IXIARO®

Japanese Encephalitis Vaccine, Inactivated, Adsorbed

JAPANESE ENCEPHALITIS (JE) IS A DANGEROUS, POTENTIALLY DEADLY DISEASE.[1]

TRAVELERS TO CERTAIN AREAS OF ASIA MAY BE AT RISK.[2]

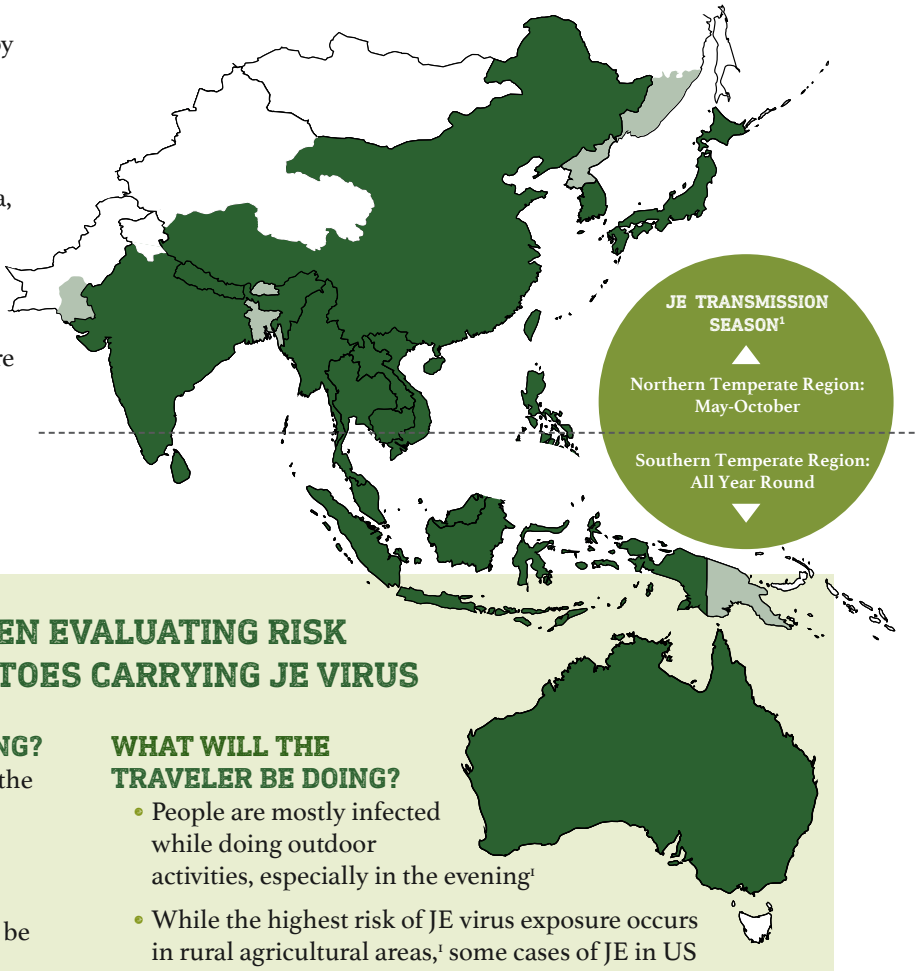
WHAT IS JE?

- JE, a mosquito-borne viral disease, is a form of encephalitis, or inflammation of the brain, caused by JE virus that can lead to brain damage or death[1]
- JE virus is the most common vaccine preventable cause of encephalitis in Asia[1]
- JE is endemic in 25 countries in Asia, Southeast Asia, and parts of the western Pacific[2]

WHAT ARE THE CONSEQUENCES OF JE?

- Although the majority of human infections with JE virus have been asymptomatic, 68,000 cases of JE are estimated to occur each year in Asia[3]
- Up to 30% of cases prove to be fatal[1]
- Of those who survive, up to 50% will suffer from neurologic or psychiatric complications[1]

GEOGRAPHIC DISTRIBUTION OF JE[2]



FACTORS TO CONSIDER WHEN EVALUATING RISK FOR EXPOSURE TO MOSQUITOES CARRYING JE VIRUS

WHERE AND WHEN IS THE TRAVELER GOING?

- JE occurs throughout most of Asia and parts of the western Pacific[2]
- In temperate areas, peak transmission season is summer and fall (see map)[1]
- In tropics or subtropics, transmission times can be sporadic or year-round (see map)[1]

WHAT IS THE DURATION OF THE TRIP?

- As trip duration is one factor that increases risk of exposure, most cases have been reported in longer-term travelers (eg, >1 month)[4]
- However, more than 1/3 of travelers who developed JE were on shorter-term trips (eg, <1 month)[4]

WHAT WILL THE TRAVELER BE DOING?

- People are mostly infected while doing outdoor activities, especially in the evening[1]
- While the highest risk of JE virus exposure occurs in rural agricultural areas,[1] some cases of JE in US travelers to Asia were in urban and peri-urban regions[5,6]

WHERE IS THE TRAVELER STAYING?

- Staying in accommodations with no air conditioning, screens or bed nets increases the risk of exposure[1]

HOW CERTAIN IS THE TRAVELER'S ITINERARY?

- Travelers uncertain of activities, destinations, and accommodations are at increased risk of exposure[1]

INDICATION

IXIARO® is a vaccine indicated for the prevention of disease caused by Japanese encephalitis (JE) virus, approved for use in individuals 2 months of age and older.

IMPORTANT SAFETY INFORMATION

Contraindications

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of IXIARO, any other Japanese Encephalitis Virus vaccine, or any component of IXIARO, including protamine sulfate, is a contraindication to administration of IXIARO. Because of uncertainty as to which component of the vaccine may be responsible, individuals with a history of severe allergic reaction to another Japanese Encephalitis vaccine may be referred to an allergist for evaluation if immunization with IXIARO is considered.

