

## 8. Details of Manufacturer

**BE** **Biological E. Limited**

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Web site: [www.biologicale.com](http://www.biologicale.com)

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## 9. Details of permission or licence number with date

**Permission No:** MF-456/2011

**Date of issue:** 29 Sep 2011

## 10. Date of revision

Nov 2025

You can help by reporting any side effects that you may get after vaccination to Biological E. Limited (BE), who is the manufacturer of **JEEV**<sup>®</sup> on:

E-mail at [pharmacovigilance@biologicale.com](mailto:pharmacovigilance@biologicale.com)

For adverse event reporting online: <https://www.biologicale.com>

For more information, read this Package Insert carefully.

# Japanese Encephalitis Inactivated Vaccine (Human) (Purified Inactivated Vaccine - Adsorbed)

## JEEV<sup>®</sup>

## 1. Name of the Medicinal Product

JEEV<sup>®</sup> is a suspension for injection.

Japanese Encephalitis Inactivated Vaccine (Human)

## 2. Composition

Each 0.5 ml contains:

Purified Inactivated Japanese Encephalitis

Virus Vaccine Strain (SA<sub>11</sub>-14-2) : 3µg

Aluminium as Aluminium Hydroxide : 0.1%w/w

Thiomersal BP : 0.005% w/w

Phosphate Buffer Saline : q.s

produced in Vero cells

The vaccine is formalin inactivated

For full list of excipients, see section 6.1

## 3. Pharmaceutical Form

Suspension for injection

Appearance of the vaccine is clear liquid with a white precipitate. A white, cloudy liquid/ suspension forms upon agitation

## 4. Clinical Particulars

## 4.1. Therapeutic Indications

JEEV<sup>®</sup> is indicated for active immunization against Japanese encephalitis in children (between ≥ 1 to < 3 years of age).

It should be used in children at risk of exposure through travel into areas where JE is endemic, spending a month or longer in endemic areas during the transmission season, especially if travel will include rural areas, or in the course of their occupation or residing in areas where JE is endemic or epidemic JE vaccine should also be considered for short-term (<1 month) travelers whose itinerary or activities might increase their risk for exposure to JE virus. JE vaccine is not recommended for short-term travelers whose visit will be restricted to urban areas.

## 4.2. Posology and Method of Administration

Method of administration

The vaccine should be administered by intramuscular route. The preferred site is anterolateral aspect of the thigh for children. Do not administer the vaccine intravenously, intradermally, or subcutaneously.

Posology

The immunization schedules for Japanese Encephalitis Vaccine should be based on official recommendations.

The primary vaccination series consists two separate doses of 0.5ml each according to the following schedule:

First dose : day 0

Second dose: 28 days after first dose

It is recommended that vaccinees who received first dose of BE's JEEV<sup>®</sup> should receive their 2<sup>nd</sup> dose of vaccination course with BE's JEEV<sup>®</sup> only.

The vaccine has to be administered by a qualified healthcare professional.

Immunization series should be completed at least 1 week prior to potential exposure to JEV. Before administration, shake the vial well to obtain a white, homogeneous suspension. Do not administer if particulate matter remains following shaking or if discoloration is observed.

## 4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients or to any residuals

Individuals who show hypersensitivity reactions after receiving first dose of the vaccine should not be given the second dose.

Vaccine must not be given to individuals with known or suspected hypersensitivity to any constituent of the vaccine.

Administration must be postponed in persons with acute severe febrile conditions.

## 4.4. Special Warnings and Precautions for Use

As with all injectable vaccines, appropriate medical treatment and supervision should always be available to treat rare cases of anaphylactic reactions following the administration of the vaccine.

JEEV<sup>®</sup> is an intramuscular vaccine and under no circumstance be administered intravenously.

As with any other vaccine, vaccination with JEEV<sup>®</sup> may not result in protection in all cases. JEEV<sup>®</sup> will not protect against encephalitis caused by other micro-organisms.

Like other intramuscular injections, this vaccine should not be administered to persons with thrombocytopenia, haemophilia or other bleeding disorders.

