the MenACWY vaccine should be a designated vaccine in the Determination for people with asplenia and hyposplenia, complement deficiency or undergoing eculizumab treatment. The ESC noted that the at-risk population are currently eligible to receive MenACWY vaccination through the NIP.

6.7 Details of the key trials presented in the submission to support the clinical claims are provided in Table 3.

Table 3: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
MET51	Phase III, modified double-blind, randomised, parallel-group, active controlled, multi-centre trial to compare the immunogenicity and describe the safety of a single dose of MenACYW conjugate vaccine to a single dose of a licensed quadrivalent meningococcal serogroups A, C, W, and Y tetanus toxoid conjugate vaccine (MenQuadfi) in toddlers in the European Union who are either meningococcal vaccine naïve or received MenC vaccination during infancy	December 2018
MET54	A Phase II, randomised, parallel-group, open-label, active-controlled, multi-centre, single country study to describe the safety and immunogenicity of MenACYW conjugate vaccine compared to Nimenrix in toddlers 12 to 23 months of age.	June 2016
	Vesikari T, Borrow R et al. Immunogenicity and safety of a quadrivalent meningococcal tetanus toxoid-conjugate vaccine (MenACYW-TT) in healthy toddlers: a Phase II randomised study.	*Human vaccines & immunotherapeutic 2020*; 16 (6): 1306-1312.
MET50	A Phase II, open-label (the laboratory technicians were blinded to group assignment), randomised, parallel-group, active-controlled, multi-centre single-country study to evaluate the immunogenicity and safety profile of a single dose of MenACYW conjugate vaccine compared to that of the licensed vaccine Menveo, and when MenACYW conjugate vaccine is given with Tdap and HPV vaccines, in healthy adolescents 10 to 17 years of age in the US.	July 2018
	Chang L, Hedrick J el al. A Phase II, randomised, immunogenicity and safety study of a quadrivalent meningococcal conjugate vaccine, MenACYW-TT, in healthy adolescents in the United States.	*Vaccine 2020;* 38: 3560-3569.
	Hedrick J, Christensen S et al. Study of the Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) When Co-administered with Other Vaccines in Healthy Adolescents	*Open Forum Infectious Diseases*, 2018; 5 (Supplement_1): 570

Source: compiled during the evaluation based on the Excel spreadsheet 'Annotated Results' provided in the submission.

6.8 The key features of the trials are summarised in Table 4.

Table 4: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
MenQuadfi vs Nimenrix					
MET51	918 (612 MenC naïve, 306 Men C primed)	Phase III, RCT, modified double blind[1]	Low	Children 12-23 months Mixed MenC naïve or primed	Seroresponse rate (hSBA antibody titre ≥ 1:8)
MET54	188	Phase II, RCT, OL (laboratory technicians were blinded)	Low	Children 12-23 months	Antibody responses to antigens (serogroups A, C, Y, and W) measured by hSBA and rSBA collected at 30 days post vaccination.
MenQuadfi vs Menveo					
MET50	1,715[2]	Phase II, RCT, OL (laboratory technicians were blinded)	Low	Children and adolescents age 10-17 years	Seroresponse rate (hSBA titre ≥ 1:8).

Source: Table 2.2 of the submission.
OL = open label; RCT = randomised clinical trial. hSBA=human serum bactericidal antibody; rSBA=rabbit serum bactericidal antibody
1. Vaccine administrator was unblinded
2. Including 300 patients who only received HPV+tdap

Comparative effectiveness

6.9 The results of the clinical evidence from the three key trials are presented in Table 5.

6.10 The primary outcome for MET51 was to assess the seroresponse rate (hSBA antibody titre ≥ 1:8) in MenQuadfi (vaccine naïve) arm vs Nimenrix (vaccine naïve) arm, and MenQuadfi (either vaccine naïve or MenC primed arm) vs Nimenrix (either vaccine naïve or MenC primed). The seroresponse rate (hSBA≥1:8) at 30 days post vaccination are:

<u>For meningococcal vaccine-naïve children:</u>

- The proportion of children achieving hSBA≥1:8 in the MenQuadfi group are similar compared with the Nimenrix group for serogroup A (90.8% vs 89.5%), serogroup W (83.6% vs 83.4%) and serogroup Y (93.2% vs 91.6%) at 30 days post vaccination.
- The proportion of children achieving hSBA≥1:8 for MenC is higher in the MenQuadfi group compared with the Nimenrix group (99.3% vs 81.4%) and the difference is statistically significant (18.0%, 95% confidence interval (CI): 13.6%, 22.8%).
- The lower limit of the two-sided 95% CI of the difference of the seroprotection rate (antibody titres ≥ 1:8 30 days post vaccination) was greater than -10% for all four serogroups. Therefore, MenQuadfi was non-inferior compared to Nimenrix for all serogroups in terms of the hSBA≥1:8 outcome, given that the chosen non-inferiority margin was set at -10%.

