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

The medicine is dispensed with a physician's prescription only

Retrovir Capsules 250 mg

Each Retrovir capsule 250 mg contains 250 mg zidovudine.

Inactive and allergenic ingredients in the preparation - see section 6 "Further information" and section 2 "Important information about some of the ingredients of the medicine".

Read this 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?

Retrovir is used together with additional anti-retroviral medicines to treat adults and children infected with human immunodeficiency virus (HIV).

Preventive treatment with Retrovir is indicated for pregnant and HIV-positive women (after the 14th week of pregnancy) to prevent intrauterine infection of the fetus and for primary prevention of HIV infection in a newborn baby.

Therapeutic group: The active ingredient in Retrovir is zidovudine. Retrovir belongs to a group of medicines called *nucleoside analogue reverse transcriptase inhibitors (NRTIs)*.

Retrovir does not eliminate the HIV virus; it reduces the amount of virus in your body, and keeps it at a low level. Retrovir increases the CD4 *cell count* in your blood. CD4 cells are a type of white blood cells that are important in helping your body to fight infection.

HIV infection is spread by sexual contact with someone who is infected, or by transfer of infected blood (for example, when sharing injection needles).

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- **you are sensitive** (allergic) to the active ingredient or any of the additional ingredients contained in the medicine (as listed in section 6).
- **you have a very low white blood cell count** (*neutropenia*) **or a very low red blood cell count** (*anemia*).

Retrovir for newborn babies:

Retrovir must not be given to some newborn babies with liver problems, including:

- some cases of *hyperbilirubinemia* (increased amounts in the blood of a substance called *bilirubin* which may make the skin appear yellow).
- other problems which cause high levels of liver enzymes in the blood.

Special warnings regarding use of this medicine

Some people taking Retrovir or combination therapy for HIV are at higher risk of serious side effects. You need to be aware of the extra risks:

- **if you have ever had liver disease** (including hepatitis B or C)
- **if you are seriously overweight** (especially if you are a woman)

→ **Talk to your physician if any of these apply to you.** You may need extra check-ups, including blood tests, while you are taking your medicine. **See Section 4 for more information.**

Pay attention to important symptoms

Some people taking medicines to treat HIV infection, develop other problems, which can be serious. You need to know about important signs and symptoms to look out for while you are taking Retrovir.

Read the information in Section 4 of this leaflet. If you have any questions about this information or the advice given:

→ **Consult with the physician.**

Tests and follow-up

For as long as you are taking Retrovir, your physician will refer you to regular blood tests to monitor side effects. Further information regarding these side effects appears in Section 4 of this leaflet.

Other medicines and Retrovir

If you are taking, or have recently taken, other medicines, including non-prescription medicines or nutritional supplements, tell the physician or pharmacist. Remember to inform your physician or the pharmacist if you start taking a new medicine during treatment with Retrovir.

Especially inform the physician or pharmacist if you are taking:

Do not take these medicines with Retrovir:

- **stavudine**, used to treat **HIV infection**
- **ribavirin** or injections of ganciclovir to treat **viral infections**
- **rifampicin**, which is an **antibiotic**.

Some medicines can make it more likely that you will have side effects, or make side effects worse.

These include:

- **sodium valproate**, used to treat **epilepsy**
- **aciclovir, ganciclovir** or **interferon**, used to treat **viral infections**
- **pyrimethamine**, used to treat **malaria** and other parasitic infections
- **dapsone**, used to prevent **pneumonia** and treat **skin infections**
- **fluconazole** or **flucytosine**, used to treat **fungal infections** such as **candida**
- **pentamidine** or **atovaquone**, used to treat parasitic infections such as **PCP**
- **amphotericin** or **co-trimoxazole**, used to treat **fungal and bacterial infections**
- **probenecid**, used to treat **gout** and similar conditions, and given with some antibiotics to increase their effectiveness
- **methadone**, used as a **heroin substitute**
- **vincristine, vinblastine** or **doxorubicin**, used to treat **cancer.**

→ **Tell your physician** if you are taking any of these.

Some medicines interact with Retrovir

These include:

- **clarithromycin**, which is an **antibiotic**
- **phenytoin**, used for treating **epilepsy**

→ **Tell your physician** if you are taking clarithromycin or phenytoin. Your physician may need to monitor you while you are taking Retrovir.

Pregnancy, breastfeeding and fertility

Pregnancy

If you are pregnant, become pregnant, or are planning to become pregnant:

→ **Talk to your physician** about the risks and benefits of taking Retrovir.

If pregnant women who are HIV-positive take Retrovir, they are less likely to pass the HIV infection on to their unborn babies.

