



Japanese Encephalitis Vaccine, Inactivated (Adsorbed, Human)



SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC)



Japanese Encephalitis Vaccine, Inactivated (Adsorbed, Human)



1. NAME OF THE MEDICINAL PRODUCT:

Name of the product: Japanese Encephalitis Vaccine, Inactivated (Adsorbed, Human)

Strength:

Each dose of 0.5mL contains:

Vero Cell derived, Purified, Inactivated Japanese Encephalitis Virus
(JEV Strain 821564-XY) protein Potency NLT 5.0 µg
Pharmaceutical Form: Suspension for Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each dose of 0.5mL contains:

Vero Cell derived, Purified, Inactivated Japanese Encephalitis Virus
(JEV Strain 821564-XY) protein Potency NLT 5.0 µg
Aluminium Hydroxide Gel equivalent to Aluminium (Al+++) ... 0.25 mg
Thiomersal IP 0.025 mg
Phosphate Buffered Saline q.s to 0.5 mL

3. PHARMACEUTICAL FORM:

Suspension for Injection.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications:

- **JENVAC[®]** is indicated for active immunization against Japanese Encephalitis infection aged one year and above

4.2 Posology and method of administration:

JENVAC[®] is administered intramuscularly into the deltoid region of the upper arm for adults and anterolateral region of thigh for children <2 years of age.

Do not administer intravenously, subcutaneously or intradermally.

The vaccination consists of a single dose of 0.5mL to be administered by a qualified healthcare professional. Shake the vaccine container well to obtain uniform suspension before administration.

4.3 Contraindications:

JENVAC[®] should not be administered or repeated to persons to be hypersensitivity to any of the components.

Administration must be postponed in persons with fever or other conditions as deemed necessary by the administering physician.

4.4 Special warnings/precautions:

- Do not administer intravenously, intradermally, or subcutaneously.
- Do not administer if the particulate matter remains following shaking or if the discoloration is observed.
- Like with all other vaccines, supervision and appropriate medical treatment should always be available for the treatment of any anaphylactic reactions that may occur after immunization.
- **JENVAC[®]** will not protect against encephalitis caused by other micro-organisms.

4.5 Interaction with other medicinal products

For concomitant administration of other injectable product, use different injection sites and separate syringes. **JENVAC[®]** should not be mixed with any other vaccine or medicinal product, because the interactions with other vaccines or medicinal products have not been established.

4.6 Pregnancy and lactation:

Safety and efficacy have not been established in pregnant women and in nursing mothers. It is not known whether this vaccine is excreted in human milk.

4.7 Effect on the ability to drive and use machines:

No studies on the effect of **JENVAC[®]** on the ability to drive and use machines have been performed.

4.8 Undesirable effects:

The safety of **JENVAC[®]** vaccine was established in controlled clinical trials in healthy volunteers in comparison with a licensed JE vaccine. General adverse events such as fever headache, body ache and local adverse events such as pain, redness and swelling at the injection site were the frequently reported adverse events after administration of **JENVAC[®]**. They usually occurred within the first 48 hours after vaccination and dissipate within 2 days.

Within each system organ class, the adverse reactions are ranked under headings of frequency using the following convention:

- Very common : $\geq 10\%$
Common : $\geq 1\%$ and $< 10\%$
Uncommon : $\geq 0.1\%$ and $< 1\%$
Rare : $\geq 0.01\%$ and $< 0.1\%$
Very rare : $< 0.01\%$

Using the above convention, the reported adverse events were:

- Very common : Fever
Common : Headache, Body ache, Pain, Swelling and Redness at the injection site
Uncommon : Nausea, Vomiting, Diarrhea, Cold, Cough, Myalgia

4.9 Overdose:

No case of overdose with **JENVAC**[®] has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Encephalitis vaccines, ATC code: J07BA02 Japanese Encephalitis is a disease caused by the mosquito-borne JE virus. **JENVAC**[®] is a Vero-cell based purified inactivated vaccine that is known to act by inducing antibodies that neutralize live JEV.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Pre-clinical safety data

