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

The medicine is dispensed according to a physician's prescription only

Hepsera

Tablets

Each tablet contains 10 mg Adefovir dipivoxil.

For the list of the inactive and allergenic ingredients in the medicine, see section 2 – "Important information about some of the ingredients in the medicine" and section 6 – "Additional information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the physician or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Hepsera is used to treat chronic hepatitis B in adults with:

- compensated liver disease with evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active liver inflammation and fibrosis.
  Initiation of Hepsera treatment should only be considered when the use of an alternative antiviral agent with a higher genetic barrier to resistance is not available or appropriate.
- decompensated liver disease in combination with a second agent without cross-resistance to Hepsera.

Therapeutic group:

Hepsera belongs to a group of medicines called antiviral medicines.

Infection with the hepatitis B virus leads to damage to the liver. Hepsera reduces the amount of the virus in your body, and has been shown to reduce liver damage.

Compensated liver disease – a disease in which the liver is damaged, but still functions at a certain level.
Decompensated liver disease – a liver disease in which the liver is seriously damaged and is not capable of functioning properly.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to adefovir, adefovir dipivoxil or to any of the additional ingredients contained in this medicine (listed in section 6).
- **Tell your physician at once** if you could be allergic to adefovir, adefovir dipivoxil or any of the additional ingredients of Hepsera.

Special warnings regarding use of the medicine

Before the treatment with Hepsera, tell the physician if:

- **you have had kidney disease,** or if tests have shown problems with your kidneys. Hepsera can affect the way your kidneys work. The risk of this occurring is increased with long-term use of Hepsera. Your physician should run tests to check your kidneys and liver are working properly, before and during your treatment. Depending on the results, your physician may change how often you take Hepsera.
- you are over 65 years of age; your physician may monitor your health more closely.
- **Do not stop taking Hepsera** without your physician's advice.
- **After stopping treatment with Hepsera, tell your physician immediately** about any new, unusual or worsening symptoms that you notice after stopping treatment. Some patients have had symptoms or blood tests indicating that their hepatitis has worsened after stopping treatment with Hepsera. It is best for your physician to monitor your health after stopping treatment with Hepsera. You may need blood tests for several months after treatment.
- **Once you start taking Hepsera:**

- look out for possible signs of lactic acidosis – see section 4, “Side effects”.
- your physician will perform blood tests every three months to check that Hepsera is keeping your chronic hepatitis B infection under control.

- Take care not to infect other people. Hepsera does not reduce the risk of passing on HBV to others through sexual contact or blood contamination. You must continue to take precautions to avoid this. A vaccine is available to protect people at risk from becoming infected with HBV.
- If you are a carrier of HIV, this medicine will not control your HIV infection.

Children and adolescents

- Do not use Hepsera in children or adolescents under 18 years of age.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the physician or pharmacist.

- Do not take Hepsera if you are taking any medicines containing tenofovir.

- It is especially important to tell your physician if you are taking, or have recently taken, any of the following medicines which may damage your kidneys, or interact with Hepsera:
  - vancomycin and aminoglycosides, to treat bacterial infections
  - amphotericin B, to treat fungal infections
  - foscarnet, cidofovir or tenofovir disoproxil fumarate, to treat viral infections
  - pentamidine, to treat other types of infection.

Using the medicine and food

Hepsera can be taken with or without food.

Pregnancy, breast-feeding and fertility

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

- Tell your physician immediately if you are pregnant or planning to become pregnant. It is not known whether Hepsera is safe to use during pregnancy.

- **Use an effective method of contraception** to avoid becoming pregnant if you are a woman of child-bearing age taking Hepsera.
- **Do not breast-feed while taking Hepsera.** It is not known whether the active substance in this medicine passes into breast milk.

Driving and using machines

It is unlikely that this medicine will affect your ability to drive or use machines.

Important information about some of the ingredients of the medicine

Hepsera contains lactose. If you are lactose-intolerant, or if you have been told that you have an intolerance to some sugars, talk to your physician before taking Hepsera.

Hepsera contains sodium

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

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions. This is to make sure that your medicine is fully effective and to reduce the development of resistance to the treatment. Check with the physician or pharmacist if you are uncertain about the preparation dosage and treatment regimen.

