

Package leaflet: Information for the user

Harvoni 90 mg/400 mg film-coated tablets ledipasvir/sofosbuvir

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine 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 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.

What is in this leaflet

1. What Harvoni is and what it is used for
2. What you need to know before you take Harvoni
3. How to take Harvoni
4. Possible side effects
5. How to store Harvoni
6. Contents of the pack and other information

If Harvoni has been prescribed for your child, please note that all the information in this leaflet is applicable to your child (in this case please read “your child” instead of “you”).

1. What Harvoni is and what it is used for

Harvoni is a medicine that contains the active substances ledipasvir and sofosbuvir. Harvoni is given to treat chronic (long-term) hepatitis C virus infection in **adults and children 3 years of age and older**.

Hepatitis C is a virus that infects the liver. The active substances in the medicine 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. What you need to know before you take Harvoni

Do not take Harvoni

- **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 any of these conditions apply to you, **do not take Harvoni and tell your doctor immediately.**

Warnings and precautions

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.

Children and adolescents

Do not give this medicine to children under 3 years of age. The use of Harvoni in children under 3 years of age has not yet been studied.

Other medicines and Harvoni

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

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.

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.

Harvoni 90 mg/400 mg and 45 mg/200 mg film-coated tablets contain 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 90 mg/400 mg film-coated tablets 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 Harvoni

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

Recommended dose

Harvoni is to be taken as advised by your doctor. The recommended dose of Harvoni **in adults** is **one 90 mg/400 mg film-coated tablet once a day**. Your doctor will tell you for how many weeks you should take Harvoni.

The recommended dose of Harvoni in children aged 3 years and above is based on weight. Take Harvoni as advised by your doctor.

Swallow the tablet(s) whole with or without food. 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 you should contact your doctor or nearest emergency department immediately for advice. Keep the tablet bottle with you so that you can easily describe what you have taken.

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 Harvoni

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.

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. 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).

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 also report side effects directly via the *Yellow Card Scheme*

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

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

5. How to store Harvoni

Keep this medicine out of the sight and reach of children.

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.

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. Contents of the pack and other information

What Harvoni contains

- **The active substances are** ledipasvir and sofosbuvir. Each film-coated tablet contains 90 mg ledipasvir and 400 mg sofosbuvir or 45 mg ledipasvir and 200 mg sofosbuvir.
- **The other ingredients are**
Tablet core:
Copolydione, lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, colloidal anhydrous silica, magnesium stearate

Film-coating:
Polyvinyl alcohol, titanium dioxide, macrogol, talc, and for the 90 mg/400 mg tablet only; sunset yellow FCF (E110)

What Harvoni looks like and contents of the pack

Harvoni 90 mg/400 mg 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.

Harvoni 45 mg/200 mg film-coated tablets are white, capsule-shaped, debossed with “GSI” on one side and “HRV” on the other side. The tablet is approximately 14 mm long and 7 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 for the 90 mg/400 mg and the 45 mg/ 200 mg film-coated tablets.
- outer cartons containing 3 bottles of 28 (84) film-coated tablets for the 90 mg/400 mg film-coated tablets only. Not all pack sizes may be marketed.

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