

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS REGULATIONS
(PREPARATIONS) - 1986

This medicine is marketed upon doctor's prescription only

ZEPATIER®
50 mg/100 mg
Tablets

Each tablet contains:

elbasvir 50 mg and grazoprevir 100 mg

For a list of inactive ingredients see section 6.1 "What **ZEPATIER** contains?".

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

- This leaflet contains concise information about **ZEPATIER**. If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their ailment seems similar to yours.
- Your doctor may prescribe **ZEPATIER** with a medicine called ribavirin. **If you take ZEPATIER and ribavirin, be sure you read the patient leaflet for ribavirin.**
- This medicine is intended for adults above 18 years of age.
- Before you take this medicine, be sure you understand what it is for and how to take it safely.

What is the most important information I should know about ZEPATIER?

ZEPATIER can cause serious side effects, including:

Hepatitis B virus reactivation: Before starting treatment with **ZEPATIER**, your doctor will do blood tests to check for hepatitis B virus infection. If you have ever had hepatitis B virus infection, the hepatitis B virus could become active again during or after treatment of hepatitis C virus infection with **ZEPATIER**. Hepatitis B virus becoming active again (called reactivation) may cause serious liver problems including liver failure and death. Your doctor will monitor you if you are at risk for hepatitis B virus reactivation during treatment and after you stop taking **ZEPATIER**.

For more information about side effects, see section 4 "Side Effects".

1. WHAT IS ZEPATIER INTENDED FOR?

ZEPATIER is a prescription medicine to treat chronic (long-lasting) hepatitis C genotypes 1 or 4 infection in adults.

THERAPEUTIC GROUP: elbasvir- HCV NS5A inhibitor; grazoprevir- HCV NS3/4A protease inhibitor.

2. BEFORE USING ZEPATIER

2.1 Do not use ZEPATIER if:

- you are sensitive (allergic) to elbasvir, grazoprevir or any of the other ingredients of **ZEPATIER** (see section 6.1 "What **ZEPATIER** contains?").
- you have certain liver function disorders
- you are taking any of the following medicines:
 - carbamazepine
 - cyclosporine
 - HIV treatments that include: efavirenz, atazanavir, darunavir, lopinavir, saquinavir, or tipranavir
 - phenytoin
 - rifampin
 - St. John's wort (*Hypericum perforatum*)

2.2 Special warnings concerning use of ZEPATIER

Before starting treatment with ZEPATIER, tell your doctor about all of your medical conditions, including if you:

- have ever had hepatitis B virus infection
- suffer from liver problems other than hepatitis C
- have ever taken any medicine for hepatitis C
- are a carrier of the HIV virus
- have had or are waiting for a liver transplant

2.3 Blood tests and monitoring

The doctor will refer you for blood tests to evaluate liver functions before and during treatment with ZEPATIER.

2.4 Interactions with other medicines

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, you should inform the doctor or pharmacist. ZEPATIER may affect the way other medicines work, and other medicines may affect how ZEPATIER works.

Especially if you are taking:

- bosentan
- a combination HIV treatment containing cobicistat, elvitegravir, emtricitabine, and tenofovir
- etravirine
- oral ketoconazole
- modafinil
- nafcillin
- tacrolimus
- certain statins (atorvastatin, fluvastatin, lovastatin, rosuvastatin, or simvastatin)

Also see section 2.1 "Do not use ZEPATIER if".

- Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist when you get a new medicine.
- If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking ZEPATIER.

2.5 Taking ZEPATIER with food

Take ZEPATIER with or without food.

2.6 Pregnancy and breastfeeding

- Tell your doctor if you are pregnant or trying to get pregnant. ZEPATIER has not been studied in pregnant women. We do not know if ZEPATIER will harm your baby while you are pregnant.
 - **Males and females who take ZEPATIER and ribavirin should also read the ribavirin patient leaflet for important pregnancy, contraception, and infertility information.**
- Tell your doctor if you are breastfeeding or plan to breastfeed. We do not know if ZEPATIER gets in your breast milk and gets passed to your baby.
 - **Talk to your doctor about the best way to feed your baby during treatment with ZEPATIER.**

2.7 Children and adolescents

It is not known if ZEPATIER is safe or effective in children under 18 years old.

3. HOW SHOULD YOU USE ZEPATIER?

Always take **ZEPATIER** as instructed by the doctor. You should check with your doctor or pharmacist if you are not sure.

The dosage and treatment regimen will be determined by the doctor only.

