

Patient leaflet in accordance with the Pharmacists' (Products) Regulations - 1986

This medicine is to be supplied by doctor's prescription only

VOSEVI[®]

Film-coated tablets

Active ingredients: Each tablet contains –
sofosbuvir 400 mg
velpatasvir 100 mg
voxilaprevir 100 mg

Inactive and allergenic substances: see section 6 “*Additional information*”.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you. This leaflet contains essential information about this medicine. If you have any further questions, ask your doctor or pharmacist. This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if it seems that their medical condition is similar to yours.

Hepatitis B virus reactivation:

Before starting treatment with Vosevi, your healthcare provider will do blood tests to check for hepatitis B virus infection. If you have or had in the past an infection with hepatitis B virus, treatment with Vosevi might cause reactivation of hepatitis B, which in some cases might be fatal or cause serious liver problems (such as liver failure).

Reactivation of hepatitis B can occur during treatment or at the end of treatment with Vosevi. If you are at risk of hepatitis B reactivation you must be monitored closely during and after treatment with Vosevi.

For additional information on side effects, refer to section 4.

1. What is Vosevi intended for?

Vosevi is given to adults of 18 years and older to treat a chronic (long-term) viral infection of the liver called hepatitis C.

Therapeutic group:

- **Velpatasvir, voxilaprevir and sofosbuvir** are direct-acting antivirals.

Vosevi is a medicine that contains the active substances sofosbuvir, velpatasvir and voxilaprevir in a single tablet. The active substances in this medicine work together by blocking three different proteins that the hepatitis C virus needs to grow and reproduce itself, causing the infection to be eliminated from the body.

2. Before taking Vosevi

Do not take this medicine:

- **If you are allergic** to sofosbuvir, velpatasvir, voxilaprevir or any of the other ingredients of this medicine (listed in section 6 of this leaflet).

→If this applies to you, **do not take Vosevi and tell your doctor immediately.**

- **If you are currently taking any of the following medicines:**
 - **rifampicin** and **rifabutin** (antibiotics used to treat infections, including tuberculosis);
 - **St. John's wort** (a herbal medicine used to treat depression);
 - **carbamazepine, phenobarbital** and **phenytoin** (medicines used to treat epilepsy and prevent seizures);
 - **rosuvastatin** (a medicine used to treat high blood cholesterol or decrease the risk of certain cardiovascular events);
 - **dabigatran** (a medicine used to prevent blood clots);
 - **ethinylestradiol** containing medicines, including many contraceptives.

Special warnings relating to the use of this medicine

Talk to your doctor if you:

- **have liver problems** other than from hepatitis C, for instance
 - **if you have** a current or previous infection with the **hepatitis B** virus, since your doctor may want to monitor you more closely;
 - **if you have had a liver transplant.**
- **are taking treatment for human immunodeficiency virus (HIV) infection**, since your doctor may want to monitor you more closely.

Talk to your doctor or pharmacist before taking Vosevi if:

- you currently take, or have taken in the last few months, the medicine amiodarone to treat irregular heartbeats, as it may result in a life-threatening slowing of your heart beat. Your doctor may consider alternative treatments if you have taken this medicine. If treatment with Vosevi is needed, you may require additional heart monitoring.
- you have diabetes. You may need closer monitoring of your blood glucose levels and/or adjustment of your diabetes medication after starting Vosevi. Some diabetic patients have experienced low sugar levels in the blood (hypoglycaemia) after starting treatment with medicines like Vosevi.

Tell your doctor immediately if you currently take, or have taken in the last months, any medicines for heart problems and during treatment you experience:

- slow or irregular heartbeat, or heart rhythm problems;
- shortness of breath or worsening of existing shortness of breath;
- chest pain;
- light-headedness;
- palpitations;
- near fainting or fainting.

Blood tests

Your doctor will test your blood before, during and after your treatment with Vosevi. This is so that:

- Your doctor can decide if you should take Vosevi and for how long;
- Your doctor can confirm that your treatment has worked and you are free of the hepatitis C virus.

Children and adolescents

Do not give this medicine to children and adolescents under 18 years of age. The use of Vosevi in children and adolescents has not yet been studied.

Other medicines and Vosevi

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including non-prescribing medicines and food supplements.

If you are not sure talk to your doctor or pharmacist.