Retrovir and similar medicines may cause side effects in unborn babies. If you have taken Retrovir during pregnancy, your physician may refer you for regular blood tests and other diagnostic tests to monitor the development of your child. In children whose mothers took NRTI medicines during pregnancy, the benefit from protection against contraction of HIV outweighed the risk of side effects.

Breastfeeding

Women who are HIV-positive must not breastfeed, because HIV infection can be passed on to the baby in breast milk.

A small amount of the ingredients in Retrovir can also pass into your breast milk.

If you are breastfeeding, or thinking about breastfeeding:

→ **Consult with your physician immediately.**

Driving and operating machinery

Retrovir can make you dizzy and have other side effects that make you less alert.

→ **Do not drive or operate machinery** unless you are feeling well.

Stay in regular contact with your physician

Retrovir helps to control your condition, but it does not cure the HIV infection. You need to keep taking it every day to stop your illness from getting worse. You may still develop other illnesses and infections linked to HIV infection.

→ **Keep in touch with your physician, and do not stop taking Retrovir** without your physician's advice.

Protect other people

HIV infection is spread by sexual contact with a person who has the infection, or by transfer of infected blood (for example, by sharing injection needles). You can still pass on HIV when taking this medicine, although the risk is lowered with effective anti-retroviral therapy.

Discuss with your physician the precautions needed to avoid infecting other people.

Important information about some of the ingredients of the medicine

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

3. HOW SHOULD YOU USE THE MEDICINE?

Always use this preparation according to the physician's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

Swallow the capsule whole with water. The dosage and treatment regimen will be determined by the physician only.

There is no information regarding opening and dispersing the capsule.

The usual dosage is generally:

Adults and adolescents weighing at least 30 kg:

The usual dose of Retrovir is 250 mg, twice a day. Take each dose 12 hours apart.

Children:

Your child can take Retrovir in liquid form or as 100 mg capsules.

Pregnancy, childbirth and newborn babies:

Do not take Retrovir during the first 14 weeks of pregnancy. After week 14, the usual dose is 500 mg each day, given as a 100 mg capsule, five times per day, until you go into labor. During the labor and birth, your physician may give you injections of Retrovir, until your baby's umbilical cord has been clamped. Your newborn baby may also be given Retrovir to help prevent it from becoming infected with HIV.

People with kidney or liver problems:

If you have severe kidney or liver problems, you may be given a lower dose of Retrovir, depending on how well your kidneys or liver are functioning. Follow your physician's advice.

Do not exceed the recommended dose.

If you accidentally took a higher dosage, refer to your physician or pharmacist for advice. If possible, show them the Retrovir pack.

If you **accidentally took a higher dosage** or if a child has accidentally swallowed the medicine, refer immediately to a physician or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine at the scheduled time, do not worry. You can take your next dose as soon as you remember, but not within two hours of your next dose. If you remember within two hours of your next dose, skip the dose you missed and take the next dose at the usual time. Then continue your treatment as before.

Do not take a double dose to make up for a missed dose.

Adhere to the treatment regimen as recommended by the physician. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the physician.

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

During HIV therapy, there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and lifestyle, and in the case of blood lipids, sometimes to the HIV medicines themselves. Your physician will test for these changes.

Treatment with zidovudine (Retrovir) often causes a loss of fat from legs, arms and face (lipoatrophy). This loss of body fat has been shown to be not fully reversible after discontinuation of zidovudine. Your physician should monitor for signs of lipoatrophy. Tell your physician if you notice any loss of fat from your legs, arms and face. When these signs occur, stop Retrovir treatment. The physician will change your HIV treatment.

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

Some side effects may show up in your blood tests, and may not appear until 4-6 weeks after you start taking Retrovir.

If you get any of these effects, and if they are severe, your physician may advise you to stop taking Retrovir.

→ **As well as the effects listed below**, other effects can develop during combination therapy for HIV. It is important to read the information in 'Other possible side effects of combination therapy for HIV'.

Very common side effects

These may occur **in more than 1 in 10** people taking Retrovir:

- headaches
- nausea.

Common side effects

These may occur **in up to 1 in 10** people taking Retrovir:

- vomiting
- diarrhea
- stomach pains
- feeling dizzy
- aching muscles
- generally feeling unwell.

Common side effects that may show up in your blood tests are:

- a low red blood cell count (*anemia*) or low white blood cell count (*neutropenia or leucopenia*)
- an increase in the level of liver enzymes
- an increased amount in the blood of *bilirubin* (a substance produced in the liver) which may cause your skin to appear yellow.

Uncommon side effects

These may occur **in up to 1 in 100** people taking Retrovir:

- skin rash (red, raised or itchy skin)
- feeling breathless (choking)
- fever
- general aches and pains
- wind (flatulence)
- weakness.