<u>For both meningococcal naïve children and MenC primed groups combined:</u>

- The seroresponse rates for MenQuadfi were non-inferior compared with Nimenrix separately for all four serogroups, given the non-inferiority margin of -10%.

- The proportion of children achieving hSBA≥1:8 for MenA was lower in the MenQuadfi group (90%) compared with Nimenrix (92%), but the difference was not statistically significant (-2.03%, CI: -5.84%, 1.78%).
- However, ATAGI was not concerned about the results for MenA (primed with MenC) because they do not expect many MenC-primed infants in Australia and serogroup A disease is extremely rare in Australia.

6.11 The MET54 trial showed that the proportion of subjects achieving rSBA≥1:8 was higher in the MenQuadfi group (100%) compared with the Nimenrix group (98.8%) for MenC at 30 days post vaccination. All subjects achieved rSBA≥1:8 in the MenQuadfi group and the Nimenrix group for MenA, MenY, and MenW.

6.12 The MET50 trial compared MenQuadfi and Menveo in adolescents aged 11-17 years.

- The proportion of individuals that achieved seroprotection (hSBA titres ≥ 1:8 for subjects with pre-vaccination hSBA titres < 1:8 or at least a 4-fold increase in hSBA titres for subjects with pre-vaccination hSBA titres ≥ 1:8) in the MenQuadfi group are higher compared with the Menveo group for all serogroups: serogroup A (75.6% vs 66.4%), serogroup C (97.2% vs 72.6%), serogroup W (86.2% vs 66.6%) and serogroup Y (97.0% vs 80.8%) at 30 days post vaccination.
- MenQuadfi was non-inferior to Menveo for each serotype, given that the lower limit of the two-sided 95% CI of the difference of the seroprotection rate was greater than -10% for all four serogroups.

Table 5: Seroresponse at 1 month post-vaccination across the studies

Serogroup	Vaccine	MET51 12 -23 months vs Nimenrix n/M, % (95% CI)		MET54 12 – 23 months vs Nimenrix n/M, % (95% CI)		MET50 10-17 years vs Menveo n/M, % (95% CI)
		hSBA ≥ 1:8		rSBA GMT ≥ 1:8		hSBA ≥ 1:8 or 4-X increase
		Vaccine naïve Day 30	Both Naïve and MenC-primed Day 30	Day 0 (baseline)	Day 30	Day 30
MenA	MenQuadfi	266/293 90.8% (86.9; 93.8)	443/490 90% (87.4; 92.9)	30/91 33.0% (23.5; 43.6)	91/91 100.0% (96.0; 100.0)	350/463 75.6% (71.4; 79.4)
	Nimenrix	264/295 89.5% (85.4; 92.7)	361/394 92% (88.4; 94.2)	15/86 17.4% (10.1; 27.1)	86/86 100.0% (95.8; 100.0)	-
	Menveo	-	-	-	-	308/464 66.4% (61.9; 70.7)
	Vaccine group difference (95% CI)	1.3% (-3.60; 6.20)	-2.03% (-5.84; 1.78)	-	-	9.2% (3.4; 15.0)
MenC	MenQuadfi	291/293 99.3% (97.6; 99.9)	485/489 99% (97.9; 99.8)	2/91 2.2% (0.3; 7.7)	91/91 100.0% (96.0; 100.0)	449/462 97.2% (95.2; 98.5)
	Nimenrix	240/295 81.4% (76.4; 85.6)	337/394 86% (81.7; 88.9)	3/86 3.5% (0.7; 9.9)	85/86 98.8% (93.7; 100.0)	-
	Menveo	-	-	-	-	336/463 72.6% (68.3; 76.6)
	Vaccine group difference (95% CI)	18.0% (13.6; 22.8)	12.1% (8.16; 16.1)	-	-	24.6% (20.3; 29.0)
MenW	MenQuadfi	245/293 83.6% (78.9; 87.7)	415/489 85% (81.4; 87.9)	3/91 3.3% (0.7; 9.3)	91/91 100.0% (96.0; 100.0)	399/463 86.2% (82.7; 89.2)
	Nimenrix	247/296 83.4% (78.7; 87.5)	331/394 84% (80.0; 87.5)	3/86 3.5% (0.7; 9.9)	86/86 100.0% (95.8; 100.0)	-
	Menveo	-	-	-	-	309/464 66.6% (62.1; 70.9)
	Vaccine group difference (95% CI)	0.2% (-5.85; 6.18)	0.5% (-4.37; 5.28)	-	-	19.6% (14.2; 24.8)
MenY	MenQuadfi	273/293 93.2% (89.7; 95.8)	462/490 94% (91.8; 96.2)	14/91 15.4% (8.7; 24.5)	91/91 100.0% (96.0; 100.0)	448/462 97.0% (95.0; 98.3)
	Nimenrix	271/296 91.6% (87.8; 94.5)	362/395 92% (88.5; 94.2)	9/86 10.5% (4.9; 18.9)	86/86 100.0% (95.8; 100.0)	-
	Menveo	-	-	-	-	375/464 80.8% (76.9; 84.3)
	Vaccine group difference (95% CI)	1.6% (-2.76; 6.03)	2.4% (-1.34; 6.19)	-	-	16.2% (12.3; 20.2)

