



## CALL FOR STAKEHOLDER COMMENTS ON THE PRELIMINARY RECOMMENDATION OF THE HEALTH TECHNOLOGY ASSESSMENT (HTA) COUNCIL ON JAPANESE ENCEPHALITIS VACCINE FOR THE PREVENTION OF JAPANESE ENCEPHALITIS AMONG CHILDREN 9 TO 59 MONTHS OLD IN HIGH RISK AREAS

Published as of 26 May 2025

As of 26 May 2025, the Health Technology Assessment (HTA) Council has completed the evidence appraisal on the assessment of *Japanese encephalitis vaccine* for the prevention of Japanese encephalitis among children 9 to 59 months old in high risk areas as defined in the <u>DOH</u> <u>Omnibus Health Guidelines (OHG) for Children under 10 years (2023)</u>, for possible government financing. The HTA Council hereby releases its preliminary recommendation on the said health technology for stakeholder feedback and comments from 26 May (Monday) to 10 June (Tuesday) 2025.

The population, intervention, and comparator (PIC) set by the HTA Council for the said evaluation are shown in the table below, for your reference:

Population	Children aged 9 to 59 months old		
Intervention	<ul> <li>Live, attenuated, recombinant Japanese Encephalitis vaccine</li> <li>Inactivated Japanese Encephalitis vaccine</li> </ul>		
Comparator	No vaccination		

As of review, there are two (2) Philippine FDA-approved JE vaccines (i.e., live, attenuated, recombinant, vero cell; and, inactivated adsorbed, vero cell) eligible for HTA. The use of JE vaccine was reviewed against national clinical practice guidelines (CPGs) *[local and approved by the Department of Health (DOH); and/or international, but locally adopted guidelines],* existing recommendations by the World Health Organization (WHO), and DOH Omnibus Health Guidelines (OHG). Further, a costing analysis was also performed.

As a preliminary recommendation, the **HTA Council positively recommends both JE vaccines to be rolled out in high risk areas** (as defined by DOH) **contingent to the budget and resource availability**, acknowledging that despite its high cost and impact to the NIP budget, it will be beneficial for the target population as it mitigates JE and its complications. With this, the HTAC **strongly recommends JE vaccine for price negotiation to further lower down its cost**.

The HTA Council's preliminary recommendation was based on the following considerations:

### a. Responsiveness to Magnitude and Severity

- JE is the main cause of viral encephalitis according to the <u>World Health Organization</u> (WHO) (2015). It is endemic in 24 countries across Southeast Asia and Western Pacific regions, including the Philippines. JE primarily affects children with an annual global incidence of 5.4 per 100,000 among children under 15 years old.
- Recent data from the Philippine Integrated Diseases Surveillance and Response (PIDSR) shows that in 2021, the Philippines reported a total of 112 laboratory-confirmed JE cases and four (4) confirmed JE-related deaths, with Regions I and II having the highest case counts (<u>PIDSR, 2021</u>). This rose to 123 cases in 2022 and 2023. However, a decrease in cases was observed in 2024, with only 25 confirmed JE cases reported. This is probably due to incomplete processing of data in the late months of 2024.
- The data on hospitalized cases included cases from mild to severe indicating that even mild cases are admitted. The average length of hospital stay is two to three weeks (ranging from 16 to 22 days) according to Lopez et al (2021).

Postal Address	: DOST Main Building, DOST Complex,	Tel. Nos.	: Trunkline (+632) 8837-2071	WILLIPPINE O	
	General Santos Avenue, Central Bicutan,	Website	: www.dost.gov.ph	* PIL PLA	TUVNORD
	Taguig City 1631			0	TÜV NORD Philippines Inc.
P.O. Box	: 3596 Manila Central Post Office	Email	: email@dost.gov.ph	E	
					ISO 9001
				*#CELLENCE	tuv-nord.com/ph

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- Data from Acute Meningo-Encephalitis Syndrome (AMES, which is combined JE and bacterial meningitis) surveillance showed that both cases and mortality were consistently and significantly higher in the <18 age group from 2019 to 2023. The local incidence of JE among children under 15 years old is 0.7 per 100,000, with 35.1% of confirmed cases among children aged >2 months to <5 years (Lopez et al, 2021).
- According to the <u>DOH OHG 2023</u>, the following are declared as areas with high burden of high risk for JE:
  - Luzon Nueva Ecija, Tarlac, Metro Manila, Bulacan, Laguna, Mindoro, Pampanga, Camarines Norte, Camarines Sur;
  - Visayas Northern Samar, Iloilo, Negros Oriental;
  - Mindanao North Cotabato
- Compared to dengue infection which has a high number of reported cases yearly, JE has a low incidence. Despite this, JE has a case fatality rate of 20-30% and a severe disease sequelae, with 30-50% of survivors having permanent neurologic, cognitive, or psychiatric symptoms (<u>US CDC, 2022</u>).

