เอกสารกำกับยาภาษาอังกฤษ

Dengvaxia MD, powder and solvent for suspension for injection
Dengue tetravalent vaccine (live, attenuated)

WARNING

- Tell your doctor, pharmacist or nurse before receiving Dengvaxia MD if you or your child have never been infected by dengue virus before or if you don't know whether you or your child have ever been infected by dengue virus. Doctor will consider prescribing vaccination after having carefully considered the benefits and the risks of vaccination.
- Dengvaxia MD is not recommended for individuals who have never been infected by dengue virus before vaccination because you may have an increased risk of a severe dengue illness that may lead to hospitalization if you are later bitten by a dengue-infected mosquito **(see Section Warnings and precautions).**

SEE PRESCRIBING INFORMATION FOR COMPLETE INFORMATION.

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 vaccine 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 5.

What is in this leaflet

1 Indication

Dengvaxia MD is a vaccine used to help protect you or your child against dengue disease caused by dengue virus serotypes 1, 2, 3 and 4. Dengvaxia MD is given to adults, adolescents and children 9 through 45 years of age living in endemic areas (where dengue infections regularly occur).

Dengvaxia MD contains dengue virus serotypes 1, 2, 3 and 4 that have been weakened. Dengvaxia MD works by stimulating the body's natural defenses (immune system), which produces its own protection (antibodies) against the viruses that cause dengue disease.

Dengue is a viral infection transmitted to humans through the bite of an infected *Aedes* mosquito. Dengue is not transmitted directly from person-to-person. Nevertheless the virus which replicates in an infected individual can be transmitted to other humans through mosquito bites for 4–5 days (maximum 12 days) after the first symptoms appear.

Dengue disease results in a wide range of symptoms including fever, headache, pain behind the eyes, muscle and joint pain, nausea, vomiting, swollen glands or skin rash. Symptoms usually last for 2–7 days. Dengue disease can also be asymptomatic.

However, occasionally dengue can be severe and potentially lead to hospitalization and in rare cases to death. Severe dengue is characterized by high fever and any of the following symptoms: severe abdominal pain, persistent vomiting, rapid breathing, severe bleeding, bleeding in stomach, bleeding gums, fatigue, restlessness, coma, seizure and organ failure.

2 Contraindication, Warning and Precaution for Dengvaxia MD

To make sure that Dengvaxia MD 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 MD if you or your child

- are allergic (hypersensitive) to the active substances or any of the other ingredients of Dengvaxia MD listed in Section 8,
- have developed an allergic reaction after prior administration of Dengvaxia MD. Signs of an allergic reaction may include an itchy rash, shortness of breath and swelling of the face and tongue,
- are suffering from a disease with mild to high fever or acute disease. In this case, your doctor will postpone the administration of Dengvaxia MD until you or your child have recovered,
- have a weakened immune system, for example due to a genetic defect, HIV infection or therapies that affect the immune system (for example, high-dose corticosteroids or chemotherapy),
- are pregnant,
- are breastfeeding.

Warnings and precautions

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

- have never been infected by dengue virus before or if you don't know whether you or your child have ever been infected by dengue virus. Doctor will consider prescribing vaccination after having carefully considered the benefits and the risks of vaccination. Dengvaxia MD is not recommended for individuals who have never been infected by dengue virus before vaccination because you may have an increased risk of a severe dengue illness that may lead to hospitalization if you are later bitten by a dengue-infected mosquito.
- are taking an immunosuppressive treatment (prednisone or equivalent 20 mg or 2 mg/kg body weight for 2 weeks or more). Your doctor will postpone administration of Dengvaxia MD until 4 weeks after you stop taking the treatment.
- have experienced any health problems after prior administration of any vaccines. Your doctor will carefully consider the risks and the benefits of vaccination.

As with all vaccines, Dengvaxia MD may not protect 100% of persons who have been vaccinated. Vaccination with Dengvaxia MD is not a substitute for protection against mosquito bites. You should take appropriate precautions for you and your child to prevent mosquito bites, including the use of repellents, adequate clothing, and mosquito nets.

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.

Fainting, sometimes accompanied by falling, can occur (mostly in adolescents) following, or even before, any injection with a needle. Therefore tell the doctor, pharmacist or nurse if you or your child fainted with a prior injection.

Travelers

Tell your doctor if you currently live in an area where dengue infections do not regularly occur. Unless you have been previously infected by dengue, vaccination is not recommended if you plan to travel to an area where dengue infections regularly occur.

Children
Dengvaxia MD should not be administered in children less than 9 years of age.

Using other medicines and Dengvaxia MD
Dengvaxia MD may not have an optimal effect if it is used at the same time as medicines that suppress the immune system such as corticosteroids or chemotherapy.

Please, tell your doctor, pharmacist or nurse if you or your child are taking or have recently taken any other vaccines or any other medicines, including medicines obtained without a prescription.

Pregnancy and breastfeeding
Dengvaxia MD must not be given to pregnant or breastfeeding women.

If you or your child:
- are of child-bearing age, you should take the necessary precautions to avoid pregnancy for 1 month following administration of Dengvaxia MD.
- are pregnant or breastfeeding, think you or your child may be pregnant or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before receiving Dengvaxia MD.

Driving and using machines
No data are available on the effects of Dengvaxia MD on the ability to drive or use machines.

3 Recommended dose and Mode of Administration

Dengvaxia MD is given by your doctor or nurse as an injection underneath the skin (subcutaneous route) in the upper arm.

You or your child will receive 3 injections of 0.5 mL each at 6-month intervals. The first injection will occur at the chosen or scheduled date; the second injection, 6 months after the first injection; and the third injection, 6 months after the second injection. Dengvaxia MD should be used according to the local vaccination schedule.