CI: confidence interval; MenA: *Neisseria meningitidis* serogroup A; MenC: *Neisseria meningitidis* serogroup C; MenW: *Neisseria meningitidis serogroup W; MenY: Neisseria meningitidis serogroup Y. n=number of subjects experiencing the endpoint listed in the first*

three columns; M=number of subjects with valid serology results for the particular serogroup and time point; N= number of subjects in per-protocol analysis set; Percentages are based on M.
Source: Table 2.14, p36 of the submission; Table 5.2, MET54 CSR; Table 2.31, p44 of the submission.

6.13 The ATAGI acknowledged 'the absence of studies of MenQuadfi in populations with medical conditions associated with an increased risk of IMD. The comparator Nimenrix has been studied in limited populations with medical risk conditions. A non-randomised, prospective study of 40 individuals with asplenia/hyposplenia had similar immunogenicity after two doses of Nimenrix compared to age-matched healthy controls. Given that Nimenrix is currently recommended for individuals with medical risk conditions and ATAGI is satisfied that MenQuadfi is immunogenic and comparable to Nimenrix for healthy individuals aged ≥12 months, ATAGI believes that MenQuadfi should be similarly immunogenic after the same number of doses, and would be clinically beneficial in individuals with medical conditions associated with an increased risk of IMD'.

Comparative harms

6.14 The ATAGI did not have any specific concerns regarding the safety of MenQuadfi in any age group, compared to Nimenrix and other registered MenACWY vaccines including Menveo that should preclude its use on the NIP, either alone or concomitantly with other routine vaccines, subject to approval of registration of MenQuadfi by the TGA.

6.15 The safety results across the main studies are summarised in Table 6. Overall, the safety results appear very similar between treatment arms in the trials.

Table 6: Summary of key adverse events in the trials

MET51	**MenQuadfi (N=506)**			**Nimenrix (N=408)**		
Subjects experiencing at least one:	n/M	%	(95% CI)	n/M	%	(95% CI)
Within 30 minutes after vaccine injection						
Immediate unsolicited AE	0/506	0.0	(0.0; 0.7)	0/408	0.0	(0.0; 0.9)
Immediate unsolicited AR	0/506	0.0	(0.0; 0.7)	0/408	0.0	(0.0; 0.9)
Within 7 days after vaccine injection						
Solicited reaction	388/506	76.7	(72.7; 80.3)	311/407	76.4	(72.0; 80.5)
Grade 3 solicited reaction	41/506	8.1	(5.9; 10.8)	24/407	5.9	(3.8; 8.6)
Solicited injection site reaction	261/506	51.6	(47.1; 56.0)	214/407	52.6	(47.6; 57.5)
Solicited systemic reaction	318/506	62.8	(58.5; 67.1)	237/407	58.2	(53.3; 63.1)
During the study						
SAE	4/506	0.8	(0.2; 2.0)	3/408	0.7	(0.2; 2.1)
Related SAE	0/506	0.0	(0.0; 0.7)	0/408	0.0	(0.0; 0.9)
Death	0/506	0.0	(0.0; 0.7)	0/408	0.0	(0.0; 0.9)
AESI	2/506	0.4	(0.0; 1.4)	0/408	0.0	(0.0; 0.9)
MET54	**MenQuadfi (N=94)**			**Nimenrix (N=94)**		
Subjects experiencing at least one:	n/M	%	(95% CI)	n/M	%	(95% CI)
Within 30 minutes after vaccine injection						
Immediate unsolicited AE	0/94	0.0	(0.0; 3.8)	0/94	0.0	(0.0; 3.8)
Immediate unsolicited AR	0/94	0.0	(0.0; 3.8)	0/94	0.0	(0.0; 3.8)
Within 7 days after vaccine injection						
Solicited reaction	75/94	79.8	(70.2; 87.4)	78/94	83.0	(73.8; 89.9)
Solicited injection site reaction	46/94	48.9	(38.5; 59.5)	50/94	53.2	(42.6; 63.6)
Solicited systemic reaction	58/94	61.7	(51.1; 71.5)	65/94	69.1	(58.8; 78.3)
Death	0/94	0.0	(0.0; 3.8)	0/94	0.0	(0.0; 3.8)
During the study						
SAE	1/94	1.1	(0.0; 5.8)	0/94	0.0	(0.0; 3.8)
Related SAE	0/94	0.0	(0.0; 3.8)	0/94	0.0	(0.0; 3.8)
Death	0/94	0.0	(0.0; 3.8)	0/94	0.0	(0.0; 3.8)
Fever	7/94	7.4	(3.0; 14.7)	4/91	4.4	(1.2; 10.9)
MET50	**MenQuadfi (N=503)**			**Menveo (N=501)**		
Subjects experiencing at least one:	n/M	%	(95% CI)	n/M	%	(95% CI)
During the study						
SAE	4/503	0.8	(0.2; 2.0)	4/501	0.8	(0.2; 2.0)
Related SAE	0/503	0.0	(0.0; 0.7)	0/501	0.0	(0.0; 0.7)
Death	0/503	0.0	(0.0; 0.7)	0/501	0.0	(0.0; 0.7)
Within 30 days after visit 1 injections						
SAE	2/503	0.4	(0.0; 1.4)	1/501	0.2	(0.0; 1.1)
Related SAE	0/503	0.0	(0.0; 0.7)	0/501	0.0	(0.0; 0.7)
Solicited reaction	315/496	63.5	(59.1; 67.8)	316/492	64.2	(59.8; 68.5)
Death	0/503	0.0	(0.0; 0.7)	0/501	0.0	(0.0; 0.7)

