Protocol for Japanese Encephalitis Vaccine (IXIARO®)

1. What's New

A. Updated references to reflect the updated 2024 CDC Yellow Book.

2. Immunization Protocol

A. Administer a 0.5- mL dose, IM, of Japanese Encephalitis (JE) vaccine to persons ≥7 years of age according to age and schedule if indicated.

B. IXIARO® can be given with all other ACIP-recommended vaccines.

3. Vaccine Schedule

JE Vaccine (IXIARO®) [1] Dose and Route – 0.5-mL IM				
Age	**Dose in Series**	**Acceptable Age Range**	**Dose Volume**	**Booster**
7-17 years	2 doses at 0 and 28 days	≥ 7 years	0.5 mL	≥ 1 year after primary series†
18-64 years	2 doses at 0 and 7-28 days*			
≥ 65 years	2 doses at 0 and 28 days			

* This is the only age group for which an accelerated schedule is approved.

† If ongoing exposure or re-exposure to JE virus is expected.[2]

4. Licensed Vaccine[3]

Product Name	Vaccine Components	Presentation	FDA Approved Age Range	Thimerosal
IXIARO®[1] (JE-VC)‡	6 antigen units purified, inactivated JEV proteins and 250 µg of aluminum hydroxide per 0.5-mL dose	0.5 mL suspension in a pre-filled single dose syringe	2 months – 65 years	None

‡JE-MB (JE-VAX) is no longer manufactured in the United States.

5. Recommendations for Use[2]

A. JE vaccination is recommended for the following:
   a. Persons moving to JE-endemic countries.
   b. Travelers who plan to spend a month or longer in endemic areas.
   c. Laboratory personnel who work with live, wild-type JE virus strains.[3]

B. Vaccine should also be considered for the following:
   a. Shorter-term travelers (e.g. less than 1 month) with an increased risk of exposure to JE based on planned travel duration, season, location, activities, and accommodations.[2]
   b. Travelers going to endemic areas, but who are uncertain of specific destinations, activities, or duration of travel.

C. Booster doses
   a. A booster dose should be given ≥1 year after completion of the primary JE-VC series if ongoing exposure or re-exposure to JE virus is expected.

b. The 2-dose primary series of JE-VC vaccine should be given to persons who received JE-MB (JE-VAX®) † and need a booster.
c. Vaccinated, at-risk laboratory personnel should receive appropriate booster doses of JE vaccine or be evaluated regularly for JE virus-specific neutralizing antibodies to assure adequate titers.

6. Contraindications

A. Severe allergic reaction (e.g., anaphylaxis) to a previous dose or to any vaccine component.[1]

Vaccine	Contains
IXIARO® (JE-VC)	Protamine sulfate, aluminum hydroxide and phosphate buffered saline (sodium chloride, potassium dihydrogen phosphate, disodium hydrogen phosphate)[1]

7. Warnings and Precautions

A. Hypersensitivity to protamine sulfate[1]
B. Other vaccines: Studies of concomitant administration of JE vaccine with hepatitis A vaccine and JE vaccine with rabies vaccine have showed noninferiority compared to administering each vaccine alone. An additional study of concomitant administration of JE vaccine, rabies vaccine and meningococcal conjugate vaccine showed protective responses to all administered vaccines.[3]
C. Pregnancy: No studies of JE-VC in pregnant women have been conducted. Pregnancy is a precaution for use of JE-VC and in most instances, its administration to pregnant women should be deferred. However, pregnant women who must travel to an area where risk for JE virus infection is high should be vaccinated when the theoretical risk of immunization is outweighed by the risk of infection.[2]
D. Newborns: JE vaccine has not been tested in individuals ≤2 months of age.[3] Older adults: In a post-licensure study, seroprotection and gross mean titers were substantially lower among adults ≥65 years of age compared to younger persons. No data exists on the safety or immunogenicity of an additional dose or early booster dose of JE vaccine for adults ≥65 years of age. [3]

8. Other Considerations [1-3]

A. Although ≤1% of JEV infections results in clinical disease, JE is a devastating illness that has a case-fatality rate of 20%–30% and neurologic or psychiatric sequelae in 30%–50% of survivors. No specific treatment exists.[3]
B. In all instances, travelers are advised to take personal precautions to reduce exposure to mosquito bites.[2]
C. The decision to use JE-VC should balance the risks for exposure to the virus and for developing illness, the availability and acceptability of repellents and other alternative measures, and the side effects of vaccination.[2]
D. Risk assessments should be interpreted cautiously because risk can vary within areas and from year to year.[2]

E. Risk of JE for travelers to highly endemic areas during the transmission season can reach 5 to 50 cases per 100,000; the risk for most short-term travelers may be 1 per million or less.[2]
F. Adverse Events: epinephrine hydrochloride solution (1:1,000) and other appropriate agents and equipment must be available for immediate use in case of anaphylactic or acute hypersensitivity reaction.[4]
G. Immunocompromised: individuals with altered immunocompetence may have reduced immune responses. Immunosuppressive therapies may decrease the immune response to IXIARO®[1]
H. Lactation: Breastfeeding is not a contraindication or precaution to JE vaccine.[3]

9. Side Effects and Adverse Reactions[1]

Adverse Events	Frequency
Infants and Children	
Pain, itching, redness or swelling at the injection site	Up to 20%
Fever	Up to 10%
Allergic reactions	Rare
Adults	
Soreness, redness or itching at the injection site, headache, fatigue	Up to 30%
Vomiting, fever, chills, rash	Up to 5%
Allergic reactions	Rare

10. Storage and Handling

A. IXIARO® is a clear liquid with a white precipitate. Before administration, shake the syringe well to obtain a white, opaque, homogeneous suspension.
B. Store medications according to OAR 855-041-1036.

Vaccine	Temp	Storage Issues	Notes
IXIARO®[1]	2°– 8°C (36˚F–46˚F)	Do not freeze. Store in original container. Protect from light.	No natural rubber latex. Do not use after manufacturer's expiration date on product label.

11. References

1. IXIARO® (2018) package insert, available at: www.fda.gov/media/75777/download. Accessed 12 April 2023.
2. Hills, Lindsey, & Fischer. (n.d.). Japanese Encephalitis. 2024 Yellow Book Health Information for International Travel. Available at: https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/japanese-encephalitis. Accessed 17 January 2024.
3. CDC. Japanese Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunization Practices. MMWR 2019; 68(RR-2): 1–33. Available at: www.cdc.gov/mmwr/volumes/68/rr/pdfs/rr6802a1-H.pdf. Accessed 12 April 2023.

4. Kroger AT, Bahta L, Long S, Sanchez P. General Best Practice Guidelines for Immunization. Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP). https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html. Accessed 12 April 2023.

12. Appendix

A. N/A