Some medicines must not be taken with Vosevi. Taking Vosevi with any of these may stop your medicines from working properly, or make any side effects worse:

- **rifampicin** and **rifabutin** (antibiotics used to treat infections, including tuberculosis);
- **St. John's wort** (a herbal medicine used to treat depression);
- **carbamazepine, phenobarbital** and **phenytoin** (medicines used to treat epilepsy and prevent seizures);
- **rosuvastatin** (a medicine used to treat high blood cholesterol or decrease the risk of certain cardiovascular events);
- **dabigatran** (a medicine used to prevent blood clots);
- **ethinylestradiol** containing medicines, including many contraceptives.

Tell your doctor or pharmacist if you are taking any of the medicines below:

- **amiodarone**, used to treat irregular heartbeats;
- **rifapentine** (an antibiotic used to treat infections, including tuberculosis);
- **oxcarbazepine** (medicine used to treat epilepsy and prevent seizures);
- **tenofovir disoproxil fumarate**, or any medicine containing tenofovir disoproxil fumarate, used to treat HIV infection;
- **atazanavir, efavirenz** or **lopinavir**, used to treat HIV infection;
- **digoxin**, used to treat heart conditions;
- **modafinil**, used to treat sleep disorders;
- **atorvastatin, pravastatin, or other statins**, used to treat high cholesterol;
- **ciclosporin**, used to suppress the immune system.

Taking Vosevi with any of these may stop your medicines from working properly, or make any side effects worse. Your doctor may need to give you a different medicine or adjust the dose of medicine you are taking.

- **Get advice from a doctor or pharmacist** if you take medicines used to treat **stomach ulcers, heartburn or acid reflux** as they can decrease the amount of velpatasvir in your blood. These medicines include:
 - antacids (such as aluminium/magnesium hydroxide or calcium carbonate). These should be taken at least 4 hours before or 4 hours after Vosevi;
 - proton pump inhibitors (such as omeprazole, lansoprazole, rabeprazole, pantoprazole and esomeprazole). If you need high doses of these medicines your doctor may give you a different medicine instead or adjust the dose of the medicine you are taking;
 - H₂-receptor antagonists (such as famotidine, cimetidine, nizatidine or ranitidine). If you need high doses of these medicines your doctor may give you a different medicine instead or adjust the dose of the medicine you are taking.

These medicines can decrease the amount of Vosevi in your blood. If you are taking one of these medicines your doctor will either give you a different medicine for stomach ulcers, heartburn or acid reflux, or recommend how and when you take that medicine.

- **Get advice from a doctor or pharmacist** if you take **warfarin or other similar medicines** called vitamin K antagonists used to thin the blood. Your doctor may need to increase the frequency of your blood tests to check how well your blood can clot.
- Your liver function may change with treatment of hepatitis C and therefore may affect other medications (e.g. medicines used to suppress your immune system, etc.). Your doctor may need to closely monitor these other medicines you are taking and make adjustments after starting Vosevi.

Pregnancy, breast-feeding and fertility

If you are pregnant, think you may be pregnant, are breast-feeding your baby, or are planning to have a baby ask your doctor for advice before taking this medicine.

Pregnancy

Vosevi is not recommended during pregnancy. The effects of Vosevi during pregnancy are not known.

Breast-feeding

Do not breast-feed during treatment with Vosevi. Some of the active substances of Vosevi may pass into human breast milk.

Driving and using machines

Vosevi should not affect your ability to drive or use any tools or machinery.

Vosevi contains lactose

- **Tell your doctor if you are lactose intolerant or intolerant to other sugars.** Vosevi contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Vosevi?

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Usual dosage

The usual dose is **one tablet once a day for 8 or 12 weeks.**

Do not exceed the recommended dose.

Swallow the tablet whole with food. There is no information available regarding the crushing/splitting of the product. Do not chew, crush or split the tablet as it has a very bitter taste.

Kidney problems

Tell your doctor if you **have kidney problems** or if you are on **kidney dialysis**, since Vosevi has not been fully tested in patients with severe kidney problems.

Liver problems

Vosevi should not be used if you have moderate or severe liver problems.

If you are taking an antacid, take it at least 4 hours before or at least 4 hours after Vosevi.

If you are sick (vomit) after taking Vosevi it may affect the amount of Vosevi in your blood. This may make Vosevi work less well.

- If you are sick (vomit) **less than 4 hours after** taking Vosevi, take another dose.
- If you are sick (vomit) **more than 4 hours after** taking Vosevi, you do not need to take another dose until your next scheduled dose.

If you take more Vosevi than you should

If you accidentally take more than the recommended dose of Vosevi or if a child has accidentally swallowed this medicine, you may be at increased risk of side effects with this medicine (*see section 4 Side effects*).