AE: adverse event; AR: adverse reaction; SAE: serious adverse event1.
n=number of subjects experiencing the endpoint listed in the first column M=number of subjects with available data for the relevant endpoint. N=number of subjects in the safety analysis. Percentages are based on M.
Source: Table 2.39, p49 of the submission; Table 2.40, p50 of the submission; Table 2.41, p51 of the submission.

Clinical claim

6.16 The submission described MenQuadfi as non-inferior in terms of effectiveness and safety compared with Nimenrix in children aged approximately 12 months and in adolescents aged 14-19 years.

6.17 The submission stated that 'while there are no reliable data available regarding the comparative effectiveness and safety of the ATAGI-recommended 2 x primary plus booster dose regimens of MenQuadfi and Nimenrix among the target populations of medically at-risk subjects aged ≥12 months, there is equally no evidence or clinical expectation that the therapeutic relativity here would differ from that of a single dose regimen in other populations'.

6.18 Children 12 months:

- The submission claimed that MenQuadfi was non-inferior to Nimenrix in terms of immunogenicity and safety.
- The ATAGI considered this claim was reasonable.
- However, none of the trials collected clinical efficacy data in terms of cases of MenACWY avoided. Immunogenicity does not necessarily correlate to efficacy of a vaccine to prevent a disease. Given meningococcal disease is relatively rare, it would be difficult to design a trial of the effectiveness of vaccines in reducing incidence of meningococcal disease.
- The ESC noted that PBAC had previously accepted the use of immunogenicity as a surrogate outcome for IMD (Menitorix Public Summary Document (PSD), November 2010; Nimenrix PSD, March 2018; Menveo PSD, July 2018).

6.19 Adolescents:

- There was no direct head to head trial comparing MenQuadfi with Nimenrix in adolescents aged 14-19 years.
- The submission claimed that MenQuadfi is non-inferior to Nimenrix given that (a) MenQuadfi was non-inferior to Menveo in MET50, and (b) that the PBAC has previously concluded that Menveo is non-inferior to Nimenrix.
- The ATAGI considered this claim was reasonable.
- Additionally, the ATAGI considered it valid to extrapolate the finding that MenQuadfi is non-inferior to Nimenrix in terms of immunogenicity in children aged 12–23 months to the adolescent population, on the basis that immune responses to meningococcal conjugate vaccines are typically similar or stronger in older children.
- It may be reasonable to claim that MenQuadfi is non-inferior to Nimenrix given the above ATAGI advice, given that MenQuadfi was non-inferior to Menveo in MET50 and given that the PBAC previously considered Menveo non-inferior to Nimenrix. The evaluation considered this claim uncertain given the lack of direct randomised evidence comparing MenQuadfi and Nimenrix in adolescents.

6.20 Medically at-risk population:

- No trial data was available for the medically at-risk population. However, the ATAGI considered that 'given that Nimenrix is currently recommended for

individuals with medical risk conditions and ATAGI is satisfied that MenQuadfi is immunogenic and comparable to Nimenrix for healthy individuals aged ≥12 months, ATAGI believes that MenQuadfi should be similarly immunogenic after the same number of doses, and would be clinically beneficial in individuals with medical conditions associated with an increased risk of IMD'.

- The PBAC previously recommended MenACWY for the medically at-risk population in consideration of the clinical need for vaccination and the current best practice guidelines such as the Australian Immunisation Handbook and the Therapeutic Guidelines.

