**PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER**

**Dengvaxia®, powder and solvent for suspension for injection in multidose containers**
Dengue tetravalent vaccine (live, attenuated).

**Read all of this leaflet carefully before you or your child is vaccinated because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you or your child only. Do not pass it on to others.
- If you or your child get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See Section 4.

**In this leaflet**:


## 1. WHAT Dengvaxia IS AND WHAT IT IS USED FOR

Dengvaxia is a vaccine. It is used to help protect you or your child against "dengue disease" caused by dengue virus serotypes 1, 2, 3 and 4. It contains versions of these 4 varieties of the virus that have been weakened so that they cannot cause the disease.

Dengvaxia is given to adults, young people and children (from 6 to 45 years of age) with prior dengue virus infection confirmed by a test (also see sections 2 and 3).

Dengvaxia should be used according to official recommendations.

**How the vaccine works**
Dengvaxia stimulates the body's natural defences (immune system), to produces antibodies that will help protect against the viruses that cause dengue disease if the body is exposed to them in the future.

**What is dengue and dengue disease?**
Dengue is a viral infection which spreads through the bite of an infected Aedes mosquito. The virus from an infected person can spread to other people through mosquito bites for about 4 to 5 days (maximum 12 days) after the first symptoms appear. Dengue is not transmitted directly from person-to-person.

Dengue disease results in symptoms including fever, headache, pain behind the eyes, muscle and joint pain, feeling sick (nausea), being sick (vomiting), swollen glands or skin rash. Symptoms usually last for 2 to 7 days. You can also have dengue but show no symptoms (called "asymptomatic").

Occasionally dengue can be severe enough for you to have to go to hospital and in rare cases it can cause death. Severe dengue can give you a high fever and any of the following: severe abdominal (belly) pain, persistent sickness (vomiting), rapid breathing, severe bleeding, bleeding in the stomach, bleeding gums, feeling tired, feeling restless, coma, having fits (seizures) and organ failure.

## 2. BEFORE YOU OR YOUR CHILD USE Dengvaxia

To make sure that Dengvaxia is suitable for you or your child, it is important to tell your doctor, pharmacist or nurse if any of the points below apply to you or your child. If there is anything you do not understand, ask your doctor, pharmacist or nurse to explain.

**Do not use Dengvaxia if you or your child**
- Know you are allergic to the active substances or any of the other ingredients of Dengvaxia (listed in section 6).

- had an allergic reaction after using Dengvaxia before. Signs of an allergic reaction may include an itchy rash, shortness of breath and swelling of the face and tongue.
- have a weak immune system (the body's natural defences). This may be due to a genetic defect or HIV infection.
- are taking a medicine that affects the immune system (such as high-dose corticosteroids or chemotherapy). Your doctor will not use Dengvaxia until 4 weeks after you stop treatment.
- are pregnant or breast-feeding.

**Take special care with Dengvaxia**
If you or your child have never been infected by dengue virus before vaccination, you may have an increased risk of a more serious dengue illness that may lead to hospitalisation if you are later bitten by a dengue-infected mosquito.
Before the administration of Dengvaxia, your doctor, pharmacist or nurse will check if you or your child have ever been infected by dengue virus, and will tell you if a test has to be performed. Individuals who have not been previously infected by dengue virus should not be vaccinated because of an increased risk of hospitalisation for dengue and clinically severe dengue observed during the long-term follow up of the clinical trials in vaccinated individuals not previously infected.

Tell your doctor or nurse before receiving Dengvaxia if you or your child:

- a mild to high fever or acute disease. You will not get Dengvaxia until you or your child have recovered.
- ever had any health problems when given a vaccine. Your doctor will carefully consider the risks and benefits of vaccination.
- ever fainted from an injection. Fainting, and sometime falling, can occur (mostly in young people) following, or even before, any injection with a needle.

**Travelers**
Vaccination is not recommended if you have never lived in an area where dengue infections regularly occur and if you plan to only occasionally travel to an area where dengue infections regularly occur.

**Important information about the protection provided**
As with any vaccines, Dengvaxia may not protect everybody who has been vaccinated. You must continue to protect yourself against mosquito bites even after vaccination.

After vaccination, you should consult a doctor if you or your child believe you might have a dengue infection, and develop any of the following symptoms: high fever, severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, tiredness, restlessness and blood in vomit.

