

## **5.12 MENINGOCOCCAL (GROUPS A,C,W-135 AND Y) OLIGOSACCHARIDE CRM197 CONJUGATE VACCINE (Men ACWY-CRM), Solution for Injection (0.5 mL), Menveo<sup>®</sup>, Glaxosmithkline Australia Pty Ltd**

### **1 Purpose of Submission**

- 1.1 The Committee Secretariat submission requested the listing of the new solution for injection form of meningococcal serogroup A, C, W-135 and Y oligosaccharides conjugated individually to *Corynebacterium diphtheriae* CRM197 protein (MenACWY-CRM) vaccine (Menveo<sup>®</sup> solution for injection) as a designated vaccine on the *National Health (Immunisation Program – Designated Vaccines) Determination 2014 (No. 1)* for adolescents for the prevention of invasive meningococcal diseases (IMDs) caused by *Neisseria meningitidis* serogroups A, C, W-135 and Y under the same circumstances as MenACWY-CRM Menveo solution and powder for reconstitution.

### **2 Background**

- 2.1 Menveo solution and powder for reconstitution is a designated vaccine under the National Immunisation Program (NIP) Schedule for prevention of IMDs in:
- (a) a person aged at least 14 years old but less than 17 years old as part of a school-based program; or
  - (b) a person aged at least 14 years old but less than 19 years old who did not receive the vaccination as part of a school-based program (including the catch-up program).

#### **Registration status**

- 2.2 Menveo solution for injection was approved by the TGA on 26 September 2023. The sponsor provided the TGA Delegate's Overview, the minutes from the Advisory Committee on Vaccines (ACV) and the TGA approval letter during the evaluation.
- 2.3 The approved indication for Menveo solution for injection is:
- “MENVEO is indicated for active immunisation of children (from 2 years of age), adolescents and adults to prevent invasive disease caused by *Neisseria meningitidis* serogroups A, C, W135 and Y. The use of this vaccine should be in accordance with official recommendations.”
- 2.4 It was noted during the evaluation that Menveo solution for injection is indicated for persons from 2 years of age while the solution and powder for reconstitution is indicated for persons from 2 months of age. The ACV advised that “use of MenACWY

Liquid in infants and children aged 2 months to 23 months was not supported at this time. This age group requires 2, 3 or 4 doses of Menveo, and these schedules have not been tested with the MenACWY Liquid formulation. In the absence of data there is uncertainty on immunogenicity and safety. “(p6, ACV minutes). The PBAC noted this difference would not impact the request for the solution for injection to be used under the NIP for prevention of IMDs in adolescents.

### **Previous PBAC consideration**

- 2.5 This is the first PBAC submission for Menveo solution for injection for the prevention of IMDs caused by *Neisseria meningitidis* serogroups A, C, W-135 and Y in adolescents.
- 2.6 Menveo solution and powder for reconstitution was recommended at the July 2018 PBAC meeting. The PBAC recommended it as a designated vaccine for the purposes of the *National Health Act 1953* for the prevention of IMDs caused by *N. meningitidis* serogroups A, C, W135 and Y as a single dose for adolescents as part of a school based immunisation program for year 10 students (aged 14-16) and via a catch-up program for a single dose for adolescents aged up to 19 years old. The PBAC considered that the claim that there is no evidence of a difference in the immunogenicity or safety between the Menveo solution and powder for reconstitution and meningococcal polysaccharide serogroups A, C, W135 and Y tetanus toxoid conjugate (Nimenrix®) vaccines was reasonable. Recommendation was made on a cost minimisation basis, with equi-effective doses of 0.5 mL Menveo and 0.5mL Nimenrix.

## **3 Requested listing**

- 3.1 The submission requested the following new listing under the NIP.

Vaccine	Brand	Formulation	Active ingredient and strength	Number and timing of doses
Meningococcal (Groups A,C,W-135 and Y) Oligosaccharide CRM197 Conjugate Vaccine (Men ACWY-CRM)	Menveo	Injection (0.5mL)	Each 0.5 mL dose contains: (a) 10 µg Meningococcal polysaccharide serogroup A conjugated to 16.7–33.3 µg Corynebacterium diphtheriae CRM197 protein (b) 5 µg Meningococcal polysaccharide serogroup C conjugated to 7.1–12.5 µg C. diphtheriae CRM197 protein (c) 5 µg Meningococcal polysaccharide serogroup W-135 conjugated to 3.3–8.3 µg C. diphtheriae CRM197 protein (d) 5 µg Meningococcal polysaccharide serogroup Y conjugated to 5.6–10 µg C. diphtheriae CRM197 protein	1 dose
Circumstances Vaccine may be provided to: (a) a person aged at least 14 years old but less than 17 years old as part of a school based program; or (b) a person aged at least 14 years old but less than 19 years old who did not receive the vaccination as part of a school based program				

- 3.2 The submission claimed that Menveo solution for injection contains the same amount of each antigen as the solution and powder form and there are no changes to the drug substance manufacturing process. Additionally, the submission noted the main qualitative and quantitative differences between the dosage forms are the absence of sucrose and potassium phosphate in Menveo solution for injection, as these were added to form the lyophilisation matrix of MenA conjugate component.
- 3.3 The submission claimed the Menveo solution for injection will simplify vaccine administration by removing the need for reconstitution and potentially preventing reconstitution errors.
- 3.4 The sponsor noted in the pre-PBAC response that it did not intend to delist or discontinue Menveo solution and powder for reconstitution at the time of this consideration.

