4.8 JAPANESE ENCEPHALITIS

4.8.1 Virology

Japanese encephalitis (JE) is caused by a mosquito-borne RNA flavivirus.

4.8.2 Clinical features

The disease is typically an acute neurological illness, characterised by headache, fever, convulsions, focal neurological signs and depressed level of consciousness. It has a high case-fatality rate (approximately 30%) and there is a high prevalence of neurological sequelae (up to 50%) in those who survive the acute illness. Less commonly, the disease may present as an acute flaccid paralysis. Milder forms include febrile illness with headache, and aseptic meningitis. It is recognised, however, that most infections are asymptomatic; published estimates of the symptomatic to asymptomatic infection ratio vary in different populations from 1:25 to 1:1000.

4.8.3 Epidemiology

JE is a significant public health problem in many parts of Asia, including the Indian subcontinent, Southeast Asia and China. In recent decades the disease has extended beyond its traditionally recognised boundaries to eastern Indonesia (including Bali) and Papua New Guinea. Occasional outbreaks have also occurred in the Torres Strait, and 1 case in north Queensland.

The first ever outbreak of Japanese encephalitis (JE) in Australia occurred in the remote outer islands of the Torres Strait in 1995, with 3 cases, 2 of them fatal. There have been 5 cases to date acquired in Australia. JE virus has only been detected infrequently in sentinel animal surveillance in the outer islands. The sentinel pig surveillance system has been gradually disbanded since 2006, with surveillance of the last remaining herd on Cape York ceasing from the 2011–2012 wet season.

There has not been a case of JE in the Torres Strait since 1998 and the risk of JE has diminished considerably in the outer islands since the mid-1990s. Most communities have relocated pigs well away from homes, and major drainage works on most islands have markedly reduced potential breeding sites for vector mosquitoes. Between 2001 and 2014, only 9 cases of JE virus infection were notified in Australia, all having been acquired overseas.

The JE virus is essentially a zoonosis of pigs and wading birds, and is transmitted between these animals by culicine mosquitoes. The virus replicates, leading to a transient high-level viraemia, within these ‘amplifying’ hosts, but not within other large vertebrates such as horses and humans. Indeed, humans are an incidental host, infected when living in close proximity to the enzootic cycle; this usually occurs in rural areas where there is prolific breeding of the vectors in flooded rice fields.

Two epidemiological patterns of JE in endemic regions were recognised historically. In the temperate or subtropical regions of Asia (northern Thailand, northern Vietnam, Korea, Japan, Taiwan, China, Nepal and northern India), the disease principally occurred in epidemics during the summer or wet season months (April to May until September to October). In the tropical regions (most of Southeast Asia, Sri Lanka, southern India), the disease occurs throughout the year, but particularly during the wet season. A 2006 study confirmed that JE virus is endemic in Bali, that it causes substantial human illness, and that it circulates year round. In some countries (Japan, Taiwan, South Korea and some provinces of China), the incidence of JE has declined considerably in recent decades, and it has been eradicated from Singapore. Immunisation, changes in pig husbandry, a reduction in land utilised for rice farming, and improved socioeconomic circumstances have all contributed to these changes. Because JE virus is maintained in an enzootic cycle, susceptible individuals may still be at risk when visiting areas where there are few human cases due to established immunisation programs.

Updated information regarding JE virus activity and/or risk in travel destinations should be sought from a reputable source prior to travel (for example, Health information for international travel [the ‘Yellow book’] published by the US Centers for Disease Control and Prevention, available at www.cdc.gov/travel/yellowbook).

4.8.4 Vaccines

- **Imojev** – Sanofi-Aventis Australia Pty Ltd (live attenuated recombinant Japanese encephalitis virus). Lyophilised powder in a monodose vial with separate diluent. Each 0.5 mL reconstituted dose contains 4.0–5.8 log plaque-forming units (PFU) of live attenuated recombinant Japanese encephalitis virus; mannitol; lactose; glutamic acid; potassium hydroxide; histidine; human serum albumin. No adjuvants or antibiotics are added.