Please see Important Safety Information on next page and full Prescribing Information.

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IXIARO is a vaccine indicated for the prevention of disease caused by Japanese encephalitis (JE) virus. IXIARO is approved for use in individuals 2 months of age and older.[7]

- IXIARO is the only JE vaccine available in the US and has a well-studied safety and tolerability profile[7-9]
- Most common side effects are headache, fever, and myalgia. The most common injection-site reactions are pain and tenderness[7]
- For adults aged 18–65 years, the vaccine is given in 2 doses, 7 days apart or 28 days apart, and vaccination should be completed 7 days before departure[7]
- For pediatric (2 months to <18 years) and older adult (66+ years) travelers, the vaccine is given in 2 doses, 28 days apart, and vaccination should be completed 7 days before departure[7]
- For travelers who were vaccinated at least 11 months previously, a booster dose may be given if ongoing exposure or re-exposure is expected[7]*

HOW TRAVELERS STAY PROTECTED FROM JE?

- Avoid mosquito bites by using personal protective measures such as bed netting, screens, and insect repellents. However, these are only partially effective[10]
- For recommendations on who should get the JE vaccine, please see graphic to the right

*Children from 14 months to <3 years of age should receive a single 0.25 mL booster dose. Individuals 3 years of age and older should receive a single 0.5 mL booster dose.[7]

Please note that children from 2 months to <3 years of age receive two 0.25 mL doses spaced 28 days apart. Children and adults >3 years of age receive two 0.5 mL doses spaced 28 days apart on this schedule.

THE THREE O'S OF JE VACCINATION[1]

Protect travelers from the risk of exposure when traveling to Asia

ONGOING TRAVEL

GIVE **IXIARO**[7]

Frequent Traveler

Long-term Traveler

Traveler Taking Residence

OUTDOORS

CONSIDER RISK, PROTECT WITH **IXIARO**[7]

Season, Location, Duration

Activities Outside

Accommodation (No air conditioning, screens, or bed nets)

OTHER PLANS

CONSIDER RISK, PROTECT WITH **IXIARO**[7]

Uncertain Destinations

Uncertain Activities

Uncertain Travel Duration

JE vaccine is NOT recommended for travelers with very low-risk itineraries, such as shorter-term travel limited to urban areas or outside of the virus transmission season.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

IXIARO contains protamine sulfate, a compound known to cause **hypersensitivity reactions** in some individuals. Appropriate medical care should be readily available in case of anaphylactic reaction.

Syncope (fainting) can occur in association with administration of injectable vaccines including IXIARO. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope.

Vaccination with IXIARO may not protect all individuals.

Immunocompromised individuals may have a diminished immune response to IXIARO.

Adverse Reactions

In infants 2 months to <1 year of age, the most common injection site reaction was redness (>15%); the most common solicited systemic adverse reactions were fever (>20%), irritability (>15%) and diarrhea (>10%). In children 1 to <3 years of age, the most common solicited systemic adverse reaction was fever (>20%). In children 3 to <12 years of age, the most common solicited systemic adverse reaction was fever (>10%). In adolescents 12 to <18 years of age, the most common solicited injection site reactions were pain (15%) and tenderness (10%). In adults 18 years of age and older, the most common injection site reactions were pain (>25%) and tenderness (>25%); the most common solicited systemic adverse reactions were headache (>20%) and myalgia (>10%).

Use in Special Populations

Pregnancy

There are no adequate and well-controlled studies of IXIARO in pregnant women, and human data available from clinical trials and post-marketing experience with IXIARO are insufficient to establish the presence or absence of drug-associated risk during pregnancy.

To report SUSPECTED ADVERSE REACTIONS, contact Valneva at 1-844-349-4276 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov. Healthcare practitioners are also encouraged to report inadvertent use in pregnant women to Valneva at 1-844-349-4276.

Please see full Prescribing Information.

References: 1. Hills SL, Walter EB, Atmar RL, Fischer M. Japanese encephalitis vaccine: recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2019;68(2):1-33. 2. Geographic distribution of Japanese encephalitis virus. Centers for Disease Control and Prevention. Updated April 7, 2023. Accessed April 30, 2024. https://www.cdc.gov/japaneseencephalitis/maps/index.html 3. Japanese encephalitis—Australia. World Health Organization. Published April 28, 2022. Accessed April 30, 2024. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON365 4. Turtle L, Driver C. Risk assessment for Japanese encephalitis vaccination. *Hum Vaccin Immunother.* 2018;14(1):213-217. 5. Janatpour ZC, Boatwright MA, Yousif SM, et al. Japanese encephalitis in a U.S. traveler returning from Vietnam, 2022. *Travel Med Infect Dis.* 2023;52:102536. 6. Chen L, Peek M, Stokich D, et al. Japanese encephalitis in two children—United States, 2010. *MMWR Morb Mortal Wkly Rep.* 2011;60(9):276-278. 7. IXIARO®. Prescribing Information. Valneva USA Inc.; 2022. 8. Japanese encephalitis vaccine. Centers for Disease Control and Prevention. Updated February 7, 2023. Accessed April 30, 2024. https://www.cdc.gov/japaneseencephalitis/vaccine/index.html 9. Cramer JP, Dubischar K, Eder S, et al. Immunogenicity and safety of the inactivated Japanese encephalitis vaccine IXIARO® in elderly subjects: open-label, uncontrolled, multi-center, phase 4 study. *Vaccine.* 2016;34(38):4579-4585. 10. Rogers B, Bunn WB, Connor BA. An update on travel vaccines and issues in travel and international medicine. *Workplace Health Saf.* 2016;64(10):462-468.

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