6.21 The ATAGI considered that 'There is also a lack of data on duration of clinical protection or on persistence of antibody levels induced by MenQuadfi. Despite this uncertainty, the post-vaccination geometric mean titres (GMT) trend higher after vaccination with MenQuadfi than with Nimenrix (in children aged 12–23 months) and MenACWY (Menveo/ Menactra) adolescents for most covered serogroups. As both MenQuadfi and Nimenrix are similar tetanus toxoid protein–conjugated vaccines, ATAGI expects MenQuadfi persistence to be at least similar to the current comparator Nimenrix.

6.22 Overall, the ATAGI did not have significant safety concerns regarding the use of MenQuadfi in the proposed population groups.

6.23 The ESC considered the claim that MenQuadfi was non-inferior in terms of effectiveness and safety compared to Nimenrix in children and adolescents was reasonably supported by the evidence presented.

6.24 The PBAC considered that the claim of non-inferior comparative effectiveness (based on immunogenicity data) was reasonable.

6.25 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

6.26 The submission presented a cost-minimisation analysis versus the currently listed MenACWY vaccine, Nimenrix.

6.27 The submission stated that the sponsor would match the revealed NNP of Nimenrix if MenQuadfi was recommended for listing on the NIP. The submission proposed a proxy price of $[redacted] for MenQuadfi and Nimenrix.

6.28 Menveo was identified as a near-market comparator in the submission but no equi-effective dose was provided and it was not included in the economic evaluation as it was not listed on the NIP at the time of submission. The ESC considered this was reasonable but noted Menveo had recently been included on the Determination for the adolescent cohort (amendment dated 27 August 2020).

6.29 The key components and assumptions of the cost-minimisation analysis are presented in Table 7.

Table 7: Key components and assumptions of the cost-minimisation analysis

Component	Claim or assumption
Therapeutic claim: effectiveness	Based on evidence presented, MenQuadfi is assumed to be non-inferior to Nimenrix.
Therapeutic claim: safety	Based on evidence presented, MenQuadfi is assumed to be non-inferior to Nimenrix.
Evidence base	Direct comparison of MenQuadfi and Nimenrix for children 12-23 months old. Direct comparison of MenQuadfi and Menveo for adolescent population. No direct evidence available vs Nimenrix. No data available for medically at-risk population.
Equi-effective doses	Children 12 months old*. A single dose of (0.5 mL) of MenQuadfi = a single dose (0.5 mL) of Nimenrix Adolescents (14-19 years): A single dose of (0.5 mL) of MenQuadfi = a single dose (0.5 mL) of Nimenrix Medically at-risk individuals (≥12 months) **: Two doses of (0.5 mL) of MenQuadfi = Two doses (0.5 mL) of Nimenrix
Direct medicine costs	The submission stated that the sponsor would 'match the revealed NNP list price of Nimenrix' if MenQuadfi is recommended for listing on the NIP.
Other costs or cost offsets	None

*the submission stated children 12-23 months old, but the current NIP is listed as children 12 months old.
**modified to ≥12 months, instead of all ages given that MenQuadfi is indicated for use in individual ≥12 months
Source: Compiled during the evaluation based on the information provided in Section 2 and Section 3 of the submission.

6.30 The equi-effective doses were estimated as MenQuadfi (1 x 0.5 mL) and Nimenrix (1 x 0.5 mL) for children (12 months) and adolescents (14-19 years old). The proposed dose for the children and adolescent populations was consistent with the draft MenQuadfi PI provided with the submission.

6.31 The equi-effective doses were estimated as MenQuadfi (2 x 0.5 mL) and Nimenrix (2 x 0.5 mL) for medically at-risk individuals (≥12 months)[3]. The evaluation considered this was reasonable as the ATAGI proposed 'a 2 dose schedule with an interval of 8 weeks between doses for those with a specified medical condition associated with an increased risk of IMD'.

6.32 The submission did not include the cost to the GP or costs of treating adverse events associated with the administration of MenQuadfi. However, these costs are likely to be equal for MenQuadfi and Nimenrix. Further, the totals costs per patient were likely to be equal for MenQuadfi and Nimenrix given that the sponsor would match the NPP of Nimenrix if MenQuadfi was recommended for inclusion on the Determination.

[3] The recommended dose for Nimenrix is 2 to 4 in medically at-risk individuals. Children under 12 months of age receive 3 or 4 doses which does not apply to MenQuadfi.

Estimated NIP usage & financial implications

6.33 This submission was not considered by DUSC. The submission used a market share approach to estimate the use and financial impact of the proposed vaccination program.

6.34 The submission based its financial estimates on Nimenrix, the NIP-listed vaccine at the time of submission. The key data sources data applied were ABS population projections for Australian infants 12 months old and adolescents aged 14-19 years. The submission assumed 500 to < 5,000 medically at-risk individuals per annum. The evaluation considered this to be uncertain. The detailed data sources and parameter values applied in the utilisation and financial estimates are summarised in Table 8.