Reconstitution instructions intended for medical and healthcare professionals are included at the end of the leaflet.

If you or your child forget an injection of Dengvaxia MD
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 return visits for the follow-up injection. If you forget or are not able to go back to your doctor, pharmacist or nurse at the scheduled time, ask him/her for advice.
If you have any further questions on the use of this product, ask your doctor, pharmacist or nurse.

4 Pharmacodynamics/Pharmacokinetics

Mechanism of action
Dengvaxia MD contains live attenuated viruses. Following administration, the viruses replicate locally and elicit neutralizing antibodies and cell-mediated immune responses against the four dengue virus serotypes.

No pharmacokinetic studies have been performed on Dengvaxia MD.

5 Undesirable Effects

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

Serious allergic reactions
If any of these symptoms occur after leaving the place where you or your child received an injection, you must consult a doctor IMMEDIATELY:

- difficulty in breathing,
- blueness of the tongue or lips,
- a rash,
- swelling of the face or throat,
- low blood pressure causing dizziness or collapse
- sudden and serious malaise with drop in blood pressure causing dizziness and loss of consciousness, accelerated heart rate associated with respiratory disorders.

When these signs or symptoms (signs or symptoms of anaphylactic reactions) occur they usually develop quickly 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 user in 10 000).

Other undesirable effects
The following side effects were reported during clinical studies in children, adolescents and adults. Most of the reported side effects occurred within 3 days after the injection of Dengvaxia MD.

- Very common: (may affect more than 1 user in 10)
    - headache
    - muscle pain (myalgia)
    - generally feeling unwell (malaise)
    - feeling of weakness (asthenia)
    - injection site pain
    - fever
- Common: (may affect up to 1 user in 10)
    - injection site reactions: redness (erythema), bruising (hematoma), swelling, and itching (pruritus)
- Uncommon: (may affect up to 1 user in 100)
    - infections of the upper respiratory tract
    - dizziness
    - sore throat (oropharyngeal pain)
    - cough
    - runny nose (rhinorrhea)
    - nausea
    - skin eruption (rash)
    - neck pain
    - hardening of skin at the injection site (injection site induration)
- Very rare: (may affect up to 1 user in 10 000)
    - allergic reactions

Additional undesirable effects in adults:

- Uncommon: (may affect up to 1 user in 100)
    - swollen glands (lymphadenopathy)
    - migraine
    - joint pain (arthralgia)
    - flu-like symptoms (influenza-like illness)

Additional undesirable effects in children and adolescents (from 9 to and including 17 years of age):

- Uncommon: (may affect up to 1 user in 100)

- itchy rash (urticaria)

For some people who have not been infected by dengue before vaccination, there may be an increased risk of getting a severe dengue illness requiring hospitalization if they become bitten by a dengue-infected mosquito later. By monitoring subjects 9 years of age or older in a 5 year follow-up clinical trial, it was estimated that there were 5 additional hospitalized dengue cases or 2 additional severe dengue cases per 1000 vaccinees with no previous dengue infection could occur following vaccination. This increased risk may mainly occur during the third year following the first injection and was not observed in people who have been previously infected by dengue before vaccination.

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

6 Overdose and Treatment

No cases of overdose have been reported in clinical studies with Dengvaxia MD.

7 Storage condition for Dengvaxia MD

Keep Dengvaxia MD out of the reach and sight of children.

Do not use Dengvaxia MD 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 - 8°C).

Do not freeze.
Keep the vaccine in the outer carton in order to protect it 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.

8 Contents of the pack and product description

After reconstitution, one dose (0.5 mL) contains 4.5 - 6.0 log10 $CCID_{50}$* of each serotype of the CYD dengue virus** (1, 2, 3 and 4).
* $CCID_{50}$: 50% Cell Culture Infectious Dose.
** Produced in serum-free Vero cells by recombinant DNA technology.

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

What Dengvaxia MD looks like and contents of the pack

Dengvaxia MD is a powder and solvent for suspension for injection. Dengvaxia MD 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 MD 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 clear, colorless liquid.

After reconstitution with the solvent provided, Dengvaxia MD is a clear, colorless liquid with the possible presence of white to translucent particles.

The following information is intended for doctors, pharmacists or nurses only:

Before administering any biological, the person responsible for administration must take all precautions to prevent allergic or other reactions. 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 MD.

- Epinephrine (1:1000) and other appropriate agents used to control immediate allergic reactions must be available to treat unexpected events such as anaphylaxis.
- Once Dengvaxia MD has been completely reconstituted using the solvent provided, it is administered by subcutaneous (SC) injection. The recommended injection site is the deltoid region.
- Dengvaxia MD must not be mixed with other medicinal products in the same syringe.
- Dengvaxia MD must not be administered by intravascular injection under any circumstances.
- 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.
- Separate syringes and needles, separate injection sites and preferably separate limbs must be used if any other vaccine(s) or medicinal product(s) is/are concomitantly administered.

Dengvaxia MD 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. The vial is then gently swirled. 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.

The suspension should be visually inspected prior to administration. After reconstitution, Dengvaxia MD is a clear, colorless liquid with the possible presence of white to translucent particles (of endogenous nature).

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

After reconstitution with the solvent provided, Dengvaxia MD must be used as soon as possible. Any remaining vaccine doses should be discarded at the end of the immunization session or within 6 hours after reconstitution, whichever comes first.

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

A partially used multi-dose 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, preferably by heat inactivation or incineration, in accordance with local regulations.

9 Marketing Authorization Holder

Sanofi Pasteur Ltd, Bangkok

10 Date of Revision of Package Insert

01/2018