As a part of pre-clinical studies to assess the safety of the vaccine, a 42-day intramuscular toxicity study was conducted in Wistar rats and New Zealand white rabbits with **JENVAC**[®] days 0, 7, 14 and 28. The animals were observed for clinical signs of toxicity due to the administration of **JENVAC**[®] for 42 days. Purified viral vaccines produced in tissue cultures are generally well tolerated by humans and animals; hence no maximal tolerable dose studies were conducted. No significant changes were observed due to the administration of **JENVAC**[®]. The vaccine is found to be safe at the rate of 64.8 times of human equivalent dose as a single dose by intramuscular route in Wistar rats and at the rate of 12.7 times of human equivalent dose as a single dose by intramuscular route in New Zealand white rabbits. Further, it was confirmed that the safety and immunogenicity of **JENVAC**[®] were equivalent to JENCEVAC.

A study on the potency of inactivated Japanese encephalitis vaccines in adult female Swiss albino mice was conducted by the Center for Vaccine Development, Mahidol University, Thailand. **JENVAC**[®] and Beijing JE vaccine conferred higher GMT than the Korean Green Cross JE Vaccine, but **JENVAC**[®] conferred 100% seroconversion rate after 2 doses, while the other 2 vaccines did not.

Clinical Trial Experience

Phase 1 randomized, double-blind, placebo-controlled study was conducted to evaluate the safety, tolerability and immunogenicity of 2-dose (D0 & D28) and 3-dose (D0, D7, D28) **JENVAC**[®] in 60 healthy adult volunteers aged between 18 to 50 years, two doses (Day 0 & 28) and three doses (Day 0, 7 & 28) showed significant immunogenicity. With one dose itself, there was 100% seroprotection and 90% seroconverted above 4-fold (seen at the end of Day 28). Seroconversion above 4-fold was seen in 100% at Day 56. However, between two or three doses, there was no difference. No seroconversion was seen in the placebo group.

Phase II/III, clinical trial was a randomized, single-blind, active-controlled study to evaluate the immunogenicity and safety of **JENVAC**[®] vs. Chinese SA14-14-2 (live attenuated JE vaccine) in 644 healthy volunteers aged between 1 year and 50 years. In this study, the proportion of subjects achieving

seroprotection after a single dose of respective vaccine, was significantly higher in **JENVAC**[®] group (98.7%) compared to that in the SA14-14-2 arm (77.56%), 28 days post-vaccination. Seroconversion and Seroprotection percentages on Day 28 between **JENVAC**[®] and SA14-14-2 vaccine groups were statistically significant ($p < 0.001$).

Post-Marketing, a phase IV, an open-labeled, comparative, randomized, active-controlled study was conducted to evaluate the immunogenicity and safety of a single dose of **JENVAC**[®] vs. SA14-14-2 vaccine in healthy volunteers. While the proportion of subjects being seronegative or seropositive for JE antibodies was similar in both treatment groups at the baseline, the proportion of subjects achieving seroprotection was significantly higher in the **JENVAC**[®] treatment arm (92.4%) compared to that in the SA14-14-2 arm (71.4%), 4 weeks after vaccination. Further, the higher seroprotection rate was persistent till 2 years of follow up among the subjects receiving **JENVAC**[®]; 88.54% vs 68.29%.

In the follow-up of the above-mentioned phase IV study, 178 participants were recalled and a booster dose of **JENVAC**[®] or SA 14-14-2 was administered interchangeably. The study results have revealed that booster dose of **JENVAC**[®] is more immunogenic in both the groups who were primarily administered either with **JENVAC**[®] (**JENVAC**[®] to **JENVAC**[®]) or with SA 14-14-2 (SA14-14-2 to **JENVAC**[®]).

