New drugs

Meningococcal B vaccine

Approved indication: immunisation

Bexsero (Novartis)

0.5 mL pre-filled syringe containing suspension for injection

Australian Medicines Handbook section 20.1

Meningococcal disease is caused by the Gram-negative bacterium *Neisseria meningitidis*. Asymptomatic carriage of meningococci in the nasopharynx is relatively common (5–10% of people), but occasionally the bacteria invade and cause septicaemia or meningitis. Infection can be rapid and fatal and mainly affects children under two years. However, there is also a peak of incidence in adolescents associated with increased carriage rates.

More than 80% of cases of meningococcal disease in Australia are caused by serogroup B isolates. Up until now, the only vaccines available protect against serogroups A, C, W and Y (Aust Prescr 2011;34:29-30). Vaccines based on the serogroup B capsule have been poorly immunogenic, probably because of similarities with carbohydrate residues found on human tissue.

This is the first vaccine to be approved for serogroup B disease. It contains the following components from serogroup B *N. meningitidis* strains:

- heparin binding protein
- adhesin A
- factor H binding protein
- outer membrane vesicles containing the porA P1.4 protein.

These antigens are adsorbed to the adjuvant aluminium hydroxide.

The immunogenicity of the vaccine has been investigated in babies and adolescents. As protection from meningococcal disease correlates with antibodies that kill meningococci, efficacy was inferred by measuring bactericidal antibody titres to several serogroup B reference strains. These were measured in sera one month after vaccination. A four-fold increase in titres from baseline is considered to be protective against invasive disease.[1]

In a phase III study of 2627 babies, the vaccine was immunogenic after three intramuscular injections at 2, 4 and 6 months of age (given with routine childhood vaccinations). Most babies developed antibody titres that correlated with protection. In an extension study, waning antibody titres were boosted by a fourth injection at 12 months.[2]

In a dose-finding trial of 1631 adolescents (aged 11–17), two doses of the vaccine given 1–6 months apart resulted in protective antibody titres.[3] In a cohort of 257 teenagers from the study, 77–94% maintained protective antibody titres 18–24 months after the initial immunisation of two doses.[4]

There are numerous different circulating serogroup B strains in the population. It is not clear if antibodies to this vaccine will be cross-protective against other serogroup B strains. However, preliminary results of a survey of 373 invasive isolates from Australia predicted that 76% of the strains would be killed by sera from vaccinated individuals. Similar results were observed in a study of European isolates.[5]

The safety of the vaccine has been assessed in a cohort of 6555 individuals. In babies and toddlers, the most common adverse events were irritability (93%), injection-site reactions and fever. Fever within six hours of the injection was more common when the vaccine was given concomitantly with routine immunisations compared to when routine vaccinations were given alone (65.3% vs 32.2% babies).[2] Paracetamol is recommended if fever develops. Sleepiness (87%), unusual crying (85%), diarrhoea (44%), vomiting (27%) and rash (13%) were also very common.[2] In adolescents and adults, injection-site reactions, malaise, headache, nausea, myalgia and arthralgia were the most common events.

The vaccine is indicated from two months of age and is given by intramuscular injection. Three primary doses are recommended for babies aged 2–5 months and two doses for those aged 6–11 months. These children should also have a booster dose at 12–23 months. Children over one year and adults should have two doses. It is unclear whether they need a booster injection.

The vaccine produces bactericidal antibody titres that correlate with protection against serogroup B reference strains. However, the actual efficacy of the vaccine including the coverage and duration of protection will not be known until after marketing. Parents should be warned that fever is very common with this vaccine and advised to use paracetamol if this occurs.

[X] manufacturer did not respond to request for data

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

REFERENCES †A

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3. Santolaya ME, O'Ryan ML, Valenzuela MT, Prado V, Vergara R, Munoz A, et al; V72P10 Meningococcal B Adolescent Vaccine Study group. Immunogenicity and tolerability of a multicomponent meningococcal serogroup B (4CMenB) vaccine in healthy adolescents in Chile: a phase 2b/3 randomised, observer-blind, placebo-controlled study. Lancet 2012;379:617-24.
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5. Vogel U, Taha MK, Vazquez JA, Findlow J, Claus H, Stefaelli P, et al. Predicted strain coverage of a meningococcal multicomponent vaccine (4CMenB) in Europe: a qualitative and quantitative assessment. Lancet Infect Dis 2013;13:416-25.

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The Transparency score (T) is explained in 'New drugs: T-score for transparency', Aust Prescr 2014;37:27.

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).

A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/industry/pm-auspar.htm)