Table 8: Data sources and parameter values applied in the utilisation and financial estimates

Data	Value applied and source	Comment
Eligible population		
Children 12 months old	ABS cat. No.3222.0 [redacted][1](Yr1) to [redacted][1] (Yr6)	-
Adolescents 14 years old	ABS cat. No.3101.0 [redacted][1] (Yr1) to [redacted][1] (Yr6)	The current NIP school program is for adolescents aged 14- 16 years (e.g. in NSW, it is for students in year 10). Thus, to estimate the number of school aged adolescents, the evaluation considered it may be more appropriate to use the 15 years old population data instead of 14 years old. The ESC agreed with the PSCR that using the 15 year old population would have little impact on the financial estimates.
Adolescents 15-19 years total (for school catch up program)	ABS cat. No.3101.0 [redacted][2] (Yr1) to [redacted][2] (Yr6)	-
Adolescents 15-19 years (eligible)	Calculated. The submission estimated the total amount of adolescents who are not vaccinated and eligible for the catch up program as the total number of adolescents (aged 15-19) above minus the number vaccinated through the school program and the catch up program in the previous year. [redacted][3] (Yr1) to [redacted][4] (Yr6)	-
Medically at-risk (≥12 months)	Assumed to be [redacted][5] individuals per annum, source of reference not given.	The evaluation considered this was uncertain.
Treatment utilisation		
Uptake rate children 12 months Uptake rate school program (14-16 years) Uptake rate school catch up (all ages before 19)	Estimated based on National centre for immunisation research and surveillance (NCIRS 2019) Children 12 months: 90% (Yr1 to Yr6) School program: 85% (Yr1 to Yr6) School catch up: 20% (Yr1 to Yr6)	The evaluation considered this was uncertain
Medically at-risk (≥12 months)	Assumed to be 100%. Source of reference not given.	The evaluation considered this was uncertain
Doses per subject (children 12 months)	1 dose for both MenQuadfi and Nimenrix per vaccination, based on MenQuadfi Draft PI and Nimenrix PI, respectively	-
Doses per subject (adolescent 14 -19 years)	1 dose for both MenQuadfi and Nimenrix per vaccination, based on MenQuadfi Draft PI and Nimenrix PI, respectively	-
Doses per subject (medically at-risk age ≥12 months)	2-dose schedule with an interval of 8 weeks between doses, as per ATAGI advice	-
MenQuadfi	Proxy price, the submission stated that the sponsor would 'match the revealed [NNP] list price of Nimenrix' if both are listed on the NIP	-

Data	Value applied and source	Comment
Nimenrix	Proxy cost of $[redacted] based on a recently published Australian cost effectiveness analysis of MenACWY in Australia adolescents (Si, Zomer et al.2019)	-
Patient co-payment	No patient co-payment for vaccines	-

Source: Table 4.1 of the submission and section 4 budget impact Excel spreadsheet.
The redacted values correspond to the following ranges
[1] *300,000 to < 400,000*
[2] *1,000,000 to < 2,000,000*
[3] *800,000 to < 900,000*
[4] *200,000 to < 300,000*
[5] *500 to < 5,000*

6.35 The estimated number of children (12 months old), adolescents (14-19 years old) and medically at-risk people (≥12 months old) receiving routine MenACWY vaccine (both MenQuadfi and Nimenrix) is presented in Table 9.

6.36 The submission estimated that 4,000,000 to < 6,000,000 people would receive routine MenACWY vaccination (MenQuadfi or Nimenrix) over the next six years, split by subpopulation as follows:

- 1,000,000 to < 2,000,000 children aged 12 months.
- 1,000,000 to < 2,000,000 adolescents through school program.
- 500,000 to < 600,000 adolescents through the catch-up program.
- 5,000 to < 10,000 medically at-risk people (≥12 months).

Table 9: Estimated number of eligible patients (children 12 months; adolescent aged 14-19 years; medically at-risk ≥12 months) participating in the proposed vaccine program and the cost of listing MenQuadfi and Nimenrix on the NIP

	2021	2022	2023	2024	2025	2026
Total Australian population						
Children 12 months old	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Adolescents 14 years	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Adolescents 15-19 total	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Adolescents 15-19 eligible	[redacted][3]	[redacted][4]	[redacted][5]	[redacted][6]	[redacted][6]	[redacted][6]
At risk subjects ≥12 months	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]
Uptake rate						
Children program	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%
School based program	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%
Catch up program	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
At risk subjects ≥12 months	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Estimated total number of people receiving MenACWY vaccine						
Children program	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
School based program	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]
Catch up program	[redacted][8]	[redacted][8]	[redacted][9]	[redacted][10]	[redacted][11]	[redacted][11]
At risk subjects ≥12 months	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]
Doses MenACWY per subject						
Children and adolescents	1	1	1	1	1	1
At risk subjects ≥12 months	2	2	2	2	2	2
Estimated total number of MenACWY doses required						
Children program	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
School based program	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]
Catch up program	[redacted][8]	[redacted][8]	[redacted][9]	[redacted][10]	[redacted][11]	[redacted][11]
At risk subjects ≥12 months	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]
Cost of MenQuadfi (assuming 50% market share)	$[redacted][12]	$[redacted][12]	$[redacted][12]	$[redacted][12]	$[redacted][12]	$[redacted][12]
Reduction in cost of Nimenrix	-$[redacted][12]	-$[redacted][12]	-$[redacted][12]	-$[redacted][12]	-$[redacted][12]	-$[redacted][12]
NET cost to NIP	$[redacted][13]	$[redacted][13]	$[redacted][13]	$[redacted][13]	$[redacted][13]	$[redacted][13]

