PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

HARVONI 90 mg/400 mg film-coated tablets

ledipasvir/sofosbuvir

Contains sugar (165 mg lactose per tablet)

Read all of this leaflet carefully before you start taking HARVONI

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- HARVONI has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

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

1. WHAT HARVONI IS AND WHAT IT IS USED FOR

HARVONI is used to treat an infection of your liver caused by a hepatitis C virus, in adults and adolescents 12 to less than 18 years of age.

HARVONI works by blocking two different proteins that the virus needs to grow and reproduce itself.

HARVONI is sometimes taken with other medicines like Ribavirin.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE HARVONI

Do not take HARVONI:

- If you are hypersensitive (allergic) to ledipasvir, sofosbuvir or any of the other ingredients of Harvoni (listed in section 6)
- If you are currently taking any of the following medicines:
    - rifampicin and rifabutin (used to treat tuberculosis);
    - St. John's wort (*Hypericum perforatum* – 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 you are pregnant or breastfeeding your baby and you are treated with Harvoni with or without ribavirin.

If you are using ribavirin with HARVONI, you **must** use effective contraception to prevent you becoming pregnant. Ribavirin will cause serious harm to your unborn baby.

You should ask your doctor or pharmacist to provide you with the Patient Information Leaflet of Ribavirin, which contains the information you must read in the “Do not take Ribavirin section”. It will also provide you with the other information you will need to know about Ribavirin.

Warnings and precautions

Take special care with HARVONI:

- Talk to your doctor or pharmacist if you have severe kidney problems or if you are on kidney dialysis.

- If you have been diagnosed with hepatitis B infection, the infection may be re-activated by treatment with HARVONI and you may develop severe liver inflammation, liver failure or death. Your doctor will closely monitor your liver function while you are using HARVONI.

- If you have been diagnosed with a liver disorder in addition to hepatitis C (for example, cirrhosis or if you are awaiting a liver transplantation), your doctor will do further investigations and closely monitor your liver function before deciding on treatment with Harvoni.

- If you receive 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 (your doctor may consider alternative treatments if you have taken this medicine).
- 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 are taking any medicines for heart problems and during treatment you experience:

- shortness of breath
- light-headedness
- palpitations
- fainting

Blood tests

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

- Decide what other medicines you should take with HARVONI and for how long.
- Confirm that your treatment has had the desired effect.

Children and adolescents

Do not give this medicine to children under 12 years of age. The use of HARVONI in children younger than 12 years has not yet been studied.

Other medicines and HARVONI

Always tell your health care provider if you are taking any other medicine. This includes all complementary or traditional medicines.

Warfarin and other similar medicines called vitamin K antagonists used to prevent blood clotting. 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.

- Do not take any of these medicines with HARVONI:
  - rifapentine, rifabutin or rifampicin (used to treat tuberculosis);
  - oxcarbazepine (a medicine used to treat epilepsy and prevent seizures);
  - simeprevir (a medicine used to treat hepatitis C infection);
  - tipranavir (used to treat HIV infection).

- 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 prevent blood clotting;
  - statins used to treat high cholesterol.

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.

Please discuss the use of the following medicines used to treat stomach ulcers, heartburn or acid reflux, in combination with HARVONI with your doctor or pharmacist:

- 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;
- H_2-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 should take that medicine.

HARVONI with food and drink

HARVONI can be taken with or after a meal.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, you should not be treated with Harvoni, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

Pregnancy:

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 HARVONI.

Pregnancy must be avoided if you are taking HARVONI with ribavirin. Ribavirin will cause serious harm to your unborn baby. Therefore, you and your partner must use appropriate and effective contraceptive methods if you are a woman of child-bearing age and there is a chance for pregnancy to occur.

If you or your partner becomes pregnant during HARVONI treatment or in the months that follow, you must contact your doctor immediately.
It is very important that you read the “Pregnancy” section in the ribavirin Patient Information Leaflet very carefully.

Contraception:

You and your partner must use appropriate and effective contraceptive methods to avoid pregnancy. You must use an effective birth control method while taking HARVONI together with ribavirin and continue with contraception for 6 months after treatment has been stopped. Ask your doctor for an effective contraceptive method suitable for you.

Breastfeeding

You should not use HARVONI if you are breastfeeding your baby, It is not known if ledipasvir or sofosbuvir, the two active substances of HARVONI passes into human breast milk.

Driving and using machines

HARVONI may affect your ability to drive and use machines. It is not always possible to predict the extent HARVONI may interfere with your daily activities. You should not drive and use machines until you know how treatment with HARVONI affects you.

HARVONI contains lactose

Patients with the hereditary conditions of lactose/fructose or galactose intolerance should not take HARVONI.

3. HOW TO TAKE HARVONI

Do not share medicines prescribed for you with any other person.

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

The usual dose of HARVONI is one tablet once a day.

Your doctor will tell you how long your treatment with HARVONI will last. Do not stop treatment early because your infection will not be treated properly. If you have the impression that the effect of HARVONI is too strong or too weak, tell your doctor or pharmacist.

Swallow the tablet 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 it 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 tablet.

If you are sick (vomit) more than 5 hours after taking HARVONI, you do not need to take another tablet until your next scheduled tablet.

No dosage adjustment is required for elderly patients or patients with liver or kidney impairment.

If you take more HARVONI than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take HARVONI

It is important not to miss a dose of Harvoni.

If you miss a dose:

- and you notice within 18 hours of the time you usually take HARVONI, you must take the tablet as soon as possible. Then take the next dose at your usual time.
- and you notice 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).

If you 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.

4. POSSIBLE SIDE EFFECTS

HARVONI can have side effects.

Not all side effects reported for HARVONI are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking HARVONI, please consult your health care provider for advice.

If any of the following happens, stop taking HARVONI and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the face, lips, tongue or throat (angioedema), which may cause difficulty in swallowing or breathing,
- 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),
- rash

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to HARVONI. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

- headache,
- tiredness.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

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

5. HOW TO STORE HARVONI

Store all medicines out of reach of children.

Store at or below 30 °C.

Do not use after the expiry date stated on the label/carton/bottle. The expiry date refers to the last day of that month.

Keep the bottle tightly closed.

Do not remove the desiccant.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

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.

The other ingredients are

Each tablet contains 165 mg lactose

Tablet core:

Copovidone, Microcrystalline cellulose (E460(i)), Croscarmellose sodium, Colloidal silicon dioxide, Magnesium stearate (E470b)

Film-coating:

Polyvinyl alcohol (E1203), Titanium dioxide (E171), Macrogol (Polyethylene glycol) 3350 (E1521), Talc (E553b).

What HARVONI looks like and contents of the pack

White, diamond-shaped, biconvex, film-coated tablets with “GSI” debossed on one side and “7985” on the other side.

HARVONI tablets are supplied in a 100mL high density polyethylene (HDPE) bottles with a polypropylene child-resistant closure containing 28 film-coated tablets with a silica gel desiccant and polyester coil.

Holder of Certificate of Registration

Gilead Sciences South Africa (Pty) Ltd

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Gauteng, 2090

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