# b. Recommendations from the World Health Organization (WHO), Department of Health (DOH), and Local Medical Societies, and Review of Country Guidelines

- The <u>WHO Strategic Advisory Group of Experts on Immunization (SAGE) Position</u> <u>Paper (2015)</u>, which was also referenced by the <u>WHO Model Lists of Essential</u> <u>Medicines (EML)</u> positively recommends the following:
  - Live, attenuated, recombinant JE vaccines as single dose (0.5mL) given subcutaneously to children 9 months of age or older for primary immunization. A booster dose is recommended 12–24 months later for those <18 years of age.</li>
  - Inactivated vero-cell vaccines as two (2) intramuscular doses administered 4 weeks apart for primary immunization; at 0.25 mL and 0.5 mL for those aged <3 and ≥3 years, respectively.</p>
  - This recommendation is based on the following:
    - High seroprotection rates at one month after primary series:
      - Live, attenuated, recombinant JE vaccines: 89.7% to 100% among children aged 9 months to 42 months.
      - Inactivated vero-cell JE vaccines: 95.7% to 99% among children aged 2 months to 18 years.
    - Favorable safety profile:
      - Post-marketing surveillance within 12 months of JE vaccines introduction in Europe, USA, and Australia reported no safety signals of concern.
      - WHO Global Advisory Committee on Vaccine Safety (GACVS) concluded that all JE vaccine types have demonstrated acceptable safety profiles.
  - Among the newer generation JE vaccines (i.e., live attenuated, live recombinant, and inactivated types), the WHO SAGE does not have a preference for one over the other. Both the live, attenuated, recombinant and inactivated vaccines are included in the WHO List of Prequalified Vaccines.
- The 2023 <u>DOH Omnibus Health Guidelines (OHG) for Children under 10 years</u> recommend JE vaccination (vaccine type not specified) for apparently healthy children aged 18 years and below residing in high risk areas, as previously identified above. This recommendation aligns with the <u>Philippine Guidelines on Periodic Health</u> <u>Examination Pediatric Immunization (PHEX) (2021)</u> recommendation (weak recommendation, very low certainty of evidence)
- The Pediatric Infectious Disease Society of the Philippines (PIDSP) (2025) recommends the use of JE vaccine, specifically the live, attenuated, recombinant type for children aged 9 months to 17 years, as included in their <u>Childhood</u> <u>Immunization Schedule (2025)</u>. The PIDSP recommends one dose for primary immunization followed by a booster dose after a minimum of 12 months.
  - According to PIDSP, the recommended JE vaccine type in their childhood immunization schedule is based on locally available vaccines with Philippine FDA authorization which may or may not be in the National Immunization Program (NIP).
  - PIDSP used <u>PHEX (2021)</u> as a basis for its childhood immunization schedule in 2025. HTAC noted that and at that time of PHEX (2021) review, only the **live, attenuated, recombinant JE vaccine at one-dose** was approved by the Philippine FDA for primary immunization in children in the Philippines.
- Upon review of 24 country guidelines where JE is noted to be endemic, JEV is
  positively recommended by 16 countries. The JE vaccine is also included in the
  national immunization programs of 13 out of the 24 JE-endemic countries. It
  was noted that JE vaccine types recommended across countries varied.

### c. Budget Impact

- Comparative cost analysis, which included the cost of vaccine, consumables, and logistics, showed the following:
  - Vaccination cost per vaccinee
    - Live, attenuated, recombinant JE vaccine for children 9 months to 59 months old: Php 1,914.91
      - Inactivated JE vaccine for the following age groups
        - Among children 9 months to less than 3 years old: Php 1,869.05
        - Among children 3 years to less than 5 years old: Php 3,729.27
  - Total Budget Impact for target population (9 months to 59 months old in high risk areas)
    - Live, attenuated, recombinant JEV: Php 7.50 billion (estimated to consume 94.25% of the 2025 NIP budget)
    - Inactivated JEV: Php 10.29 billion (estimated to consume 129.33% of the 2025 NIP budget)
- Meanwhile, treatment of Japanese encephalitis is estimated using PhilHealth case rates as follows:
  - Case rate for Japanese Encephalitis: **₱41,145.00**
  - Case rate for unspecified viral encephalitis, viral encephalomyelitis, or viral meningoencephalitis: **₱41,145.00**
  - The number of cases that were diagnosed with JE from 2020-2024 were 588 cases (across all severities) and can incur a total cost of Php 24,193,260.

While the budget impact of JE vaccine is deemed high, its introduction will avert treatment cost of Japanese encephalitis and its complications, as well as productivity loss from caregivers. This underscores the need for increased funding for the NIP with a move to introduce and cover JE vaccine.

### d. Health systems implication

 Since live, attenuated, recombinant vaccines only require a single dose for primary immunization, with a standard dose across all children aged 9 to 59 months old, implementing a vaccination campaign with live recombinant vaccines is easier than with inactivated vaccines, which require two doses for primary immunization with varying dose depending on the age of the vaccinee.

The HTA Council noted that JE vaccines are considered standard of care that can address the significant burden of Japanese encephalitis in the country. However, its current estimated budget impact is deemed unaffordable, especially given that there are no funds currently earmarked for its implementation. Given this, once there are definitive plans to introduce JE vaccine, the DOH should strongly consider conducting price negotiation to ensure the affordability of the vaccine. The DOH should ensure that the price at which JE vaccine will be procured is affordable and that introduction of JE vaccine will not displace other vaccines in the NIP.

For the supporting evidence reviewed and discussed by the HTA Council, please refer to: <u>https://tinyurl.com/JEVaccinePrelimRecomm</u>. All comments, inputs, and/or appeals on the above preliminary recommendation may be submitted until **10 June 2025 (Tuesday)**, for the consideration of the HTA Council, through email at <u>hta@dost.gov.ph</u>. Please use the prescribed form for appeals indicated in the official HTA Philippines website [<u>https://tha.dost.gov.ph/appeals-2/</u>]. Appeals not following the prescribed format, and those submitted beyond the deadline shall not be entertained.

Should you have any questions or concerns regarding the preliminary recommendation, please contact us through the same email address or *via telephone call via 8-837-2071 loc 4100*.

Thank you very much.

On behalf of the HTA Philippines:

ANNE JULIENNE G. MARFORI, RPh, MSc Division Chief, HTA Division

JACINTO BLAS V. MANTAR NG III, MD, MSc Chairperson, HTA Council