- **JEspect** – Valneva Scotland Ltd/CSL Limited (inactivated Japanese encephalitis virus). Each 0.5 mL pre-filled syringe contains 6 µg of purified inactivated Japanese encephalitis virus; 0.25 mg aluminium as aluminium hydroxide. No preservatives or antibiotics are added.

Two JE vaccines, each with different characteristics, are available for use in Australia. The inactivated mouse brain-derived JE vaccine formulation manufactured in Japan, JE-Vax, which was previously used in Australia, is no longer
manufactured. Clinical and animal studies have provided evidence in support of an immunological correlate of immunity (established by the World Health Organization as a neutralising antibody titre of ≥1:10). Both currently available JE vaccines were registered on the basis of this serological correlate in lieu of a field efficacy trial.

Imojev is a Vero cell-derived, live attenuated, monovalent viral vaccine produced using recombinant technology. Two genes of the 17D-204 yellow fever vaccine virus have been replaced with two genes, prM and E genes, from the Japanese encephalitis virus strain SA 14-14-2. About 94% of healthy adults aged 18–84 years seroconverted to a strain homologous to that in the Imojev vaccine 14 days after a single vaccine dose. Several clinical trials have demonstrated that, 28 days following vaccination with a single dose of Imojev, protective levels of neutralising antibodies against the homologous vaccine virus strain are present in 96% of vaccine-naive children aged 12–24 months and 99% of adults. Immune response was non-inferior to that attained after a 3-dose primary course of the inactivated mouse brain-derived JE vaccine that was previously used in Australia. Subjects also seroconverted to various wild-type, non-homologous, JE virus strains (70 to 97% of children aged 12–24 months and 70 to 100% of adults); 85% of adults developed neutralising antibodies against all four wild-type strains used for testing. A clinical trial of a single dose of Imojev in children aged 9–18 months reported that a comparable proportion of participants aged 9–11 and 12–18 months had protective levels of neutralising antibodies at 12 months after vaccination.

In adults, a protective antibody level to the vaccine strain was maintained in 98% of adults at 1 year after vaccination, in 92% at 3 years and in 87% at 5 years. Protective antibody levels to at least three wild-type virus strains have been demonstrated in about 65% of adults 5 years after a single vaccine dose. Establishment of immunological memory in vaccinated adult subjects has also been demonstrated. In children vaccinated at 12–24 months of age with a single dose of Imojev, protective antibody levels to the vaccine strain have been demonstrated in 87% of children at 7 months after vaccination, and in 75% at 3 years. There are no immunogenicity data for Imojev in children aged 6–17 years; immunogenicity in this age group is assumed based on studies in both younger children and adults.

Among children aged 2–5 years previously vaccinated with a mouse brain-derived JE vaccine (of whom 86% were seropositive against the vaccine strain and 72 to 81% seropositive against four wild-type strains at baseline), a dose of Imojev produced seroprotective antibody levels against the vaccine strain in 100%, and against all wild-type strains in 99%. Ninety-three per cent of these children seroconverted to the vaccine strain and 90% against all wild-type strains, and 98% maintained protective antibody against the vaccine strain at 3 years after vaccination. JEspect is a Vero cell-derived, inactivated, aluminium-adjuvanted vaccine based on the attenuated SA 14-14-2 JE virus strain. JEspect has non-inferior immunogenicity (after 2 doses, given 4 weeks apart) to 3 doses of the previously available mouse brain-derived vaccine, with seroconversion achieved in 98% of subjects. Post-vaccination geometric mean titres (GMT) in JEspect recipients were significantly higher than GMTs attained after a mouse brain-derived vaccine. After a standard 2-dose course, protective levels of neutralising antibodies have been found to persist for 6 months in 95%, for 12 months in 83% and for 24 months in 48% of JEspect-vaccinated subjects in central Europe, but in 83%, 58% and 48%, respectively, at these three time points in subjects in western and northern Europe. A suggested plausible explanation for the discrepancy between these two studies is prior vaccination with the tick-borne encephalitis (TBE) vaccine in a large proportion of subjects in the central European study. In a further study, of JEspect-vaccinated subjects who completed 5 years of follow-up, the seroprotection rate at 5 years was 64% for TBE-naive individuals and 92% for those who received TBE vaccine prior to or during the study. In an extension of the western and northern European study, those who did not have a seroprotective antibody level at either the 6- or 12-month follow-up point were given a booster dose at 11 and/or 23 months after first vaccination; seropositivity was attained in 100% of these subjects. Another study showed that a booster dose given 15 months after the primary immunisation with 2 doses of JEspect increased the GMT by 5-fold after 4 weeks, and the proportion of subjects with seroprotective antibody levels increased from 69.2% pre booster to 98.5% at 6 and 12 months post booster. Mathematical modelling has predicted that 95% of subjects would maintain seroprotective antibodies for 3.8 years after a booster dose.

