Introduction of MenC vaccine to NIP
Australia, 1997-2017, by year and bacterial serogroup

IMD Australia: Breakdown by State or Territory, 2017
Peak disease: B in SA, NSW, QLD  W in Vic, WA, NT

2006 to 2015 data shows that notification rates for meningococcal B hit 2 peaks: <5 years and aged 15-19 years
Age-specific numbers and rates of invasive meningococcal disease (IMD) in Australia, 2006-2015

IMD notification rates, Australia
By Indigenous status and age group, 2002-2018 YTD

Adapted from the Annual reports of the meningococcal surveillance program and the Department of Health, 2017. Note: ‘Other’ includes where meningococcal isolates could not be identified, other isolates not grouped and cases where serogroup was not known.


Adapted from the National Notifiable Diseases Surveillance System and Australian Government (accessed 10 Feb 2019).

Note: ‘Other’ includes where meningococcal isolates could not be identified, other isolates not grouped and cases where serogroup was not known.

Adapted from Archer BN, et al. MJA. 2017; 207(9):382-387

# Breakdown by age
Data were extracted from the NNDSS on 1 August 2018, by diagnosis date.
*NG includes where meningococcal isolates could not be identified (‘not groupable’), other isolates not grouped and where serogroup was not known.

Incidence X5 in young indigenous!
National/State-based MenACWY vaccination programs

Target adolescents, due to highest carriage rate and hi disease rate

Relevant State health departments. References provided at end of slide deck.

States and Territories may also implement additional programs on an as-needed basis.

Brand of meningococcal ACWY vaccine used varies

Commonwealth takes over April 2019

NIP childhood schedule from 1 July 2018

Changes then and now

<table>
<thead>
<tr>
<th>Age</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>2 months (from 6 weeks of age)</td>
<td>DTapa-IPV-HBV/Hib PCV13 Rotavirus</td>
</tr>
<tr>
<td>4 months</td>
<td>DTapa-IPV-HBV/Hib PCV13 Rotavirus</td>
</tr>
<tr>
<td>6 months</td>
<td>DTapa-IPV-HBV/Hib</td>
</tr>
<tr>
<td>12 months</td>
<td>MenACWY MMR PCV13</td>
</tr>
<tr>
<td>18 months</td>
<td>Hib MMRV DTapa</td>
</tr>
<tr>
<td>4 years</td>
<td>DTapa-IPV</td>
</tr>
</tbody>
</table>

a Hepatitis B vaccine should be given to all infants as soon as practicable after birth. The greatest benefit is if given within 24 hours, and

b Rotavirus vaccine: First dose must be given by 14 weeks of age, the second dose by 24 weeks of age.

Australian Immunisation Handbook (AIH): Meningococcal vaccination recommendations

*Refer also to NCIRS meningococcal fact sheet & FAQs

Adolescents

Healthy adolescents aged 15–19 years are strongly recommended to receive MenACWY vaccine

Healthy adolescents aged 15–19 years are strongly recommended to receive 2 doses of MenB vaccine

Aboriginal and Torres Strait Islander people

Aboriginal and Torres Strait Islander people aged 2 months to 18 years are strongly recommended to receive MenACWY vaccine

All Aboriginal and Torres Strait Islander people aged 2 months to 19 years are strongly recommended to receive MenB vaccine
Young adults living in close quarters

Adolescents and young adults living in close quarters are strongly recommended to receive MenACWY and MenB vaccines

Smokers

Adolescents and young adults who are current smokers are strongly recommended to receive MenACWY and MenB vaccines

Quadrivalent ACWY meningococcal vaccines¹

Meningococcal A, C, W and Y conjugate vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indication</th>
<th>Dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menveo® GSK</td>
<td>≥2 months</td>
<td>≥6 months, 4 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7-23 months, 2 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>22 years, 1 dose</td>
</tr>
<tr>
<td>Nimenrix® Pfizer</td>
<td>≥6 weeks</td>
<td>6-12 weeks, 3 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>212 months, 1 dose</td>
</tr>
<tr>
<td>Menactra® Sanofi-Aventis</td>
<td>≥9 months – 55 years</td>
<td>9-23 months, 2 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-55 years, 1 dose</td>
</tr>
</tbody>
</table>

Generally well tolerated, with the most common side effects (>10%) typically associated with vaccination

- Infection site reactions, gastrointestinal upset, headache, fatigue. Not a complete list, refer to PI for full details.²

². Menactra Product Information, Sanofi 2016
³. Thrombo Product Information, Aventis 2016