## 4 Comparator

- 4.1 The submission nominated Menveo solution and powder for reconstitution as the main comparator.
- 4.2 The submission also nominated Nimenrix as this was the NIP funded vaccine on which the pricing request was based. It is also the comparator which was accepted by PBAC for the listing of the Menveo solution and powder for reconstitution (Menveo, Public Summary Document [PSD], July and August 2018 PBAC Meeting). The submission noted that Menveo solution for injection could be listed as an alternative to Nimenrix on the NIP.

## 5 Consideration of the evidence

### Sponsor hearing

- 5.1 There was no hearing for this item.

### Consumer comments

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

### Clinical trials

- 5.3 The submission presented the following clinical studies. As a Committee Secretariat submission, no independent evaluation of the clinical evidence was undertaken.

**Table 1: Studies and associated reports presented in the submission**

Trial ID	Protocol title/ Publication title	Publication citation
V59_71 NCT03652610 Study 205343	A phase 2b, randomized, controlled, observer-blind, multicentre, non-inferiority immunogenicity and safety study of two formulations of GSK Biologicals' Meningococcal ACWY conjugate vaccine (GSK3536820A and Menveo) administered to healthy adults 18 to 40 years of age Singh VP, Tiberi P, Di Domenico GF, Romolini V, Mzolo T, Costantini M, Akhund T, Basile V, Lattanzi M, Pellegrini M. Fully Liquid MenACWY-CRM Vaccine: Results from an Integrated Safety Analysis*	January 2021  <i>Drug Safety. 2023; 46: 99-108</i>
V59_78 NCT03433482 Study 207467	A phase 2b, randomized, controlled, observer-blind, multi-center study to evaluate safety and immunogenicity of different formulations of GSK Biologicals' Meningococcal ACWY conjugate vaccine (GSK3536820A and Menveo) administered to healthy adolescents and young adults 10 to 40 years of age. Singh VP, Tiberi P, Di Domenico GF, Romolini V, Mzolo T, Costantini M, Akhund T, Basile V, Lattanzi M, Pellegrini M. Fully Liquid MenACWY-CRM Vaccine: Results from an Integrated Safety Analysis*	February 2021  <i>Drug Safety. 2023; 46: 99-108</i>

Source: Table 5, p 27 of the submission.

\*Note that the results presented in Singh et al 2023 are a pooled, post hoc analysis of two phase 2b clinical studies (V59\_71 and V59\_78).

- 5.4 The submission was based on two Phase 2b clinical studies which evaluated the immunogenicity and safety of the Menveo solution for injection against the solution and powder, after being aged either artificially for approximately 2 months or naturally for 24 and 30 months. V59\_71 assessed this in adults between 18 and 40 years of age while V59\_78 assessed the effects in persons between the ages of 10 and

40 years old. The TGA Delegate’s Overview (p20) noted “Overall, based on the data from studies V59\_71 (205343) and V59\_78 (207467), which showed a very similar immunogenicity and safety profile for MenACWY Liquid when compared to Menveo, in individuals aged 10-40 years inclusive, the benefit-risk profile of the MenACWY liquid vaccine for use in individuals aged 10-40 years appears favourable.”

### **Comparative effectiveness**

- 5.5 The submission noted that “the immunogenicity data from studies V59\_71 (205343) and V59\_78 (207467) showed a similar immune response [...] for all 4 serogroups” for Menveo solution for injection and Menveo solution and powder for reconstitution (p35, submission main body).

### **Comparative harms**

- 5.6 The submission presented safety data pooled from both studies, showing that both the Menveo solution for injection and Menveo solution and powder for reconstitution had very similar adverse event profiles.

### **Clinical claim**

- 5.7 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of Menveo solution for injection compared with Menveo solution and powder for reconstitution.
- 5.8 The submission also claimed non-inferior comparative effectiveness and non-inferior comparative safety of Menveo solution for injection compared with Nimenrix. This was on the basis that the PBAC had previously found that the claim that Menveo solution and powder for reconstitution had non-inferior comparative effectiveness and non-inferior comparative safety to Nimenrix was reasonable (Menveo PSD, July and August 2018 PBAC Meeting).
- 5.9 The PBAC considered that, for the population outlined in the proposed NIP listing, the claims of non-inferior comparative effectiveness and safety to both comparators were reasonable.