The key paediatric clinical trial of JEspect was a phase III study in children aged 2 months to 17 years in the Philippines. In subjects given age-appropriate doses of JEspect, the proportions with protective antibody titres were 99 to 100% at day 56 and 85 to 100% at month 7, with no obvious pattern by age. A phase II study in 60 Indian children aged 1–3 years also showed JEspect to be safe and immunogenic in this age group. A phase III immunogenicity study involving 64 children from non-JE endemic countries aged 2 months to <18 years (mean age 11.6 years; range 11 months to 17.9 years) showed 100% seroconversion to protective levels, with the proportion seroprotected at 6 months after the 2nd dose being 100% in the <3 years age group (n=2) and 90.6% in the ≥3 years age group (n=32). A small study among healthy military personnel observed that the immune response after 4 weeks to 1 dose of JEspect, among those who had previously received at least 3 doses of mouse brain-derived JE vaccine, was non-inferior to the response after 2 doses of JEspect in those who were naïve to JE vaccines. A small study among travellers who had received at least 2 doses of a mouse brain-derived JE vaccine 1 to 21 years previously observed that, 4 to 8 weeks after a single dose of JEspect, a high proportion attained protective antibody levels against both homologous and
heterologous strains (98% and 95%, respectively), and these proportions were non-inferior compared to those who received a booster of mouse brain-derived JE vaccine. Follow-up data from this study found seroprotection rates of 89 to 100% against wild-type strains 2 years after a single JEspect booster in individuals primed with a mouse brain-derived JE vaccine.

A phase III study in healthy adults comparing accelerated (day 0 and 7) and conventional (day 0 and 28) JEspect courses suggested non-inferior immune response, for the accelerated course of JEspect compared to the conventional course, at 28 days and 1 year after the 2nd dose.

### 4.8.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze. Protect from light.

Imojev must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine must be used within 1 hour.

### 4.8.6 Dosage and administration

Imojev can be administered to persons aged ≥9 months based on evidence from clinical studies (refer to 4.8.4 Vaccines above). The dose of Imojev for infants and children (aged ≥9 months) and adults is 0.5 mL, to be given by SC injection.

JEspect can be administered to persons aged ≥2 months. However, clinical studies of JEspect in children are limited (refer to 4.8.4 Vaccines above). The ATAGI recommends that JEspect should only be used in children aged ≥2 months to <18 years in circumstances where an alternative is not available (e.g. in infants aged ≥2 months to <9 months) or is contraindicated (refer to 4.8.13 Variations from product information below).

JEspect should be given by IM injection. When using JEspect in infants and children aged ≥2 months and <3 years, primary vaccination consists of 2 doses, each of 0.25 mL, 28 days apart (refer to Table 4.8.1 Recommended doses of JE vaccines).

When using JEspect in children aged ≥3 years and adults, primary vaccination consists of 2 doses, each of 0.5 mL, 28 days apart (refer to Table 4.8.1 Recommended doses of JE vaccines).

Do not mix either Japanese encephalitis vaccine with any other vaccine in the same syringe.