Meningococcal B vaccines¹-²

Acellular meningococcal B vaccine

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indication</th>
<th>Antigen/s</th>
<th>Dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bexsero® GSK</td>
<td>≥2 months</td>
<td>Hib⁴, NAdA⁴</td>
<td>Variable, depending on age at first administration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hib⁴, NHBA⁴, NZ PorA P1.4, Porin A</td>
<td></td>
</tr>
<tr>
<td>Trumenba® Pfizer</td>
<td>≥10 years</td>
<td>Hib⁴, subfamily A</td>
<td>Variable, depending on patient risk of IMD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[ADS]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hib⁴, subfamily B</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>[BOI]</td>
<td></td>
</tr>
</tbody>
</table>

¹. Factor H Binding Protein
². Neisseria Adhesin A protein

⁻¹. Thrombo Product Information, Aventis 2016
⁻². Menactra Product Information, Sanofi 2016

Men B vaccine PI update:

Approved dosing schedules for Bexsero in Australia

Administer by deep intramuscular injection, preferably in the anterolateral aspect of thigh in infants or deltoid muscle region of upper arm in older subjects

<table>
<thead>
<tr>
<th>Dosage:</th>
<th>Primary immunisation</th>
<th>Minimum interval between primary doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants 2-3 months*</td>
<td>2 doses</td>
<td>2 months</td>
<td>Second year of life (26 months post primary series)</td>
</tr>
<tr>
<td></td>
<td>3 doses</td>
<td>2 months</td>
<td>2 months</td>
</tr>
<tr>
<td>Infants 4-11 months</td>
<td>2 doses</td>
<td>2 months</td>
<td>Second year of life (26 months post primary series)</td>
</tr>
<tr>
<td></td>
<td>2 doses</td>
<td>2 months</td>
<td>2 months</td>
</tr>
<tr>
<td>Toddlers ≥12 months</td>
<td>2 doses</td>
<td>2 doses</td>
<td>Need not be established</td>
</tr>
<tr>
<td>Children (≥12 months)</td>
<td>2 doses</td>
<td>2 doses</td>
<td>Need not be established</td>
</tr>
<tr>
<td>Adolescents &amp; Adults</td>
<td>2 doses</td>
<td>2 doses</td>
<td>Need not be established</td>
</tr>
</tbody>
</table>

*The safety and efficacy of the vaccine in infants <2 years have not been established. No data available

Bexsero update: Real world experience

- UK: Introduction of national vaccination campaign (2+1 schedule)
- Canada: Regional vaccination campaign in Saguenay–Lac-Saint-Jean, Quebec and vaccination during a MenB outbreak at Acadia University, Nova Scotia
- USA: Vaccination during MenB outbreaks at Princeton University, University of California at Santa Barbara, and Santa Clara University

Infants ≥2 months

Adolescents
Prophylactic use of paracetamol reduces the incidence and severity of fever without affecting the immunogenicity of either Bexsero or routine vaccines (PCV7 and DTP-IPV-HBV/Hib).

The effect of antipyretics other than paracetamol on the immune response has not been studied.

**1st DOSE**
- Vaccinate
- 10 minutes
- 6 hours
- 6 hours

*1 mg/kg paracetamol within 30 minutes prior to vaccination (or as soon as practicable after).

ATAGI recommends doses of paracetamol be given 6 hours apart.

**Summary**

- IMD is a rare, but potentially fatal disease
  - difficult to diagnose early due to non-specific symptoms
  - symptoms develop rapidly
  - even with appropriate medical treatment up to 10% of cases are fatal and up to 30% of survivors suffer from permanent sequelae

- Changing epidemiology has influenced changes to funded programs
  - MenACWY vaccine provided under NIP at 12 mth encounter: July 2018 (replaced MenC + Hib)
  - From April 2019: MenACWY vaccine will be available on the NIP for 14-16 year old’s (catch-up program for those aged 15-19 years)

- In 2018 & many other years. MenB was the predominant serogroup in Australia

- In 2018, SA introduced a State-based funded MenB program for infants and (from 1 Feb 2019) adolescents

- In all other states MenB is available on private prescription

- ATAGI strongly recommend MenB and MenACWY vaccination for all-risk groups

- Bexsero PI update includes a 2+1 vaccination schedule for those aged 2-5 months

---

**Recommendations: Bexsero and Prophylactic Paracetamol, age < 2 years**

Australian Technical Advisory Group on Immunisation (ATAGI)

1. Vaccine recommendations

**Any person aged 6+ weeks who wishes to protect themselves against meningococcal to have both MenACWY & MenB vaccines**

**These vaccines are strongly recommended for:**
- Infants aged 6 weeks < 2 years
- Teens aged 15 - 19 years
- All indigenous aged 2 months – 19 years
- High risk conditions e.g. lab, crowded, smokers (15-24 years)
- Travellers e.g. “meningitis belt”, Hajj