Source: Table 4.2 of the submission and section 4 budget impact Excel spreadsheet.

The redacted values correspond to the following ranges:

[1] *300,000 to < 400,000*
[2] *1,000,000 to < 2,000,000*
[3] *800,000 to < 900,000*
[4] *600,000 to < 700,000*
[5] *400,000 to < 500,000*
[6] *200,000 to < 300,000*
[7] *500 to <5,000*
[8] *100,000 to <200,000*
[9] *80,000 to < 90,000*
[10] *40,000 to < 50,000*
[11] *50,000 to <60,000*
[12] *$10 million to < $20 million*
[13] *$0 to < $10 million*

6.37 The submission assumed that if MenQuadfi is listed on the NIP, the overall market size would not change, and the market share would be equally distributed between MenQuadfi and Nimenrix. The submission predicted that the incremental cost of listing MenQuadfi on the NIP as an alternative MenACWY vaccine to Nimenrix would be zero.

6.38 The ESC noted the uncertainty regarding the number of medically at-risk individuals, vaccine uptake and MenQuadfi market share but considered there would not be an incremental cost to the NIP if MenQuadfi was included as an alternative to Nimenrix and Menveo for MenACWY.

6.39 The ESC noted that MenQuadfi would be the third MenACWY vaccine on the NIP and considered introducing an additional vaccine may provide greater security and continuity of supply in an essential vaccine program.

Quality Use of Medicines

6.40 ATAGI did not foresee any major issues with implementation of MenQuadfi on to the NIP as an alternative vaccine to the currently funded Nimenrix. Providers may require information on the availability of MenQuadfi as an alternative MenACWY vaccine.

6.41 The ESC noted the ATAGI recommended adequate vaccination provider education regarding the lower age limit for MenQuadfi, so it was not used when considering MenACWY vaccination in children aged 6 weeks to <12 months.

6.42 ATAGI noted that as MenQuadfi is a fully liquid preparation, its preparation may be simpler for providers as there is no requirement to mix a powdered vaccine and diluent, as is the case for Nimenrix. This was particularly relevant outside of primary health care facilities, such as in schools or within a meningococcal outbreak vaccination program.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended that meningococcal serogroup A, C, W-135 and Y Polysaccharide Tetanus Toxoid Conjugate (MenACWY-TT, MenQuadfi) vaccine be a designated vaccine for the purposes of the *National Health Act 1953,* for the prevention of IMD caused by *Neisseria meningitidis* serogroups A, C, W135, and Y, for children aged 12 months, adolescents aged 14 to 19 years and at-risk individuals who are 12 months of age and older and are currently eligible for Nimenrix vaccination through the NIP, under the same provisions (see section 8). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of MenQuadfi would be acceptable if it were cost-minimised against the nominated comparator, Nimenrix.

7.2 The PBAC considered the nomination of Nimenrix as the main comparator for the three populations (children 12 months of age, adolescents aged 14 to 19 years of age and medically at risk individuals over 12 months of age) and Menveo as a 'near market' comparator for the adolescent population was appropriate. The PBAC noted Menveo was listed on the NIP for the adolescent population during evaluation of the submission.

7.3 The PBAC advised the equi-effective doses were 1 x 0.5 mL MenQuadfi and 1 x 0.5mL Nimenrix for healthy children 12 months of age and adolescents 14 to 19 years of age

and 2 x 0.5 mL MenQuadfi and 2 x 0.5mL Nimenrix for medically at-risk individuals 12 months of age or older. The PBAC noted the cost minimisation analysis should be based on the effective NNP of Nimenrix.

7.4 The PBAC noted the listing of MenQuadfi on the Determination would not result in any change to the population eligible for vaccination but would provide an additional quadrivalent meningococcal vaccine to be considered for NIP listing.

7.5 The PBAC noted the clinical claims in the submission were based on two randomised controlled trials comparing MenQuadfi to Nimenrix in children aged 12-23 months (MET51, N=918; MET54, N=188), and one randomised controlled trial comparing MenQuadfi to Menveo in children and adolescents aged 10-17 years (MET50, N=1,715). The PBAC noted the outcomes of the trials were based on immunogenicity data only, rather than avoided cases of IMD. The PBAC recalled that Nimenrix and Menveo were recommended on the basis of immunogenicity data and considered the use of immunogenicity outcomes to support the claims for MenQuadfi was reasonable.