### Table 4.8.1: Recommended doses of JE vaccines

<table>
<thead>
<tr>
<th>Age of vaccine recipient</th>
<th>Vaccine</th>
<th>Number of doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 to &lt;9 months</td>
<td>JEspect</td>
<td>2 doses*</td>
<td>Not required Refer to Note 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(28 days apart)</td>
<td></td>
</tr>
<tr>
<td>≥9 months to &lt;18 years</td>
<td>Imojev</td>
<td>1 dose</td>
<td>1–2 years after primary dose</td>
</tr>
<tr>
<td></td>
<td>JEspect</td>
<td>2 doses*</td>
<td>Not required Refer to Note 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(28 days apart)</td>
<td></td>
</tr>
<tr>
<td>≥18 years</td>
<td>Imojev</td>
<td>1 dose</td>
<td>Not required</td>
</tr>
<tr>
<td></td>
<td>JEspect</td>
<td>2 doses</td>
<td>1–2 years after primary dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(28 days apart†)</td>
<td></td>
</tr>
</tbody>
</table>

**Note 1:** JEspect can be administered to children in this age group in circumstances where an alternative is not available or is contraindicated (refer to 4.8.6 Dosage and administration above).

**Note 2:** Currently there is very limited evidence available to inform recommendations regarding the need and appropriate time interval for a booster of JEspect in children who received JEspect as primary immunisation.

* Each dose of JEspect in infants and children aged ≥2 months to <3 years is 0.25 mL.
† An accelerated primary course of JEspect (2 doses, each of 0.5 mL, 7 days apart) may be considered for adults who are at imminent risk of exposure to JE virus.

### Co-administration with other vaccines

Imojev can be given at the same time as the yellow fever vaccine and MMR vaccine using separate syringes and separate injection sites. Data on the co-administration with other vaccines is not available. If Imojev and the yellow fever vaccine or other live vaccines are not given simultaneously, they should be given at least 4 weeks apart.

JEspect can be co-administered with the hepatitis A vaccine, quadrivalent meningococcal conjugate vaccine and rabies vaccine. Co-administration with other vaccines (including yellow fever vaccine) has not been assessed.

If co-administration of either JE vaccine with other vaccines is indicated, injections should be given in separate limbs.
The need for JE vaccination is recommended for all research laboratory personnel who will potentially be exposed to the virus. Booster doses may be required for persons who are at continued risk of acquiring JE, on the basis that the risk of acquiring JE is likely to be low (<1 case per 1 million travellers), the risk is greater during prolonged travel to endemic areas, particularly rural areas, during the wet season; it is probably negligible during short business trips to urban areas.

JE vaccination is recommended for residents who will be living or working on the outer islands of the Torres Strait for a cumulative total of 30 days or more during the wet season (December to May). The period of greatest risk is from February to March and the vaccination course for non-residents should be completed before February. Those arriving in the outer islands late in the wet season (i.e. in May) will arrive after the risk period and do not require vaccination. Those visiting the outer islands in the dry season (June to November) do not require vaccination. Those visiting only the inner islands, including Thursday Island, do not require vaccination. Those visiting the outer islands in the dry season (June to November) do not require vaccination before February.

The period of greatest risk is from February to March and the vaccination course for non-residents should be completed before February. Those arriving in the outer islands late in the wet season (i.e. in May) will arrive after the risk period and do not require vaccination. Those visiting the outer islands in the dry season (June to November) do not require vaccination. Those visiting only the inner islands, including Thursday Island, do not require vaccination. Those visiting the outer islands in the dry season (June to November) do not require vaccination before February.

The risk of JE to travellers is determined by the season of travel, the regions visited, the duration of travel, the extent of outdoor activity and/or the risk in travel destinations should be sought from a reputable source prior to travel (for example, Health information for international travel [the ‘Yellow book’] published by the US Centers for Disease Control and Prevention, available at www.cdc.gov/travel/yellowbook). It is important to note that, as JE has occurred in travellers after shorter periods of travel, JE vaccination should be considered for shorter-term travellers, particularly if the travel is during the wet season, or anticipated to be repeated, and/or there is considerable outdoor activity, and/or staying in accommodation without air conditioning, screens or bed nets.

All travellers to Asia (and other tropical regions) must be fully aware of the need to take appropriate measures to avoid mosquito bites. Booster doses may be required for persons who are at continued risk of acquiring JE (refer to ‘Booster doses’ below).