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

- The recommended dosage is usually one 10 mg tablet each day, taken orally with or without food.
- **A different dosage** may be given to patients with **kidney problems.**

Do not exceed the recommended dose.

Hepsera Tablets are provided in a bottle with a child-resistant cap.

Directions for opening the bottle - in order to remove the cap, press down, while turning it to the left at the same time (counterclockwise).

Directions for closing the bottle - close the bottle well with the cap; turn it to the right (clockwise) until it is completely closed.

There is no information regarding crushing or chewing the tablets
Do not halve the tablet - there is no score line on the tablet.

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

If you forgot to take this medicine
It is important not to forget a dose.
- **If you forgot a dose** of Hepsera, take it as soon as you can, and then take your next scheduled dose at its regular time.
- **If it is nearly time for your next dose,** skip the forgotten dose. Wait and take the next dose at the regular time. Do not take a double dose to make up for a forgotten tablet (two doses close together).
- **If you vomit (are sick) less than one hour after taking Hepsera,** take another tablet. You do not need to take another tablet if you are sick more than one hour after taking Hepsera.

If you stop taking the medicine
- **Tell your physician immediately about any new,** unusual or worsening symptoms that you notice after stopping the treatment. See section 2 for more details.
- **Do not stop taking Hepsera** without your physician's instruction.

Adhere to the treatment regimen recommended by your physician. Even if your health condition improves, do not stop treatment with the medicine without consulting the physician, as your symptoms may get worse.
Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the physician or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Hepsera may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

Very rare side effects

These may affect **up to 1 in 10,000** people

- **Lactic acidosis is a serious but very rare side effect.** It can cause too much lactic acid in the blood and enlargement of the liver. Lactic acidosis occurs more often in women, particularly if they are very overweight. People with liver disease may also be at risk.

  Some of the signs of lactic acidosis are:

  • Nausea (feeling sick) and vomiting (sickness)

  • Stomach pain

  Contact your physician at once if you get any of these symptoms. They are the same as some of the common side effects of Hepsera. If you do get any of them, it is unlikely to be serious, but you need to check. Your physician will monitor you regularly while you are taking Hepsera.

Uncommon side effects

These may affect **up to 1 in 100** people:

• Damage to kidney tubule cells

Common side effects

These may affect **up to 1 in 10** people:

• Headaches

• Nausea (feeling sick)

• Diarrhoea

• Digestive problems, including wind or discomfort after meals

• Stomach pain

• Kidney problems, as shown by blood tests

Tell a physician or pharmacist if you are worried about any of these.

Very common side effects

These may affect **more than 1 in 10** people:

• Weakness

Tell a physician or pharmacist if you are worried about this.

Side effects before or after having a liver transplant

Some patients have experienced:

• Rash and itching – common

• Nausea (feeling sick) or vomiting (being sick) – common

• Kidney failure – common

• Kidney problems – very common

Tell a physician or pharmacist if you are worried about any of these.

• Also, tests may show a decrease in phosphate (common) or increases in creatinine (very common) in the blood.

Additional side effects

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

• Kidney failure

• Kidney problems that may lead to softening of the bones (which causes bone pain and sometimes leads to fractures) and muscle pain or weakness

• Inflammation of the pancreas (pancreatitis)

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult with the physician.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

https://sideeffects.health.gov.il/

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed 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 the physician.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Do not store above 30ºC. Store in the original package in order to protect from moisture. Keep the bottle tightly closed.
- Can be used within 30 days after first opening.
- Do not discard medicines in the wastewater or household waste bin. Ask the pharmacist how to dispose of medicines that are no longer in use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

- In addition to the active ingredient the medicine also contains:
  Lactose monohydrate, croscarmellose sodium, talc, pregelatinised starch, and magnesium stearate.
  Also see section 2 in this leaflet - “Important information about some of the ingredients in the medicine”.
- What the medicine looks like and the contents of the package:
  Hepsera 10 mg tablets are white to off-white, round, flat-faced tablets with a beveled edge and debossed with “GS KNU” on one side and blank on the other side. Hepsera 10 mg tablets are supplied in bottles of 30 tablets with a child-resistant cap, and with a silica gel desiccant. The silica gel desiccant is contained in either a separate sachet or a small canister and should not be swallowed.
- License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer: Patheon Inc., Mississauga, Canada.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 129-97-30889

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