### **Economic analysis**

- 5.10 As a Committee Secretariat submission, the economic analysis has not been independently evaluated.
- 5.11 The submission applied the assumption of equivalence between Menveo solution for injection and Menveo solution and powder for reconstitution, with an equi-effective dose of 0.5 mL solution for injection = 0.5 mL solution and powder for reconstitution. Therefore, the equi-effective dose to the comparator Nimenrix is also 0.5 mL Menveo solution for injection = 0.5 mL Nimenrix.
- 5.12 The submission requested the price for Menveo solution for injection to be \$████ per dose as this is the existing nationally negotiated price for MenACWY vaccine for the requested population.

### **Estimated PBS usage and financial implications**

- 5.13 The submission assumed that Menveo solution for injection would replace Menveo solution and powder for reconstitution. The submission also noted that the financial impact to the NIP would be nil as the dosage was assumed to be equivalent where a single dose vial of Menveo solution for injection = single dose vial of Menveo solution and powder for reconstitution.

## **6 PBAC Outcome**

- 6.1 The PBAC recommended the listing of meningococcal serogroup A, C, W-135 and Y oligosaccharides conjugated individually to *Corynebacterium diphtheriae* CRM197 protein (MenACWY-CRM) vaccine (Menveo® solution for injection) as a designated vaccine on the *National Health (Immunisation Program – Designated Vaccines) Determination 2014 (No. 1)* for adolescents for the prevention of invasive meningococcal diseases (IMDs) caused by *Neisseria meningitidis* serogroups A, C, W-135 and Y under the same circumstances as MenACWY-CRM Menveo solution and powder for reconstitution.
- 6.2 The PBAC considered that nomination of Menveo solution and powder for reconstitution and secondary comparator Nimenrix were appropriate.
- 6.3 The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Menveo solution for injection would be acceptable if it were cost-minimised against the nominated comparators, Menveo solution and powder for reconstitution and Nimenrix .
- 6.4 The PBAC advised the equi-effective doses to be 0.5 mL Menveo solution for injection = 0.5 mL Menveo solution and powder for reconstitution = 0.5 mL Nimenrix.
- 6.5 The PBAC noted that the submission was based on two Phase 2b clinical studies which evaluated the immunogenicity and safety of the Menveo solution for injection against the solution and powder. The PBAC noted that the TGA Delegate found that the immunogenicity and safety of Menveo solution for injection were very similar to Menveo solution and powder for reconstitution.
- 6.6 The PBAC considered that the claim of non-inferior comparative effectiveness and non-inferior comparative safety of Menveo solution for injection to both Menveo solution and powder for reconstitution and Nimenrix for the proposed population was reasonable.
- 6.7 The PBAC noted that Menveo solution for injection was not TGA approved for use in persons under the age of 2 years, whereas the comparators can be administered from 2 months (Menveo solution and powder for reconstitution) and 6 weeks (Nimenrix). The PBAC noted this difference would not impact the request for the solution for injection to be used under the NIP for prevention of IMDs in adolescents.

- 6.8 The PBAC considered there would be no net cost to government as the submission requested a cost-minimisation to the nationally negotiated price for MenACWY vaccine for the requested population and the dosage for Menveo solution for injection, Menveo solution and powder for reconstitution and Nimenrix were accepted to be equivalent. Additionally, the PBAC noted that Menveo solution for injection would likely replace Menveo solution and powder for reconstitution given the solution for injection would not need to be reconstituted. The PBAC also noted that Menveo solution for injection could also be used as an alternative to Nimenrix.
- 6.9 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

## 7 Recommended listing

### 7.1 Add new item:

Vaccine	Brand	Formulation	Active ingredient and strength	Number and timing of doses
Meningococcal (Groups A,C,W-135 and Y) Oligosaccharide CRM197 Conjugate Vaccine (Men ACWY-CRM)	Menveo	Injection (0.5mL)	Each 0.5 mL dose contains: (a) 10 µg Meningococcal polysaccharide serogroup A conjugated to 16.7–33.3 µg <i>Corynebacterium diphtheriae</i> CRM197 protein  (b) 5 µg Meningococcal polysaccharide serogroup C conjugated to 7.1–12.5 µg <i>C. diphtheriae</i> CRM197 protein  (c) 5 µg Meningococcal polysaccharide serogroup W-135 conjugated to 3.3–8.3 µg <i>C. diphtheriae</i> CRM197 protein  (d) 5 µg Meningococcal polysaccharide serogroup Y conjugated to 5.6–10 µg <i>C. diphtheriae</i> CRM197 protein	1 dose
Circumstances Vaccine may be provided to:  (a) a person aged at least 14 years old but less than 17 years old as part of a school based program; or  (b) a person aged at least 14 years old but less than 19 years old who did not receive the vaccination as part of a school based program				

## **8 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.

## **9 Sponsor's Comment**

GSK welcomes the PBAC's recommendation of Menveo® solution for injection for the prevention of invasive meningococcal diseases (IMDs) caused by *Neisseria meningitidis* serogroups A, C, W-135 and Y in adolescents.