JE vaccination is recommended for:

- residents of the outer islands in the Torres Strait
- non-residents who will be living or working on the outer islands of the Torres Strait for a cumulative total of 30 days or more during the wet season (December to May).

The dose of Imojev should be administered at least 14 days prior to potential JE virus exposure.

4.8.7 Recommendations

JE vaccines are recommended for the following groups who are at greater risk of acquiring JE. The two available JE vaccines are registered for different age groups, and have different vaccination schedules, booster dose requirements, and contraindications for use. These factors should be taken into account when deciding the most appropriate vaccine to use (refer to 4.8.6 Dosage and administration above, and ‘Booster doses’ and 4.8.9 Contraindications below).

4.8.6 Dosage and administration

The JEspect vaccine (2-dose) schedule should be completed at least 1 week prior to potential JE virus exposure.

**Travellers**

The risk of JE to travellers is determined by the season of travel, the regions visited, the duration of travel, the extent of outdoor activity and the extent to which mosquito avoidance measures are taken. While the overall risk of JE infection in travellers to JE endemic countries is likely to be low (<1 case per 1 million travellers), the risk is greater during prolonged travel to endemic areas, particularly rural areas, during the wet season; it is probably negligible during short business trips to urban areas.

JE vaccination is recommended for travellers spending 1 month or more in endemic areas in Asia and Papua New Guinea during the JE virus transmission season, including persons who will be based in urban areas but are likely to visit endemic rural or agricultural areas (refer to 4.8.3 Epidemiology above). Up-to-date information regarding JE virus activity and/or risk in travel destinations should be sought from a reputable source prior to travel (for example, Health information for international travel [the ‘Yellow book’] published by the US Centers for Disease Control and Prevention, available at www.cdc.gov/travel/yellowbook). It is important to note that, as JE has occurred in travellers after shorter periods of travel, JE vaccination should be considered for shorter-term travellers, particularly if the travel is during the wet season, or anticipated to be repeated, and/or there is considerable outdoor activity, and/or staying in accommodation without air conditioning, screens or bed nets.

All travellers to Asia (and other tropical regions) must be fully aware of the need to take appropriate measures to avoid mosquito bites. Booster doses may be required for persons who are at continued risk of acquiring JE (refer to ‘Booster doses’ below).

**Torres Strait Islands**

JE vaccination is recommended for:

- residents of the outer islands in the Torres Strait
- non-residents who will be living or working on the outer islands of the Torres Strait for a cumulative total of 30 days or more during the wet season (December to May).

The period of greatest risk is from February to March and the vaccination course for non-residents should be completed before February. Those arriving in the outer islands late in the wet season (i.e. in May) will arrive after the risk period and do not require vaccination. Those visiting the outer islands in the dry season (June to November) do not require vaccination. Those visiting only the inner islands, including Thursday Island, do not require vaccination. Timing of vaccination in residents should take into account a range of factors including age, time of year, vaccine schedule and recent epidemiology.

Booster doses may be required for persons who are at continued risk of acquiring JE (refer to ‘Booster doses’ below).

**Laboratory personnel**

JE vaccination is recommended for all research laboratory personnel who will potentially be exposed to the virus.

**Booster doses**

The need for a booster dose of JE vaccine depends on the age at which the primary vaccine course was given and the vaccine used for the primary course (refer to Table 4.8.1 in 4.8.6 Dosage and administration above).

**Interchangeability of Japanese encephalitis vaccines**

The vaccine used for a booster dose should preferably be the same as that used for the primary course. No studies have been conducted to assess the immune response to an Imojev booster in individuals who have received a primary course of JEspect, or vice versa. However, as both vaccines are derived from the same virus strain, a booster using the alternative vaccine, based on first principles, should provide a satisfactory immune response.

For individuals previously vaccinated with the mouse brain-derived JE vaccine, either Imojev or JEspect can be used for revaccination if there is an ongoing risk of JE virus exposure.