**Additional protection precautions**
You should take precautions to prevent mosquito bites. This includes using insect repellents, wearing protective clothing, and using mosquito nets.

**Younger children**
Children less than 6 years of age must not receive the vaccine.

**Using other medicines or vaccines and Dengvaxia**
Tell your doctor or pharmacist if you or your child are using, have recently used or might use any other vaccines or medicines.

In particular, tell your doctor or pharmacist if you are taking any of the following:
- medicines that affect your body’s natural defences (immune system) such as high-dose corticosteroids or chemotherapy. In this case, your doctor will not use Dengvaxia until 4 weeks after you stop treatment. This is because Dengvaxia might not work as well.
- medicines called “immunoglobulins” or blood products containing immuno globulins, such as blood or plasma. In this case, your doctor will not use Dengvaxia until 6 weeks, and preferably not for 3 months after you stop treatment. This is because Dengvaxia might not work as well.

Dengvaxia can be given at the same time as Diphtheria, Tetanus, Pertussis vaccine or recombinant Human Papillomavirus vaccines. Injections of more than one vaccine at the same time should be given at different injection sites.

**Pregnancy and breast-feeding**
Do not use Dengvaxia if you or your daughter are pregnant or breast-feeding. If you or your daughter:
- are of child-bearing age, you must use an effective method of contraception to avoid pregnancy for at least one month after each Dengvaxia dose.
- think you or your daughter may be pregnant or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before using Dengvaxia.

**Driving and using machines**
Dengvaxia has minor influence on the ability to drive and use machines.

## 3. HOW TO USE Dengvaxia

Previous dengue infection must be confirmed by a test, either documented in the medical history or performed prior to vaccination.

Dengvaxia is given by your doctor or nurse as an injection under the skin (subcutaneous injection) in the upper arm. It must not be injected into a blood vessel.

You or your child will receive 3 injections of 0.5 mL – one every 6 months.
- The first injection will be given at the chosen or scheduled date.
- The second injection, 6 months after the first injection.
- The third injection, 6 months after the second injection.

Dengvaxia should be used according to official recommendations.
Instructions for preparing the vaccine intended for medical and healthcare professionals are included at the end of the leaflet.

**If you or your child forget to use Dengvaxia**

- If you or your child miss a scheduled injection, your doctor will decide when to give the missed injection. It is important that you or your child follow the instructions of your doctor, pharmacist or nurse regarding follow-up injection.
- If you forget or are not able to go back at the schedule time, ask your doctor, pharmacist or nurse for advice.

If you have any further questions on the use of this product, ask your doctor, pharmacist or nurse.

## 4. POSSIBLE SIDE EFFECTS

Like all medicines, Dengvaxia can cause side effects, although not everybody gets them.

**Serious allergic (anaphylactic) reactions**
If any of these symptoms occur after leaving the place where you or your child received an injection, **contact a doctor immediately**:
- difficulty breathing
- blueness of the tongue or lips
- a rash
- swelling of the face or throat
- low blood pressure causing dizziness or fainting
- sudden and serious feeling of illness or unease with drop in blood pressure causing dizziness and loss of consciousness, rapid heartbeat linked with breathing difficulty

These signs or symptoms (anaphylactic reactions) usually develop soon after the injection is given and while you or your child are still in the clinic or doctor's surgery. They can also happen very rarely after receiving any vaccine (may affect up to 1 in 10,000 people).

**Other serious reactions**
For some people who have not been infected by dengue before vaccination, there may be an increased risk of getting a more serious dengue illness requiring hospitalisation if they become bitten by a dengue-infected mosquito later. This increased risk may mainly begin during the third year following the first injection.

**Other side effects**
The following side effects occurred during studies in children, young people and adults. Most of the side effects occurred within 3 days of having the injection of Dengvaxia.

