

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

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

Harvoni®
Film-coated tablets

Active ingredients: Each tablet contains –

| | |
|------------|--------|
| ledipasvir | 90 mg |
| sofosbuvir | 400 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. Keep this leaflet. You may need to read it again. 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 their signs of illness are the same as yours. If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

This medicine is intended for adults aged 18 years and over.

Hepatitis B virus reactivation:

Before starting treatment with Harvoni, 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 Harvoni 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 Harvoni. If you are at risk of hepatitis B reactivation, you must be monitored closely during or after your treatment with Harvoni. For more information about the side effects, see section 4.

1. What is the medicine intended for

Harvoni is indicated to treat chronic (long-term) hepatitis C virus infection in adults.

Therapeutic group:

- **ledipasvir and sofosbuvir** are antivirals which suppress the hepatitis C virus.

Harvoni is a medicine that contains the active substances ledipasvir and sofosbuvir in a single tablet. Hepatitis C is a virus that infects the liver. The active substances ledipasvir and sofosbuvir work together by blocking two different proteins that the virus needs to grow and reproduce itself, allowing the infection to be permanently eliminated from the body.

Harvoni is sometimes taken with another medicine, ribavirin.

It is very important that you also read the leaflets for the other medicines that you will be taking with Harvoni. If you have any questions about your medicines, please ask your doctor or pharmacist.

2. Before taking the medicine

X Do not take this medicine:

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

 - **If you are currently taking any of the following medicines:**
 - **rifampicin and rifabutin** (antibiotics used to treat infections, including tuberculosis);
 - **St. John's wort** (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 cholesterol).
- If this applies to you, **do not take Harvoni and tell your doctor immediately.**

Special warnings relating to the use of this medicine

Your doctor will know if any of the following conditions apply to you. These will be considered before treatment with Harvoni is started.

- **other liver problems** apart from hepatitis C, for instance
 - **if you are awaiting a liver transplant;**
 - **if you have a current or previous infection with the hepatitis B virus**, since your doctor may want to monitor you more closely;
- **kidney problems or if you are on kidney dialysis**, since Harvoni has not been fully tested in patients with severe kidney problems;
- **ongoing treatment for HIV infection**, since your doctor may want to monitor you more closely.

Talk to your doctor or pharmacist before taking Harvoni 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 different treatments if you have taken this medicine. If treatment with Harvoni 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 Harvoni. Some diabetic patients have experienced low sugar levels in the blood (hypoglycaemia) after starting treatment with medicines like Harvoni.

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 Harvoni. This is so that:

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

Other medicines and Harvoni

If you are taking or have recently taken other medicines, including non-prescription medicines and dietary supplements, tell your doctor or pharmacist.

Warfarin and 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 Harvoni.

If you are not sure about taking any other medicines, talk to your doctor or pharmacist.

Some medicines should not be taken with Harvoni.

- **Do not take any other medicine that contains sofosbuvir, one of the active substances in Harvoni.**
- **Tell your doctor or pharmacist** if you are taking any of the medicines below:
 - **amiodarone** used to treat irregular heartbeats;
 - **tenofovir disoproxil fumarate** or any medicine containing tenofovir disoproxil fumarate, used to treat HIV infection;
 - **digoxin** used to treat heart conditions;
 - **dabigatran** used to thin the blood.
 - **statins** used to treat high cholesterol.
 - **rifapentine** (antibiotic used to treat infections, including tuberculosis);
 - **oxcarbazepine** (a medicine used to treat epilepsy and prevent seizures);
 - **tipranavir** (used to treat HIV infection).

Taking Harvoni 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**. This includes:
 - antacids (such as aluminium/magnesium hydroxide or calcium carbonate). These should be taken at least 4 hours before or 4 hours after Harvoni;
 - proton pump inhibitors (such as omeprazole, lansoprazole, rabeprazole, pantoprazole and esomeprazole). These should be taken at the same time as Harvoni. Do not take proton pump inhibitors before Harvoni. Your doctor may give you a different medicine or adjust the dose of the medicine you are taking;
 - H₂-receptor antagonists (such as famotidine, cimetidine, nizatidine or ranitidine). Your doctor may give you a different medicine or adjust the dose of the medicine you are taking.

These medicines can decrease the amount of ledipasvir 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.

Taking the medicine and food

Swallow the tablet whole with or without food.