4.8.7 Recommendations

JE vaccines are recommended for the following groups who are at greater risk of acquiring JE. The two available JE vaccines are registered for different age groups, and have different vaccination schedules, booster dose requirements, and contraindications for use. These factors should be taken into account when deciding the most appropriate vaccine to use (refer to 4.8.6 Dosage and administration above, and ‘Booster doses’ and 4.8.9 Contraindications below).

The dose of Imojev should be administered at least 14 days prior to potential JE virus exposure.

The JEspect vaccine (2-dose) schedule should be completed at least 1 week prior to potential JE virus exposure.

**Travellers**

The risk of JE to travellers is determined by the season of travel, the regions visited, the duration of travel, the extent of outdoor activity and the extent to which mosquito avoidance measures are taken. While the overall risk of JE infection in travellers to JE endemic countries is likely to be low (<1 case per 1 million travellers), the risk is greater during prolonged travel to endemic areas, particularly rural areas, during the wet season; it is probably negligible during short business trips to urban areas.

JE vaccination is recommended for travellers spending 1 month or more in endemic areas in Asia and Papua New Guinea during the JE virus transmission season, including persons who will be based in urban areas but are likely to visit endemic rural or agricultural areas (refer to 4.8.3 Epidemiology above). Up-to-date information regarding JE virus activity and/or risk in travel destinations should be sought from a reputable source prior to travel (for example, Health information for international travel [the ‘Yellow book’] published by the US Centers for Disease Control and Prevention, available at www.cdc.gov/travel/yellowbook). It is important to note that, as JE has occurred in travellers after shorter periods of travel, JE vaccination should be considered for shorter-term travellers, particularly if the travel is during the wet season, or anticipated to be repeated, and/or there is considerable outdoor activity, and/or staying in accommodation without air conditioning, screens or bed nets.

All travellers to Asia (and other tropical regions) must be fully aware of the need to take appropriate measures to avoid mosquito bites. Booster doses may be required for persons who are at continued risk of acquiring JE (refer to ‘Booster doses’ below).

**Torres Strait Islands**

JE vaccination is recommended for:

- residents of the outer islands in the Torres Strait
- non-residents who will be living or working on the outer islands of the Torres Strait for a cumulative total of 30 days or more during the wet season (December to May).

The period of greatest risk is from February to March and the vaccination course for non-residents should be completed before February. Those arriving in the outer islands late in the wet season (i.e. in May) will arrive after the risk period and do not require vaccination. Those visiting the outer islands in the dry season (June to November) do not require vaccination. Those visiting only the inner islands, including Thursday Island, do not require vaccination. Timing of vaccination in residents should take into account a range of factors including age, time of year, vaccine schedule and recent epidemiology.

Booster doses may be required for persons who are at continued risk of acquiring JE (refer to ‘Booster doses’ below).

**Laboratory personnel**

JE vaccination is recommended for all research laboratory personnel who will potentially be exposed to the virus.

**Booster doses**

The need for a booster dose of JE vaccine depends on the age at which the primary vaccine course was given and the vaccine used for the primary course (refer to Table 4.8.1 in 4.8.6 Dosage and administration above).
A booster dose of Imojev is recommended 1 to 2 years after the primary course for children aged ≥9 months and <18 years who are at continued risk of acquiring JE (refer to risk groups above). A booster dose of Imojev is not currently recommended for adults as seroprotective antibody levels have been shown to persist in a high proportion of adults 5 years following a single dose of Imojev\textsuperscript{30} (refer to 4.8.4 Vaccines above).

A booster dose of JEspect is recommended 1 to 2 years after the primary course for adults who are at continued risk of acquiring JE (refer to risk groups above). Currently there is very limited evidence available to inform recommendations regarding the need and appropriate time interval for a booster of JEspect in children who received JEspect as primary immunisation; however, recommendations will be updated when suitable evidence becomes available.

4.8.8 Pregnancy and breastfeeding

Imojev is a live attenuated viral vaccine and is contraindicated in pregnant women. Pregnancy should be avoided for 28 days after vaccination.

There are no data on whether the Imojev vaccine virus is excreted in breast milk; the vaccine should not be given to breastfeeding women.