Another study conducted by Center for Vaccine Development, Mahidol University, Thailand showed that **JENVAC**[®] has excellent cross-protection against all major JEV G1 to G4 genotypes that are currently circulating. G-I is the new emerging subtype in India.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Phosphate buffered saline
Aluminium hydroxide gel equivalent to Aluminium (Al^{+++})
Thiomersal IP

6.2 Incompatibilities:

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

6.3 Shelf life:

The Expiry date of the vaccine is indicated on the label and carton of the product.

6.4 Special precautions for storage:

Store at $+2^{\circ}$ to $+8^{\circ}C$, Do not freeze. Discard if frozen.

Shake well before use. Keep out of reach of children. Protect from light.

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

Handling of multi dose vial:

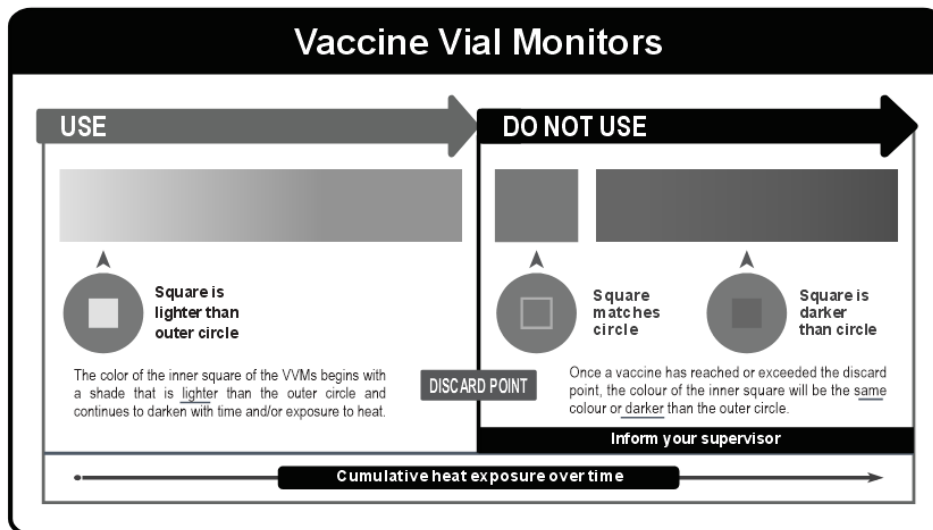
Once opened, multi dose vials of **JENVAC[®]** Vaccine from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days, provided that all of the following conditions are met:

- The expiry date of the vaccine has not passed.
- The vaccine vial has been, and will continue to be, stored at manufacturer recommended temperatures.
- 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, For multi dose vials, use different syringe at each time of vaccination.
- The vaccine vial monitor (VVM) if attached has not reached the discard point.

An opened vial must be discarded immediately if any of the following conditions applies.

- Sterile procedures have not been fully observed.
- There is even a suspicion that the opened vial has been contaminated or
- There is a visible evidence of contamination such as change in appearance of floating particles.

The Vaccine Vial Monitor (VVM7)



Vaccine Vial Monitors (VVM7) are part of the label on all **JENVAC[®]** vials. VVM7's are supplied by TEMPTIME Corporation, U.S.A. The colour dot which appears on the label of the vial is a VVM7. This 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.



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The interpretation of the VVM7 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, 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, the vial should be discarded.

6.5 Nature and contents of container

JENVAC® is presented in USP type I Glass Vial.

Single dose Vial : 0.5 mL

Multi dose Vial : 2.5 mL

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER



Bharat Biotech International Limited situated
Sy. No. 230, 231 & 235, Genome Valley,
Turkapally, Shamirpet Mandal,
Medchal, Malkajgiri District, Telangana State, India, Pin: 500078.

8. MARKETING AUTHORISATION NUMBER

MF-149/2016

9. DATE OF FIRST MARKETING AUTHORISATION

29 AUG 2016

10. DATE OF REVISION

October 2019