

5.3 Preclinical safety data

Non-clinical toxicity data is limited

A 28-day repeat dose toxicity study of Japanese encephalitis vaccine (JEEV™) 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

1. Phosphate buffer saline consisting of :
Sodium Chloride
Potassium dihydrogen phosphate
Disodium hydrogen phosphate
Water for injection
2. Aluminium as aluminum hydroxide hydrate

6.2 Incompatibilities

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

6.3 Shelf life

<2 years>

6.4 Special precautions for storage

Store in a refrigerator at 2° - 8° C (35° - 46° 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: Two withdrawals from same vial are acceptable within an interval of 28 days after the first withdrawal under refrigeration [2° to 8° C (35° to 46° F)]. There is no effect on product composition and sterility as shown by stability studies. However, as far as possible two paediatric doses from the vial should be administered within 24 hour of first dose withdrawal.

7. Presentation

Presented as 0.5 ml per Vial

0.5 ml suspension in 3 mL capacity glass vial (USP type 1 glass) with stoppers (Grey Bromobutyl rubber) and flip off Aluminium seal.

References

1. WHO model pack Insert

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory



Manufactured by:
Biological E. Limited

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JAPANESE ENCEPHALITIS INACTIVATED VACCINE (Human) (PURIFIED INACTIVATED VACCINE - ADSORBED)



1. NAME OF THE MEDICINAL PRODUCT

JEEV™ is a suspension for injection
Japanese encephalitis purified inactivated vaccine (adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Adult

1 dose (0.5mL) of JEEV™ contains:
Japanese encephalitis virus strain SA14-14-2 (Inactivated)^{1,2} 6 micrograms³
corresponding to a potency of <90 ng ID₅₀

Paediatric

1 dose (0.25mL) of JEEV™ contains:
Japanese encephalitis virus strain SA14-14-2(Inactivated)^{1,2} 3 micrograms³
corresponding to a potency of <90 ng ID₅₀

¹ produced in Vero cells

² adsorbed on aluminium hydroxide, hydrated 0.25 milligram Al³⁺

³ total protein content

The vaccine is formalin inactivated
For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suspension for injection

The appearance of the liquid is a white, clear non-uniform suspension which becomes homogenous upon shaking.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

JEEV™ is indicated for active immunization against Japanese encephalitis in adults and children.

It should be used in children and adults 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

4.2 Posology and method of administration

Method of administration

The vaccine should be administered by intramuscular route. The preferred sites are anterolateral aspect of the thigh for children or the deltoid muscle of upper arm for adults. Do not administer intravenously, intradermally, or subcutaneously.

Possology

The immunization schedules for JEEV™ should be based on official recommendations.

Adult (18 to <49 years)

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 JEEV™ should receive their 2nd dose of vaccination course with JEEV™ only.

Paediatric (Children between 1 to <3 years of age)

The primary vaccination schedule consists of two separate doses of 0.25mL each according to following schedule:

First dose : day 0

Second dose: 28 days after first dose

It is recommended that vaccinees who received first dose of JEEV™ should receive their 2nd dose of vaccination course with JEEV™ 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 (e.g. protamine sulphate).

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™ is an intramuscular vaccine and under no circumstance be administered intravenously.

As with any other vaccine, vaccination with JEEV™ may not result in protection in all cases.

JEEV™ 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™. When JEEV™ is administered concomitantly with injectable vaccines; they should be given with separate syringes at different injection sites. JEEV™ should not be mixed with any other vaccine in the same vial.

4.6 Pregnancy and lactation

Pregnancy

Safety and effectiveness have not been established in pregnant women and in nursing mothers. In animal studies findings of unclear relevance have been identified for a similar product. As a precautionary measure, the use of JEEV™ during pregnancy or lactation should be avoided.

Lactation

It is not known whether this vaccine is excreted in human milk. No effects on the breast fed new born or infants are anticipated since the systemic exposure to breast feeding woman is negligible

4.7 Effects on ability to drive and use machines

No studies on the effects of JEEV™ on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The safety of the JEEV™ vaccine was assessed in a controlled clinical trial in 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). JEEV™ 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 1:10 were protected from a lethal Japanese encephalitis virus challenge.

The World Health Organization consultation group recognizes a PRNT titer of 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 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 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 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 1:10) in both the groups at Day 56 were similar and JEEV™ is non-inferior to the licensed Comparator's JE vaccine. The study results revealed that the GMT levels increased from 9.7 at baseline to 217.9 by Day 56 with JEEV™ and the vaccine demonstrated to be non-inferior to the licensed Comparator's JE vaccine.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.