All are considered high risk

2. Menactra, Menveo, Nimenrix (ACWY)

**Age < 2 years: no preference; Menveo & Nimenrix 2/12 start, Menactra start from 9/12 of age**

- If 12-23/12 one dose Nimenrix, two doses of other 2; best not give a Tet tox vaccine 3/12 before Nimenrix (carrier interference)

- Age 2+: single dose of any, Menactra less favoured – less antibody and declines more

- Menactra not given with PCV13 as less pneumo antibody, but can give PCV13 first then 1/12 gap to Menactra

- Menactra must be given with or one month before Dip Tox, to prevent carrier interference

3. Bexsero and Trumenba

- Bexsero = recombinant, multi-component, given from 6 weeks
- Trumenba = recombinant, bivalent, from 10 years
- No preference for either if age 10+ years
- Should not mix schedules – if aged 10+ give 2 doses of each
  - (Mixing is OK with MenACWY vaccines)

**MenACWY and MenB vaccines are equally important from a clinical/public health perspective, but as yet only MenACWY is on the National Immunisation Program**
**Australian Immunisation Handbook**

### Meningococcal recommendations

<table>
<thead>
<tr>
<th>Age group</th>
<th>Healthy Aboriginal and Torres Strait Islander people</th>
<th>Healthy non-Indigenous people</th>
<th>Special risk groups (including adolescents and young adults; anyone who lives in close quarters; and laboratory workers)</th>
<th>Travellers to regions with an increased risk of exposure to MenACWY disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks–23 months</td>
<td>MenB and MenACWY</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2–4 years</td>
<td>MenB and MenACWY</td>
<td>None</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>5–16 years</td>
<td>MenB and MenACWY</td>
<td>None</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>15–19 years</td>
<td>MenB and MenACWY</td>
<td>MenB and MenACWY</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>≥20 years</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>MenB and MenACWY</td>
</tr>
</tbody>
</table>

**UK PHE MenB vaccination program**

- 74% reduction in Men B disease in the vaccinated cohort
- Men B program has prevented ~ 250 cases
- Men ACWY program has prevented ~ 50 cases
- No safety signals identified from 5 million doses administered

**UK Safety Experience with Bexsero**

- 1.28 million infants vaccinated
- No new safety signals identified
- Antigenicity did not affect compliance with subsequent doses
- The safety profile of 4CMenB was broadly as expected, with no serious safety concerns identified

**Carriage of *N. meningitidis* in high school students**

**“B Part of It” study**

- Professor Helen Marshall
- NHMRC Senior Research Fellow
- Senior Medical Practitioner and Director (VIRTU), Women’s and Children’s Health Network
- Deputy Director, Robinson Research Institute, University of Adelaide

Preliminary results presented at IPNC, USA Sep 2018

**IMD serogroup B notifications in adolescents in SA pre and post study implementation**

No IMD in 35,000 study participants

**Notifications of invasive meningococcal disease**

Australia, 1991 - 2017, by year, all cases of IMD

2019: 17 cases YTD
IMD vaccine development

Conventional approaches have not been possible for MenB

H influenzae
1 pathogenic serotype

S pneumoniae
23 pathogenic serotypes

N meningitidis
5 pathogenic serogroups

INVASIVE DISEASE

Hib Glycoconjugate vaccine

Pneumococcal Glycoconjugate vaccine

Meningococcal Glycoconjugate vaccine

Capsule poorly Immunogenic

Bexsero contains 4 antigenic components
(4CMenB vaccine)

Identified using a “reverse vaccinology” approach

Bexsero = 3 recombinant surface-exposed protein antigens + OMV

NHBA: Neisseria Heparin-Binding Antigen + GNA fusion protein

OMV: NZ PorA P1.4: porin A

NadA: Neisseria adhesin A Protein

Bexsero Consists of 3 Protein Antigens and an Outer Membrane Vesicle (OMV)

- Multicomponent (4) Meningococcal Serogroup B Vaccine
  - Has the potential to protect against the majority of MenB disease
  - Includes 4 antigen components

fHbp
NadA
NHBA
PorA 1.4 (as part of OMV)

Bexsero approvals and recommendations

More than 20 million doses distributed worldwide since launch

41 APPROVALS

- EUSA: 31 countries (plus Andorra)
- Other: Argentina, Australia, Brazil, Canada, Chile, Uruguay, USA

19 CLINICAL RECOMMENDATIONS

- Austria, Brazil, Belgium, Canada, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Mexico, Malta, Netherlands, Norway, Poland, Portugal, Spain, Sweden, UK: NIPs implemented
- USA: Category B national recommendation

9 NIPs

- Andorra, Ireland, Italy, Lithuania, Malta, Portugal, UK, USA: NIPs implemented
- USA: Category B national recommendation

Images are © Hurd Studios, 2012 and courtesy of GlaxoSmithKline