## 4.5. Interaction with other medicinal products and other forms of interaction

Interaction studies with other medicinal products have not been performed on JEEV<sup>®</sup>. When JEEV<sup>®</sup> is administered concomitantly with other injectable vaccines, they should be given with separate syringes at different injection sites. JEEV<sup>®</sup> should not be mixed with any other vaccine in the same vial.

## 4.6. Use in special populations (such as pregnant women, lactating women)

Not Applicable.

## 4.7. Effect on ability to drive and use machines

Not Applicable.

#### 4.8. Undesirable effects

The safety of the JE vaccine was assessed in a controlled clinical trial in  $\geq 1$  to  $< 3$  year old healthy Indian children in comparison with a licensed JE vaccine. Approximately 21% of vaccinated subjects can be expected to experience adverse reactions based on the clinical data. They usually occur within the first three days after vaccination, are usually mild or occasionally moderate in intensity and disappear within a few days. No increase in the number of adverse reactions was noted between first and second doses.

Most commonly reported local adverse reactions were injection site pain (8.5%) and tenderness (4.6%) and the most commonly reported systemic adverse reaction was pyrexia (11.1%). The other vaccine related adverse events reported were injection site swelling (3.29%), injection site erythema (2.63%), decreased appetite (1.32%) somnolence (1.64%) and rash (1.32%).

#### 4.9. Overdose

No case of overdose has been reported.

### 5. Pharmacological Properties

#### 5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Encephalitis Vaccines, ATC Code: J07BA02

Japanese encephalitis is a disease caused by the mosquito-borne Japanese encephalitis virus (JEV).

Japanese Encephalitis Inactivated Vaccine (Human) is a vero-cell based purified inactivated vaccine that is known to act by inducing antibodies that neutralize live JEV.

#### Mechanism of action

The mechanism of action of Japanese encephalitis (JE) vaccines is not well understood. Studies in animals have shown that the vaccine triggers the immune system to produce antibodies against Japanese encephalitis virus that are most often protective.

In other challenge studies in mice by a similar inactivated JE vaccine showed that almost all mice that had a Plaque Reduction Neutralization Test titre of at least  $\geq 1:10$  were protected from a lethal Japanese encephalitis virus challenge.

The World Health Organization consultation group recognizes a PRNT titer of  $\geq 1:10$  as being a reasonable correlate for protection

#### Clinical studies

In a phase-I study, the safety of this vaccine was established in healthy adult volunteers and the development proceeded to phase II/III study. The phase-II part of the phase-II/III study established single dose safety in healthy  $\geq 1$  to  $< 3$  year old Indian subjects which was closely monitored by an Independent Data Safety Monitoring Board.

The immunogenicity of the vaccine was further evaluated in healthy  $\geq 1$  to  $< 3$  year old Indian subjects of either gender in a multicentre, open label, parallel, randomized phase-II/III study. The objective was to evaluate both immunogenicity & safety of this vaccine administered intramuscularly to  $\geq 1$  to  $< 3$  year old healthy Indian children in 2-dose (0, 28 Day) schedule in comparison with a licensed mouse brain derived inactivated JE vaccine administered subcutaneously in 3-dose (0, 7 & 28 Day) schedule.

The primary end point was to assess whether proportion of subjects seroconverted (PRNT50  $\geq 1:10$ )

in both the groups at Day 56 were similar and JE vaccine is non-inferior to the licensed Comparator JE vaccine. The study results revealed that the GMT levels increased from 9.7 at baseline to 217.9 by Day 56 with JE vaccine and the vaccine demonstrated to be non-inferior to the licensed Comparator JE vaccine.

#### 5.2. Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

#### 5.3. Preclinical safety data

Non-clinical toxicity data is limited

A 28-day repeat dose toxicity study of Japanese encephalitis vaccine (JEEV<sup>®</sup>) administered intramuscularly to Wistar rats in 3 occasions (1, 14 and 28 day) was found to be safe and immunogenic in animal studies. Non-clinical data reveal no special hazard for humans based on repeated dose toxicity in Mice.