7.6 The PBAC considered the clinical data provided in the submission supported the claim that MenQuadfi was non-inferior in terms of immunogenicity outcomes and safety to Nimenrix for children (aged 12 to 23 months) and to Menveo for adolescents (aged 10 to 17 years).

7.7 The PBAC noted that there is a lack of direct comparative trials of MenQuadfi and the main comparator, Nimenrix, in the adolescent population. The PBAC agreed with ATAGI that it was reasonable to extrapolate the findings that MenQuadfi is non-inferior in terms of immunogenicity outcomes to Nimenrix in children to the adolescent population (paragraph 6.19). The PBAC considered that, overall, the claim that MenQuadfi is non-inferior in terms of immunogenicity outcomes and safety to Nimenrix in the adolescent population was reasonable.

7.8 The PBAC noted there were no trial data available for people with asplenia and hyposplenia, complement deficiency or undergoing eculizumab treatment. However, the PBAC noted the ATAGI advice that MenQuadfi should be similarly immunogenic to Nimenrix in this population (paragraph 6.20). The PBAC considered that, overall, the claim that MenQuadfi is non-inferior in terms of immunogenicity outcomes and safety to Nimenrix in the medically at-risk population was reasonable.

7.9 The PBAC noted a number of assumptions included in the financial estimates were uncertain (paragraph 6.34) but agreed with the ESC that including MenQuadfi on the NIP would not result in an incremental cost to the program (paragraph 6.38).

7.10 The PBAC noted that this submission is not eligible for an independent review as independent review is only relevant to requests for PBS listing.

Outcome:

Recommended

8 Recommended listing

8.1 Add new item to the Determination:

Name, restriction, manner of administration, form	Proprietary name and manufacturer
Meningococcal polysaccharide serogroups A, C, W-135 and Y conjugate Injection (0.5mL)	MenQuadfi, Sanofi-Aventis Australia Pty Ltd

Vaccine may be provided to:

a) a child who is 12 months old; or
b) a person who is at least 14 years old but less than 20 years of age; or
c) a person ≧ aged at least 12 months old who has congenital or acquired asplenia (e.g. splenectomy) or hyposplenia~~)~~; or
d) a person ≧ aged at least 12 months old who has complement deficiency; or
e) a person ≧ aged at least 12 months old undergoing eculizumab treatment.

If in circumstances (c), (d) or (e): 2 doses of a primary course plus booster doses as described in subsection 7.

For item [MenQuadfi] of Schedule 1, the following number of doses and booster doses of a designated vaccine mentioned in that item may be provided to a person who has congenital or acquired asplenia (e.g. splenectomy) or hyposplenia; a person who has complement deficiency or a person undergoing eculizumab treatment:

(a) Primary doses according to the following number of doses:

(i) if aged 12 months or older at the start of their vaccine course – 2 doses;

(b) plus booster doses according to the following number and timing of doses:

(ii) if they completed their primary schedule at less than or equal to 6 years of age - 1 booster dose 3 years after completing the primary schedule, and then 1 booster dose every 5 years after that; or

(iii) if they completed their primary schedule at 7 years of age or older - 1 booster dose every 5 years after completing the primary schedule.

8.2 A summary of the proposed MenQuadfi NIP and catch up program is provided below.

Summary of the proposed MenQuadfi NIP program

Population requested	Number of doses, timing (primary series)	Booster frequency	Program setting (all that apply)	Implications for other NIP vaccines including comparator
Children who are 12 months old.	1 dose	Not requested	GPs Specialist prescribers Child/community health clinic	NIP listings unchanged (alternative MenACWY product only)
Adolescents who are at least 14 years old but less than 20 years of age	1 dose	Not requested	Schools, years 9-10 (main program) GPs or specialist prescribers (catch-up in those up to 19 years old, as provided for in existing NIP listing for MenACWY)	As above.
Medically at-risk individuals ≥12 months of age, including those: • With congenital or acquired asplenia (e.g. splenectomy or hyposplenia); or • With complement deficiency; or • Who are undergoing eculizumab treatment.	2 doses	If primary series was completed up to and including age 6 years old: 1 booster dose 3 years after completing the primary series, and then 1 booster dose every 5 years after that; If primary series completed by age 7 years or older: 1 booster dose every 5 years after completing the primary series	GPs Specialist prescribers Child/community health clinic	As above.

Summary of the proposed MenQuadfi catch-up program

Population Requested	Number of doses and timing	Duration	Program setting (all that apply)
Included in adolescent cohort	As for adolescent cohort	As for adolescent cohort	As for adolescent cohort

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.