Contact your doctor or nearest emergency department immediately for advice. Bring the tablet bottle with you so that you can easily describe what you have taken.

If you forget to take Vosevi

It is important not to miss a dose of this medicine.

If you do miss a dose, work out how long it is since you last took your Vosevi:

- **If you notice within 18 hours** of the time you usually take Vosevi, you must take the missed dose as soon as possible. Then take the next dose at your usual time.
- **If it is 18 hours or more** after the time you usually take Vosevi, wait and take the next dose at your usual time. Do not take a double dose (two doses close together).

Do not stop taking Vosevi

Do not stop taking this medicine unless your doctor tells you to. It is very important that you complete the full course of treatment to give the medicine the best chance to treat your hepatitis C virus infection.

Do not take medicines in the dark. Check the label and the dose every time you take the medicine. Wear glasses if you need them.

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

4. Side Effects

Like all medicines, this medicine may cause side effects, although not everybody gets them. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Some side effects could be serious.

Stop taking Vosevi and seek medical help immediately if you experience any of the following symptoms:

- swelling of the face, lips, tongue or throat (angioedema) (*an uncommon side effect - may affect up to 1 in 100 people*)
- a wide-spread severe rash with peeling skin which may be accompanied by fever, flu-like symptoms, blisters in the mouth, eyes, and/or genitals (Stevens-Johnson syndrome) (*the frequency of the side effect is not known*).

Other side effects that may occur

Very common side effects

(may affect more than 1 in 10 people)

- headache
- diarrhoea
- feeling sick (nausea)

Common side effects

(may affect up to 1 in 10 people)

- stomach pain
- decreased appetite
- being sick (vomiting)
- muscle pain (myalgia)
- abnormality in a laboratory test of liver function (total bilirubin)
- rash

Uncommon side effects

(may affect up to 1 in 100 people)

- muscle spasms

If you experience side effects, if one of the side effects has worsened or you experience any side effect which is not listed in the leaflet, consult with your doctor.

Reporting of side effects

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

You can report any side effects to the Ministry of Health by clicking on the link "Report side effects due to medical treatment" that is located on the Ministry of Health homepage (www.health.gov.il) which redirects to the online form for reporting side effects or by clicking on the link: <https://sideeffects.health.gov.il>.

You can also report any side effects to the registration holder via email:

DrugSafety.Israel@gilead.com.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Vosevi

Prevent poisoning! Keep this medicine out of the sight and reach of children and/or babies. In this way you will prevent poisoning. Do not induce vomiting without a doctor's express instruction.

Do not use this medicine after the expiry date which is stated on the bottle and carton after "EXP". The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions. It is recommended to store at room temperature. Store in the original package in order to protect from moisture. Keep the bottle tightly closed.

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 protect the environment.

6. Additional information

What Vosevi contains

- **The active substances are** sofosbuvir, velpatasvir and voxilaprevir. Each film-coated tablet contains 400 mg sofosbuvir, 100 mg velpatasvir and 100 mg voxilaprevir.
- **The other ingredients are**
Tablet core:
Microcrystalline cellulose (E460), copovidone, lactose monohydrate, croscarmellose sodium (E468), magnesium stearate, colloidal anhydrous silica.

Film-coating:
Polyvinyl alcohol (E1203), titanium dioxide, macrogol/PEG 3350 (E1521), talc (E553b), iron oxide yellow, iron oxide red, iron oxide black.

What Vosevi looks like and contents of the pack

The film-coated tablets are beige, capsule-shaped tablets debossed with "GSI" on one side and "3" on the other side. The tablet is 20 mm long and 10 mm wide.

The tablets are packed in plastic bottles with child resistant caps. Each bottle contains a silica gel desiccant (drying agent) that must be kept in the bottle to help protect your tablets. The silica gel desiccant is contained in a separate sachet or canister and should not be swallowed.

The following pack size is available:

- outer cartons containing 1 bottle of 28 film-coated tablets

Registration Holder: Gilead Sciences Israel Ltd., 4 HaHarash Street, Hod Hasharon, 4524075, Israel

Manufacturer: Gilead Sciences Ireland UC, IDA Business & Technology Park, Carrigtohill, County Cork, Ireland

Revised in January 2022 in accordance with MoH guidelines.

The medicine's registration no. in the national register of medicines at the Ministry of Health: 35324

For simplicity and ease of reading, this leaflet was phrased in the masculine. Nevertheless, this medicine is intended for both sexes.

Reference: EU label from Sep 2021.

IL-JAN22-EU-SEP21 (excl. ESRD)