

## New drugs

### Live Japanese encephalitis vaccine

**Approved indication: prevention of Japanese encephalitis**

**Imojev (Sanofi Pasteur)**

**vials containing one dose of freeze-dried powder for reconstitution**

**Australian Medicines Handbook section 20.1**

The currently approved vaccine for Japanese encephalitis in Australia is an inactivated vaccine given in two doses (Aust Prescr 2009;32:82-6). This new product is a live attenuated vaccine using the yellow fever vaccine virus – strain 17D-204 – as a vector. In this virus, two of the yellow fever genes have been replaced by Japanese encephalitis genes (strain SA<sub>4</sub> 14-2) encoding a premembrane and an envelope protein. This chimeric virus is propagated in tissue culture before being freeze-dried for use.

Vaccination is recommended for people who live in or are travelling to areas where Japanese encephalitis is endemic, such as Papua New Guinea and parts of Asia. It is also recommended for people who work with the virus in laboratories. The vaccine is indicated from 12 months of age as a single subcutaneous injection.

In an early dose-finding trial, most of the 87 adults who were given the live vaccine (1.8–5.8 log<sub>10</sub> plaque-forming units subcutaneously) developed neutralising antibodies to the chimeric vaccine strain and, to a lesser degree, to the wild-type Japanese encephalitis strains Beijing-1, Nakama and 902/97. A second dose of the vaccine 30 days later did not boost this immune response.<sup>1</sup>

In a phase III immunogenicity trial of 820 adults (enrolled from Australia and the USA), one dose (4 log<sub>10</sub> plaque-forming units) of the live vaccine was comparable to three doses of an inactivated Japanese encephalitis vaccine. A month after vaccination, 99% of people in the live vaccine group were considered to have protective levels of neutralising antibody to the vaccine strain compared to 74.8% of people in the comparator group.<sup>2</sup>

In a paediatric trial, almost all children (aged 1–5 years) developed seroprotective antibody levels after a single dose of the vaccine, regardless of whether they had been previously vaccinated with an inactive vaccine. Many of the children developed neutralising antibodies that cross-reacted with other Japanese encephalitis strains.<sup>3</sup>

It is not currently known if a booster of the live vaccine will be needed, but from longer-term immunogenicity studies it seems antibody responses last for at least four years in adults and six months in children.

In adults, the most common adverse reactions to the vaccine included headache (23.9%), fatigue (21%), malaise (17%), myalgia (14.7%) and injection-site pain (11.8%). These were also common in children as well as irritability (28.5%), loss of appetite (25.9%), fever (20.7%), vomiting (19.2%) and abnormal crying (19.1%).

Vaccination should be postponed in the event of a fever or acute illness. The vaccine is contraindicated in people with impaired cellular immunity, including those on immunosuppressive therapies such as chemotherapy or high-dose steroids (for 14 days or more), and people with symptomatic HIV infection.

This vaccine should not be given to women during pregnancy and lactation as there is a theoretical risk that the virus could cross the placenta or be secreted in breast milk.

In children, other vaccines should not be given at the same time. However, in adults concomitant yellow fever vaccine can be administered in the opposite arm or leg. Prescribers should be aware that plasma products such as immunoglobulins could potentially neutralise the live virus so vaccination after receiving blood products should be avoided for at least six weeks.

This live vaccine seems to produce durable immune responses to Japanese encephalitis but its actual efficacy will not be known until after marketing. It may be preferable to the current inactivated vaccine as it is approved for use in children and only one dose is indicated.

**TT** manufacturer provided additional useful information

#### REFERENCES <sup>A</sup>

1. Monath TP, Guirakhoo F, Nichols R, Yoksan S, Schrader R, Murphy C, et al. Chimeric live, attenuated vaccine against Japanese encephalitis (ChimeriVax-JE): phase 2 clinical trials for safety and immunogenicity, effect of vaccine dose and schedule, and memory response to challenge with inactivated Japanese encephalitis antigen. *J Infect Dis* 2003;188:1213-30.
2. Torresi J, McCarthy K, Feroldi E, Méric C. Immunogenicity, safety and tolerability in adults of a new single-dose, live-attenuated vaccine against Japanese encephalitis: randomised controlled phase 3 trials. *Vaccine* 2010;28:7993-8000.
3. Chokeyhaibulkit K, Sirivichayakul C, Thisyakorn U, Sabchareon A, Pancharoen C, Bouckennooghe A, et al. Safety and immunogenicity of a single administration of live-attenuated Japanese encephalitis vaccine in previously primed 2- to 5-year-olds and naïve 12- to 24-month-olds: multicenter randomized controlled trial. *Pediatr Infect Dis J* 2010;29:1111-7.



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.

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The Transparency score (T) is explained in 'New drugs: T-score for transparency', Aust Prescr 2011;34:26-7.

- \* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA ([www.fda.gov](http://www.fda.gov)).
- † 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](http://www.ema.europa.eu)).
- <sup>A</sup> 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](http://www.tga.gov.au/industry/pm-auspar.htm))