In a similar reproductive and pre-/post-natal toxicity study with another JE vaccine, no vaccine-related effects were detected on reproduction, foetal weight, survival and development of the off-spring. However, incomplete ossification of parts of the skeleton was observed in the group receiving 2 doses, but not in the group receiving 3 doses. It is currently difficult to explain if this phenomenon is treatment related or not.

### 6. Pharmaceutical Particulars

#### 6.1. List of Excipients

- Phosphate buffer saline consisting of :
  - Sodium Chloride
  - Potassium dihydrogen phosphate
  - Disodium hydrogen phosphate
  - Water for injection
- Aluminium as aluminium hydroxide hydrate
- Thiomersal as preservative

#### 6.2. Incompatibilities

This medicinal product must not be mixed with other medicinal products.

#### 6.3. Shelf Life

$< 3$  years $>$

#### 6.4. Special precautions for Storage

Store in a refrigerator at  $2^{\circ}$  -  $8^{\circ}$  C ( $35^{\circ}$  -  $46^{\circ}$  F).

Do not freeze. Discard if the vaccine has been frozen.

Do not use the vaccine after the expiration date shown on the label.

Store in the original package in order to protect from light. During storage, a clear liquid with a white sediment can be observed.

For administration in children: Opened vial should be discarded at the end of immunization session or within 6 hours and the vaccine vial should be stored under refrigeration at  $2^{\circ}$  -  $8^{\circ}$  C ( $35^{\circ}$  -  $46^{\circ}$  F).

#### 6.5. Nature and contents of container

BE- JEEV<sup>®</sup> is filled in USP type I glass vials and closed using bromobutyl rubber stoppers and sealed with aluminium flip-off seals.

The vaccine is filled in to Multi dose presentation and is offered in the following presentations:

- Multi dose vial of 2.5 mL

The above presentations are offered in different packaging configuration as per the requirement. Not all pack sizes may be marketed.

**Handling of multi dose vial:** Once opened, multi dose vials of JEEV<sup>®</sup> Vaccine from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 4 weeks, provided that all of the following conditions are met

- the expiry date has not passed
- the vaccines are stored under appropriate cold chain conditions
- the vaccine vial septum has not been submerged in water
- Aseptic technique has been used to withdraw all doses
- The vaccine vial monitor (VVM) has not reached the discard point.

#### 6.6. Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements

#### 6.7. Patient Counselling Information

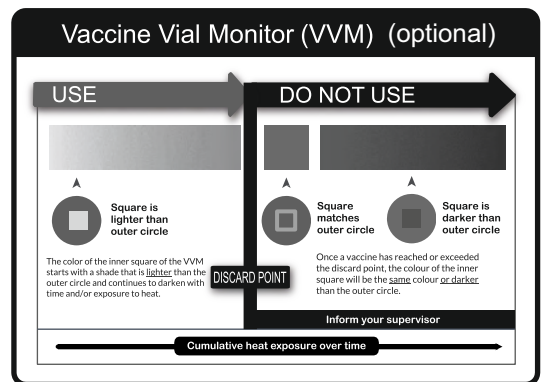
JE Vaccine is indicated for active immunization against Japanese encephalitis in children (between  $\geq 1$  to  $< 3$  years of age). The body is expected to develop an immune response against virus. The most common local adverse events reported were injection site pain, injection site erythema, injection site swelling, injection site pruritus, and tenderness. The most common systemic adverse events were pyrexia, decreased appetite, crying, Somnolence, rash, irritability, hyperhidrosis and nasopharyngitis. If the vaccinee experiences any of the above side effect(s), please contact or visit your health care provider / vaccinator / officer supervising your vaccination or immediately go to the nearest hospital.

#### 7. Instructions for use, handling and disposal

Each vaccine dose of 0.5 mL is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual.

#### 7.1. Vaccine Vial Monitoring (VVM)

The Vaccine is available with or without Vaccine Vial Monitor (VVM).



VVM is a label containing a heat-sensitive material which is placed on a vaccine vial to register cumulative heat exposure over time. The colour dot appears on the VVM label in square element is a time - temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.