1. NAME OF THE MEDICINAL PRODUCT

®

JEEV 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-14-2) : 6 μg

Aluminium as Aluminium Hydroxide                 0.1%w/v

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

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

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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JEEV (6 μg/0.5mL) is indicated for active immunization against Japanese encephalitis in individuals from the age of ≥ 3 years to ≤ 49 years.

It should be used in children, adolescents 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 is deltoid muscle of upper arm. Do not administer intravenously, intradermally or subcutaneously.

Posology

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

Children, Adolescents & Adults (≥ 3 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

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It is recommended that vaccinees who received first dose of JEEV should receive their second 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 a 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.

Booster dose recommendation (For Adults of ≥ 18 to ≤ 49 years age):

A booster dose (third dose) should be given between 12 - 14 months after the recommended primary immunization, prior to potential re-exposure to JEV. Persons at continuous risk for acquiring Japanese Encephalitis (Laboratory personnel or persons residing in endemic areas) should receive a booster dose at month 12 after primary immunization.

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 receive a second dose of the vaccine.

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 vaccine 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.

References

WHO model pack insert
In a phase-I study, (N=20) the safety of this vaccine was established in healthy adult volunteers. JEEV® is an intramuscular vaccine and under no circumstance be administered intravenously or subcutaneously. As with any vaccine, a mild reaction at the injection site may occur. 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, it 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

It is not known whether this vaccine is excreted in human milk. No studies on the effects of JEEV® on the ability to drive and use machines have been performed.

4.7 Effects on ability to drive and use machines

4.8 Undesirable effects

In a multi-centre, open label, phase IV study conducted on Indian children (n=108) aged 2-11 years, 30% of the subjects experienced at least 1 adverse event, majority being mild in nature. The most common treatment emergent local adverse events were injection site pain (44.3%), redness (14.7%) and swelling (7.4%). The most common systemic adverse events were myalgia (12.0%), fever (4.6%) and headache (4.6%). There were no serious adverse events reported for any subjects during the entire study period. In a multicentre, randomized, open label, phase IV study in Indian adults (n=162) aged 18 to 45 years, comparing JEEV® with IXIARO®, both the vaccines were found to have similar adverse event profile. Injection site pain (44.7% in JEEV®, vs. 54.2% in IXIARO®) was the most common local adverse event reported and fever (23.1% in JEEV® vs. 29.3% in IXIARO®) was the most common systemic adverse event reported. There were no serious adverse events in either of the study groups during the study period.

4.9 Overdose

No cases 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 live-attenuated virus vaccine. JEEV® is a virus-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 Pariñas Reduction Neutralization Test titre of ≥1:10 were protected from a lethal Japanese encephalitis virus challenge. The World Health Organization consultation group recognizes a PRNT titre of ≥1:10 as a reasonable correlate for protection.

Clinical studies

In a phase-I study, (N=20) the safety of this vaccine was established in healthy adult volunteers. A multi-centre open randomized study (N=162) was conducted to compare the immunogenicity and safety of 6µg/0.5mL intramuscular dose of JEEV® vaccine in ≥18 to ≤49 year old adults, to demonstrate its non-inferiority with IXIARO®. A total of 99.07% in JEEV® group and 99.15% in IXIARO® group achieved seroprotection rates (PRNT ≥1:10) at Day 56 with non-inferiority of JEEV® demonstrated. Both vaccines elicited strong immune response as seen by a large increase in anti-JEV neutralizing antibodies and the high proportion of adults seroprotected. JEEV® vaccine was found to be safe and well tolerated. Injection site pain (reported in 44.7% in JEEV® vs. 54.2% in IXIARO®) was the most frequently reported local adverse event and fever (reported in 23.7% in JEEV® vs. 29.3% in IXIARO®) was the most frequently reported systemic adverse event in both groups with no statistically significant differences between groups. No serious adverse events were reported during this study in either of the groups.

A phase-IV post marketing safety study (N=432) was conducted in ≥18 to ≤49 year old adults to obtain additional safety information on 6µg/0.5mL intramuscular dose of JEEV® vaccine. JEEV® vaccine continued to show similar clinical safety proﬁle as seen in earlier studies. Injection site pain (16.9%) was the most frequently reported local adverse event and fever (2.06%) was the most frequently reported systemic adverse event. All reported adverse events were mild to moderate in their intensity, which resolved spontaneously. In a safety and immunogenicity study (N=108) conducted in paediatric and adolescent population between ≥3 to <18 years of age, a 6µg/0.5mL intramuscular dose of JEEV® vaccine was found to be safe and highly immunogenic. Most of the reported adverse events were mild in nature and no serious adverse events were reported. The most common treatment emergent local adverse events were injection site pain (44.4%) and redness (7.4%) and the most common treatment emergent systemic adverse events were fever (4.6%) and myalgia (12.0%). Overall, 95.33% of subjects were found to be seroprotected by day 56 with a 4-fold increase in titre above the seroprotection threshold deﬁned (PRNT ≥1:10).

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical 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.

A similar reproductive and pre- and post-natal toxicity study with another JE vaccine, no vaccine-related effects were detected on reproduction, fetal 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 no evidence of harm to the fetus or the off-spring. This was not seen in the 3 dose group.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

1. Phosphate buffer saline consisting of: Sodium Chloride

2. Aluminium as aluminum hydroxide hydrate

3. Water for injection

6.2 Incompatibilities

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

6.3 Shelf life

5 years

6.4 Special precautions for storage

Store at a temperature of 2°C - 8°C (35°F - 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.

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 Cap & Seal) and a manual needle (18G x 0.5"").