Take one ZEPATIER tablet at the same time every day.

Swallow the tablet whole. Tell your doctor or pharmacist if you have problems swallowing tablets.

No information is available regarding crushing/splitting/chewing of tablets.

Do not exceed the recommended dose.

ZEPATIER comes in a blister package of individually-packaged tablets. Keep the tablets in this package until you are ready to take your dose.

Take **ZEPATIER** with or without food.

Do not stop taking **ZEPATIER** without first talking with your doctor.

If you have accidentally taken a higher dose than you should

If you take more than your prescribed dose, call your doctor right away.

If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a hospital emergency room and bring the package of the medicine with you.

If you have forgotten to take ZEPATIER

- Do not take two doses of **ZEPATIER** at the same time to make up for a missed dose.
- If you are not sure what to do, call your doctor or pharmacist. It is important that you do not miss or skip doses of **ZEPATIER** during treatment.

Complete the full course of treatment as instructed by the doctor.

Even if there is an improvement in your health, do not discontinue use of this medicine before consulting your doctor.

Do not take medicines in the dark! Check the label and the dose each time you take your 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, **ZEPATIER** can cause side effects, in some of the users.

Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

ZEPATIER can cause serious side effects, including:

Hepatitis B virus reactivation. See "What is the most important information I should know about **ZEPATIER**?"

Signs of liver problems. ZEPATIER may cause increases in your liver-related blood tests. This could be a sign of serious liver problems. Your doctor will do blood tests to check your liver before and during treatment with **ZEPATIER**. Tell your doctor right away if you get any of the following symptoms or if they get worse during treatment with **ZEPATIER**:

- loss of appetite
- nausea and vomiting
- feeling tired or weak
- confusion
- sleepiness
- vomiting of blood
- yellowing of your skin or eyes
- color changes in your stool or urine
- bleeding or bruising more easily than normal
- diarrhea
- swelling of the stomach area (abdomen) or pain in the upper right side of the stomach area

Common side effects (appear in 1-10 people in 100) of ZEPATIER when used without ribavirin include:

- feeling tired
- Headache
- Nausea
- trouble sleeping
- diarrhea
- stomach pain
- depression
- feeling irritable

Common side effects (appear in 1-10 people in 100) of ZEPATIER when used with ribavirin include:

- low red blood cell counts (anemia)
- headache
- feeling tired
- shortness of breath
- rash or itching
- feeling irritable
- stomach pain
- depression
- joint pain

If you have any side effect that bothers you or that does not go away, tell your doctor.

There may be other side effects to **ZEPATIER** that are not listed. Call your doctor for medical advice about side effects.

If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link: <https://sideeffects.health.gov.il/>

5. HOW TO STORE ZEPATIER?

- Avoid Poisoning! This medicine, as all other medicines, must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor!
- Do not use **ZEPATIER** after the expiry date (exp. date) which is stated on pack. The expiry date refers to the last day of the indicated month.
- Keep **ZEPATIER** in its original packaging (blister package) until you are ready to take it. Do not take the tablets out of the original blister package to store in another container such as a pill box. This is important because the tablets are sensitive to moisture. The package is designed to protect them.
- Store **ZEPATIER** up to 30°C.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

6.1 What ZEPATIER contains?

- The active ingredients are elbasvir and grazoprevir.
- In addition to the active ingredients the medicine also contains inactive ingredients: mannitol, copovidone, hypromellose 2910, croscarmellose sodium, sodium chloride, microcrystalline cellulose, lactose monohydrate, vitamin E polyethylene glycol succinate, sodium lauryl sulfate, magnesium stearate and colloidal silicon dioxide. The tablets are film-coated with a coating material containing the following inactive ingredients: lactose monohydrate, hypromellose 2910, titanium dioxide, triacetin, iron oxide yellow, iron oxide red, ferrousferic oxide, and carnauba wax.

6.2 What ZEPATIER looks like and contents of the pack

ZEPATIER is an oval-shaped, beige tablet with the number 770 on one side and plain on the other.

Pack size:

28 tablets - carton containing 2 packages, each package contains 14 tables.

6.3 License Holder:

Merck Sharp & Dohme (Israel-1996) Company Ltd., P.O.Box 7121, Petah-Tikva 49170.

6.4 Manufacturer:

Merck Sharp & Dohme Corp., New-Jersey, USA.

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Drug registration no. listed in the official registry of the Ministry of Health:

156-43-34620