Pregnancy and contraception

The effects of Harvoni during pregnancy are not known. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Pregnancy must be avoided if Harvoni is taken together with ribavirin. It is very important that you read the "Pregnancy" section in the ribavirin package leaflet very carefully. Ribavirin can be very damaging to an unborn baby. Therefore, special precautions in sexual activity **must be taken** if there is any chance for pregnancy to occur.

- You or your partner must use an effective birth control method during treatment with Harvoni together with ribavirin and for some time afterwards. It is very important that you read the "Pregnancy" section in the ribavirin package leaflet very carefully. Ask your doctor for an effective contraceptive method suitable for you.
- If you or your partner become pregnant during Harvoni and ribavirin treatment or in the months that follow, you must contact your doctor immediately.

Breast-feeding

Do not breast-feed during treatment with Harvoni. It is not known whether ledipasvir or sofosbuvir, the two active substances of Harvoni, pass into human breast milk.

Driving and using machines

If you feel tired after taking Harvoni you should not take part in activities that require concentration, for example, do not drive, ride a bike or operate machines.

Children and adolescents

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

Important information on the inactive ingredients of the medicine

Harvoni contains lactose

- **If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.**

Harvoni contains sunset yellow FCF (E110) which can cause allergic reactions

Tell your doctor if you are allergic to sunset yellow FCF, also called "E110" before taking this medicine.

Harvoni contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take the medicine

Always take this medicine exactly as your doctor has told you.

The dosage and treatment will be determined by the doctor only. Check with your doctor or pharmacist if you are not sure.

Usual dosage

The usual dose is **one tablet once a day**. Your doctor will tell you for how many weeks you should take Harvoni.

Do not exceed the recommended dose.

Swallow the tablet whole with or without 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. Tell your doctor or pharmacist if you have problems swallowing tablets.

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

If you are taking a proton pump inhibitor, take the proton pump inhibitor at the same time as Harvoni. Do not take it before Harvoni.

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

- If you are sick (vomit) **less than 5 hours after** taking Harvoni, take another dose.
- If you are sick (vomit) **more than 5 hours after** taking Harvoni, you do not need to take another dose until your next scheduled dose.

If you take more Harvoni than you should

If you accidentally take more than the recommended dose (overdose), or if a child has accidentally swallowed the medicine, you should contact your doctor or nearest emergency department immediately for advice, and bring the tablet bottle with you.

If you forget to take Harvoni

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 Harvoni:

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

Do not stop taking this medicine

It is important that you take your treatment as your doctor has ordered.

Even if your health improves, 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 a 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. Possible side effects

Like all medicines, this medicine may cause side effects in some patients. Do not be alarmed by reading the list of side effects. You may not experience them. If you take Harvoni you may get one or more of the side effects below:

Very common side effects

(may affect more than 1 in 10 people)

- headache
- feeling tired

Common side effects

(may affect up to 1 in 10 people)

- rash

Other effects that may be seen during treatment with Harvoni

The frequency of the following side effects is not known (frequency cannot be estimated from the available data).

- swelling of the face, lips, tongue or throat (angioedema).

Other effects that may be seen during treatment with sofosbuvir:

The frequency of the following side effects is not known (frequency cannot be estimated from the available data).

- 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).

→ If a side effect has appeared, if any of the side effects worsen or if you suffer from a side effect not mentioned in the leaflet, consult the doctor

Reporting of side effects

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 to the registration holder at the following: Drugsafety.Israel@gilead.com. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Harvoni

Prevent poisoning! This medicine and any other medicine should be stored in a closed place 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.
Store below 30°C.

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 the medicine contains

- **The active substances are** ledipasvir and sofosbuvir. Each film-coated tablet contains 90 mg ledipasvir and 400 mg sofosbuvir.
- **In addition to the active ingredients the medicine contains:**
Tablet core:
Microcrystalline cellulose, lactose monohydrate, copovidone, croscarmellose sodium, magnesium stearate, colloidal anhydrous silica.

Film-coating:
Polyvinyl alcohol partially hydrolized, titanium dioxide, macrogol/PEG 3350, talc, sunset yellow FCF (E110)

What does the medicine look like and contents of the pack

The film-coated tablets are orange, diamond-shaped tablets debossed with "GSI" on one side and "7985" on the other side. The tablet is approximately 19 mm long and 10 mm wide.

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 sizes are available:

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

Registration Holder:

Gilead Sciences Israel Ltd., 4 HaHarash Street, 4524075, Israel.

Manufacturer:

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

Revised in May 2023 in accordance with MoH Guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 34517

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

Reference: EU SmPC November 2022.

IL-MAY23(except SOLAR-2 and pediatric ind.) -EU-NOV22