- **Very common**: (may affect more than 1 in 10 people)
  - headache
  - muscle pain (myalgia)
  - generally feeling unwell (malaise)
  - weakness (asthenia)
  - injection site reactions: pain and redness (erythema)
  - fever

- **Common**: (may affect up to 1 in 10 people)
  - injection site reactions, bruising (hematoma), swelling, and itching (pruritus)

- **Uncommon**: (may affect up to 1 in 100 people)
  - infections of the nose or throat (upper respiratory tract)
  - pain or swelling of the nose or throat (nasopharyngitis)
  - feeling dizzy
  - sore throat (oropharyngeal pain)
  - cough
  - feeling sick (nausea)
  - vomiting
  - rash (skin eruption)
  - neck pain
  - chills
  - hardening of skin at the injection site (injection site induration)
  - injection site haemorrhage

- **Very rare**: (may affect up to 1 in 10,000 people)
  - allergic reactions

**Additional side effects in adults:**
- **Uncommon**: (may affect up to 1 in 100 people)
  - swollen glands (lymphadenopathy)
  - dry mouth
  - joint pain (arthralgia)
  - injection site warmth
  - fatigue

**Additional side effects in children and adolescents (from 6 to and including 17 years of age):**
- **Rare**: (may affect up to 1 in 1000 people)
  - runny nose (rhinorrhea)
  - itchy rash (urticaria)

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

## 5. HOW TO STORE Dengvaxia

Keep Dengvaxia out of the sight and reach of children.

Do not use Dengvaxia after the expiry date that is stated on the carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Keep the vaccine in the outer carton in order to protect it from light.

After mixing (reconstitution) with the solvent provided, the product must be used within 6 hours if stored between 2°C and 8°C (i.e., in a refrigerator) and protected from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

## 6. FURTHER INFORMATION

**What Dengvaxia contains:**

- After reconstitution, one dose (0.5mL) contains:

  4.5 - 6.0 log10 $CCID_{50}$* of each serotype of the chimeric yellow fever dengue virus ** (1, 2, 3 and 4) (live, attenuated).

  * $CCID_{50}$: 50% Cell Culture Infectious Dose.
  ** Produced in serum-free Vero cells by recombinant DNA technology. This product contains genetically modified organisms (GMOs).

- The other ingredients are: essential amino acids including Phenylalanine, non-essential amino acids, Arginine hydrochloride, Sucrose, Trehalose dihydrate, Sorbitol (E420), trometamol, urea, sodium chloride, water for injections.

**What Dengvaxia looks like and contents of the pack:**

Multidose presentation

Dengvaxia is a powder and solvent for suspension for injection. Dengvaxia is provided as a powder in a 5-dose vial and a solvent in a 5-dose vial (2.5 mL). The powder and the solvent must be mixed together before use.

Dengvaxia is available in packs of 5 (vaccine and solvent vials provided in the same box).

The powder is a white, homogenous, freeze-dried powder with possible retraction at the base, and may form a ring-shaped cake.

The solvent (0.9% sodium chloride solution) is a limpid, colourless solution. Use only the solvent provided.

After reconstitution with the solvent provided, Dengvaxia is limpid, colorless and may present limited white to translucent endogenous proteinaceous particles which do not prevent the use of the vaccine.