An uncommon side effect that may show up in your blood tests is:

- a decrease in the number of cells involved in blood clotting (*thrombocytopenia*), or in all types of blood cells (*pancytopenia*).

Rare side effects

These may occur in **up to 1 in 1,000** people taking Retrovir:

- lactic acidosis (excess lactic acid in the blood; see below, 'Other possible side effects of combination therapy for HIV')
- liver disorders, such as jaundice, enlarged liver or fatty liver
- inflammation of the pancreas
- chest pain, disease of the heart muscle
- fits (convulsions)
- feeling depressed or anxious, not being able to sleep (insomnia), not being able to concentrate, feeling drowsy
- indigestion, loss of appetite, taste disturbance
- changes in the color of your nails, your skin, or the skin inside your mouth
- a flu-like feeling, chills, sweating and cough
- tingling sensation in the skin (pins and needles)
- passing urine more often
- enlarged breasts in men.

A rare side effect that may show up in your blood tests is:

- a decrease in the number of a type of red blood cell (*pure red cell aplasia*).

Very rare side effects

A very rare side effect that may occur in **up to 1 in 10,000** people taking Retrovir, and may show up in blood tests is:

- a failure of the bone marrow to produce new blood cells (*aplastic anemia*).

Other possible side effects of combination therapy for HIV

A number of other effects may develop during HIV treatment.

Old infections may flare up

People with advanced HIV infection (AIDS) have weak immune systems, and are more likely to develop serious infections (*opportunistic infections*). When these people start treatment, they may find that old, hidden infections flare up, causing signs and symptoms of inflammation. These symptoms are probably caused by the body's immune system becoming stronger, so that the body starts to fight these infections.

In addition to the opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking medicines for the treatment of your HIV infection. Autoimmune disorders may occur many months after the start of treatment. If you notice any symptoms of infection or other symptoms such as muscle weakness, weakness beginning in the hands and feet and spreading up towards the trunk of the body, palpitations, tremor or hyperactivity, refer to your physician immediately to receive the necessary treatment.

If you suffer from symptoms of infection while you are taking Retrovir:

→ **Tell your physician immediately.** Do not take other medicines against the infection without consulting your physician.

Lactic acidosis is a rare but serious side effect

Some people taking Retrovir develop a condition called lactic acidosis, together with an enlarged liver. Lactic acidosis is caused by a build-up of lactic acid in the body. It is rare. If it happens, it usually develops after a few months of treatment. It can be life-threatening, causing failure of internal organs.

Lactic acidosis is more likely to develop in people who have liver diseases, or in obese (very overweight) people, especially women.

Signs of lactic acidosis include:

- **deep, rapid, difficult breathing**
- **drowsiness**
- **numbness** or **weakness** in the limbs
- **loss of appetite, weight loss**
- **nausea, vomiting**
- **stomach pain.**

During your treatment, your physician will monitor you for signs of lactic acidosis. If you have any of the symptoms listed above, or other symptoms that worry you:

→ **Refer to your physician as soon as possible.**

You may have problems with your bones

Some people receiving combination therapy for HIV develop a condition called osteonecrosis. With this condition, parts of the bone tissue die because of reduced blood supply to the bone.

People may be more likely to get this condition:

- if they have been taking combination therapy for a long time
- if they are also taking anti-inflammatory medicines called corticosteroids
- if they drink alcohol
- if their immune systems are very weak
- if they are overweight.

Signs of osteonecrosis include:

- **stiffness in the joints**
- **aches and pains** (especially in the hip, knee or shoulder)
- **difficulty moving.**

If you notice any of these symptoms:

→ **Tell your physician.**

Other effects may show up in tests

Combination therapy for HIV can also cause:

- **increased levels of lactic acid** in the blood, which on rare occasions can lead to lactic acidosis

This effect may show up in the blood tests you will undergo while taking Retrovir.

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.

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 SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, must be kept 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 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 30°C. Store in the original package.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Maize starch, microcrystalline cellulose, sodium starch glycollate, magnesium stearate, gelatin, titanium dioxide E171, indigo carmine E132, black inks opacode 10A1 or 10A2 (shellac, black iron oxide E172, propylene glycol, ammonium hydroxide 28% [in black ink opacode 10A1 only], strong ammonium solution [in black ink opacode 10A2 only], potassium hydroxide [in black ink opacode 10A2 only]).
- What the medicine looks like and the contents of the package:
  Retrovir Capsules 250 mg are marked with 'GSJV2'. They are white and blue and supplied in aluminum blister packs containing 40 capsules.
- License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer:
  1. S.C. Europharm S.A., Brasov, Romania.
  2. GlaxoSmithKline Pharmaceuticals S.A., Poznan, Poland.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 024-28-25361

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