JEspect vaccine is not routinely recommended for pregnant or breastfeeding women. However, as JE virus infection during the first and second trimesters has been associated with miscarriage, pregnant women at risk of acquiring JE should be offered JE vaccination. Although this inactivated JE vaccine might pose a theoretical risk to the developing fetus, no adverse outcomes of pregnancy have been attributed to vaccination against JE.

No specific data are available regarding the administration of JEpect to breastfeeding women. Breastfeeding women who are at increased risk of acquiring JE should be offered JE vaccination.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.8.9 Contraindications

JE vaccines are contraindicated in persons who have had:

- anaphylaxis following a previous dose of any JE vaccine
- anaphylaxis following any vaccine component.

Imojev is a live attenuated viral vaccine and must not be administered to pregnant or breastfeeding women or to any person who is immunocompromised due to either disease and/or medical treatment.

4.8.10 Precautions

JE vaccines should not be administered during an acute febrile illness.

There are few data on the safety and efficacy of JEpect vaccine in persons who are immunocompromised. Such persons may not mount an adequate immune response, but, as JEpect is an inactivated vaccine, safety and reactogenicity are not expected to be of concern in those who are immunocompromised.

Vaccination after immunoglobulin or blood product administration

Administration of live attenuated JE vaccine (Imojev) should be delayed after administration of immunoglobulin-containing products. Imojev should not be given within 6 weeks, and preferably not within 3 months, following administration of immunoglobulins or immunoglobulin-containing blood products.

4.8.11 Adverse events

Local reactions and minor systemic reactions are common to very common following vaccination against JE.

In adults, adverse events following Imojev were similar to those in placebo recipients,\textsuperscript{7,10} but occurred less often than in recipients of the mouse brain-derived JE vaccine.\textsuperscript{7} The most common adverse events in two key studies were injection site pain, headache, fatigue and malaise; most symptoms resolved within 3 days.\textsuperscript{7} Similarly, in children aged 12–24 months, the frequency of adverse events after Imojev was comparable to that after the hepatitis A vaccine. About 40% of these subjects reported injection site reactions, including pain (32%), erythema (23%) and swelling (9%), and about 50% reported at least one systemic reaction, including fever (21%), appetite loss (26%), irritability (28%) and abnormal crying (23%). Frequencies of adverse events in children aged 2–5 years who received Imojev after having been previously vaccinated with the mouse brain-derived vaccine were similar to, or lower than, those seen in children aged 12–24 months not previously vaccinated. All reactions were transient and almost all were mild. Most systemic reactions were mild or moderate, appeared within 7 days of vaccination, and lasted up to 3 days.\textsuperscript{8}

In a pooled analysis of over 4000 healthy adults who received at least 1 dose of JEpect, 54% reported injection site reactions, most commonly pain (33%), tenderness (33%) and redness (9%).\textsuperscript{34} Headache and myalgia were the most commonly reported systemic adverse events.\textsuperscript{17,22,34,36} An earlier analysis found a comparable rate of adverse events in
those who received JEspect compared with aluminium-containing placebo.\textsuperscript{35} Post-marketing surveillance reported adverse events following JEspect at a rate of about 10 per 100,000 doses distributed; no serious allergic reactions were observed during the first 12 months after marketing approval.\textsuperscript{36} The frequencies of adverse events reported following a booster dose were similar to those reported after a primary course.\textsuperscript{17,19}

4.8.12 Public health management of Japanese encephalitis

JE virus infection is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of JE, including management of cases of JE, should be obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

4.8.13 Variations from product information

JEspect is registered for use in persons aged $\geq 18$ years. The ATAGI recommends that JEspect can be administered to children aged $\geq 2$ months to $<18$ years in circumstances where an alternative is not available or is contraindicated. The ATAGI also recommends that children aged $\geq 2$ months to $<3$ years receive 0.25 mL doses of JEspect.

The product information for JEspect states that it can be given with inactivated hepatitis A vaccine. The ATAGI recommends that JEspect can also be given with quadrivalent meningococcal conjugate vaccine and rabies vaccine (refer to 4.8.6 Dosage and administration).

References

A full reference list is available on the electronic Handbook or website www.immunise.health.gov.au.


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