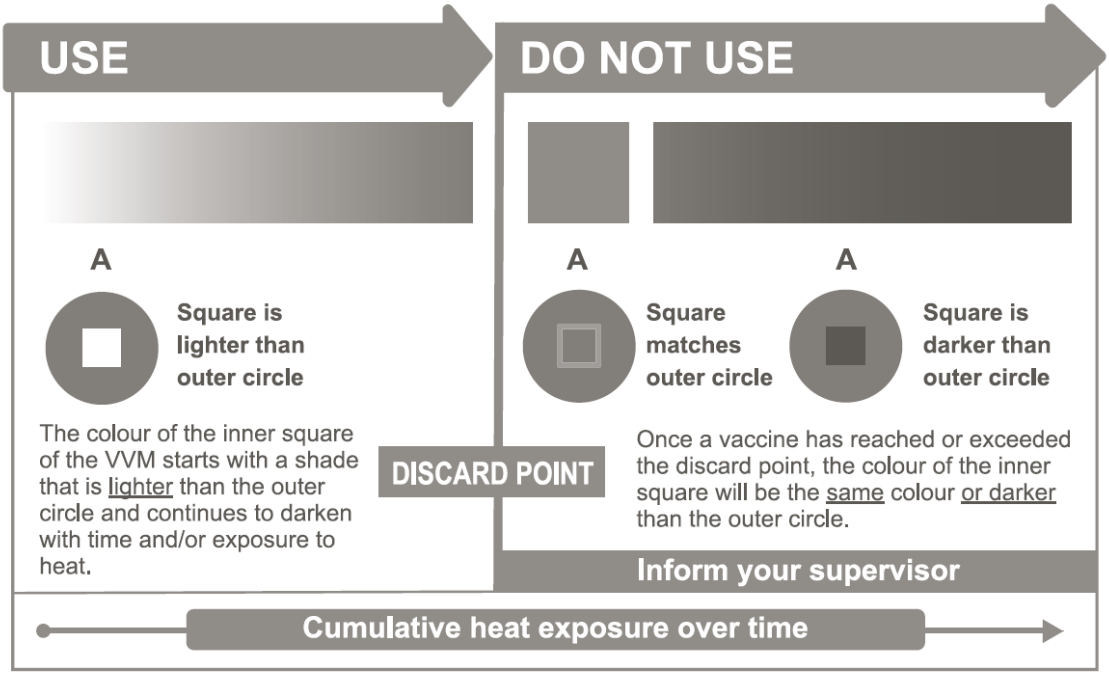
**Supplier and Manufacturer**

SANOFI PASTEUR – Zone Industrielle d'Incarville - 27100 Val de Reuil - France

**This leaflet was last approved on 01/2022.**

Detailed information on this medicinal product is available on PQTm's website (see: https://extranet.who.int/gavi/PQ_Web/.

The Vaccine Vial Monitors (VVM) are on the cap of Dengvaxia vaccine supplied through SANOFI PASTEUR. The colour dot which appears on the cap of the vial is a VVM. 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.




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 circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the circle or of a darker colour than the circle, then the vial should be discarded.

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**The following information is intended for healthcare professionals only:**

- As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Dengvaxia.
- Dengvaxia must not be mixed with other medicinal products in the same syringe.
- Dengvaxia must not be administered by intravascular injection under any circumstances.
- Immunisation should be carried out by subcutaneous (SC) injection preferably in the upper arm in the region of the deltoid.
- Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to injection with a needle. Procedures should be in place to prevent injury from falling and to manage syncopal reactions.

Reconstitution and handling of multidose presentation

Dengvaxia must be reconstituted prior to administration.

Visually inspect the lyophilized cake prior to reconstitution. The normal appearance of the vaccine is “a white powder, homogenous, freeze-dried powder with possible retraction at the base, and may form a ring-shaped cake”.
If the appearance is not conform to this description, the vaccine should be discarded.

Dengvaxia is reconstituted by transferring all of the solvent (0.9% sodium chloride solution) provided in the 5-dose vial with a dark gray flip-off cap into the 5-dose vial of freeze dried powder with a medium brown flip off cap, using a sterile syringe and needle. Use only the solvent provided.

1. Use a sterile syringe and needle for the transfer of the solvent.
2. Transfer the entire content of the solvent vial (with a dark gray flip-off cap) into the vial containing the powder (medium brown flip-off cap).
3. Swirl gently until the powder is dissolved.

After reconstitution, the suspension is limpid, colorless and may present limited white to translucent endogenous proteinaceous particles which do not prevent the use of the vaccine. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard the vial if the suspension is cloudy or contains particles other than limited white to translucent particles.

After complete dissolution, a 0.5 mL dose of the reconstituted suspension is withdrawn into a sterile syringe. A new sterile syringe and needle should be used for withdrawal of each of the 5 doses. The recommended size of the needle to be used is 23G or 25G.

Before each injection, the reconstituted suspension should be gently swirled once again.

Contact with disinfectants is to be avoided since they may inactivate the vaccine viruses.

After reconstitution with the solvent provided, Dengvaxia must be used within 6 hours.

Partially used multidose vials must be kept between 2°C and 8°C (i.e., in a refrigerator) and protected from light.

Any remaining vaccine doses should be discarded at the end of the immunization session or within 6 hours after reconstitution, whichever comes first.

A partially used multidose vial must be discarded immediately if:

- Sterile dose withdrawal has not been fully observed.
- A new sterile syringe and needle were not used for reconstitution or withdrawal of each of the previous doses.
- There is any suspicion that the partially used vial has been contaminated.
- There is visible evidence of contamination, such as a change in appearance.

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