

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

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

## **Retrovir Oral Solution**

**Each 1 ml of oral solution contains 10 mg zidovudine.**

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?**

**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 infection; 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 zidovudine or to any of the additional ingredients contained in this medicine (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 of a substance in the blood 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 the medicine

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

- **If you have ever had a 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 for HIV infection develop other conditions, which can be serious. You need to know about important signs and symptoms to look out for while you are taking Retrovir.

**Please 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 send you for regular blood tests to monitor side effects. Further information regarding these side effects appears in Section 4 of this leaflet.

### **Drug interactions**

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

Remember to tell your physician or pharmacist if you begin taking a new medicine during treatment with Retrovir.

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

### **Pregnancy and breast-feeding**

#### **Pregnancy**

If you are pregnant, if you become pregnant, or if you 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 NRTIs during pregnancy, the benefit from protection against contraction of HIV outweighed the risk of side effects.

#### **Breast-feeding**

Breast-feeding is **not recommended** for women who live with HIV, 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 breast-feeding, or thinking about breast-feeding, you should **consult your physician as soon as possible**.

### **Driving and using machines**

**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.

### **Important information about some of the ingredients in the medicine**

Retrovir oral solution contains **maltitol**, a sugar. If you have been told by your physician that you have an intolerance to some sugars, contact your physician before taking this medicine. There may be a mild laxative effect. Maltitol contains 2.3 kilocalories per gram.

This medicine contains 2 mg **sodium benzoate** per ml. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks of age).

This medicine contains 9.6 mg **propylene glycol** in each ml. If your baby is less than 4 weeks old, talk to your physician or pharmacist before giving them this medicine, in particular if the baby is given other medicines that contain propylene glycol or alcohol.

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

### **Stay in regular contact with your physician**

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

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

### 3. HOW SHOULD YOU USE THE MEDICINE?

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

#### **Adults and adolescents weighing at least 30 kg:**

The usual dose of Retrovir is 25 ml (250 mg) or 30 ml (300 mg) twice a day. Take each dose 12 hours apart.

#### **Children weighing at least 9 kg and less than 30 kg:**

Your physician will decide on the correct dosage of Retrovir for your child, according to the child's weight. Your child can also take Retrovir 100 mg capsules.

The usual dose is 0.9 ml (9 mg) per kg of bodyweight twice a day, but no more than 30 ml (300 mg) twice a day.

#### **Children weighing at least 4 kg and less than 9 kg:**

Your physician will decide on the correct dosage of Retrovir for your child, according to the child's weight.

The usual dose is 1.2 ml (12 mg) per kg of bodyweight twice a day. If your baby cannot take medicines orally, your physician may decide to give your baby an injection of Retrovir instead.

#### **Pregnancy, childbirth and newborn babies:**

You should not take Retrovir during the first 14 weeks of pregnancy. After week 14, the usual dose is 50 ml (500 mg) each day given as 10 ml (100 mg) 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.

Your physician will determine the appropriate dosage of Retrovir for your baby, according to the baby's weight.

The usual dose of Retrovir Solution is 0.2 ml/kg (2 mg/kg) starting from birth, and then every 6 hours up to the age of 6 weeks (for example, a baby weighing 3 kg will need a dose of 0.6 ml oral solution every 6 hours).

The amount of liquid medicine to be given by mouth to your baby is very small; therefore, use an appropriately sized syringe, designated for small volumes (e.g., a 1 ml syringe).

**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.**

**Step-by-step instructions**

Use the oral-dosing syringe supplied with the pack to measure your dose accurately.

1. Remove the plastic wrap from the syringe/adaptor.
2. Remove the adaptor from the syringe.
3. **Remove the bottle cap** and keep it safely. Opening instructions - to remove the cap, press down, while simultaneously twisting to the left (turning counterclockwise).
4. **Push the plastic adaptor into the neck of the bottle**, while holding the bottle firmly.
5. **Insert the syringe** firmly into the adaptor.
6. **Turn the bottle upside down.**
7. **Pull out the syringe plunger** until the first portion of your full dose is withdrawn.
8. **Turn the bottle the right way up** and remove the syringe from the adaptor.

9. **Put the syringe into your mouth**, placing the tip of the syringe against the inside of the cheek. **Slowly push the plunger in**, allowing time to swallow. Do not push too hard and squirt the liquid into the back of the throat or you may choke.
10. **Repeat steps 5 to 9 in the same way until you have taken the whole dose.**
11. **Do not leave the syringe in the bottle.** Take the syringe and the adaptor off and wash them thoroughly with clean water. Let them dry completely before you use them again.
12. **Close the bottle tightly with the cap.** Closing instructions - place cap on top of open end and twist to the right (turning clockwise) until it locks.

If you take too much Retrovir, contact your physician or pharmacist for advice. If possible, show them the Retrovir pack.

**If you accidentally have taken 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, take a dose as soon as you remember, unless the next scheduled dose is in the next two hours or before. If you remember within two hours of your next dose, just skip the dose you missed and take your 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 recommended by your physician.

Even if your health condition improves, 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 life style, 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, Retrovir should be stopped. Your 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 reading 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 to 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 affect **more than 1 in 10** people:

- headaches
- nausea.

### Common side effects

These may affect up to 1 in 10 people:

- 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 affect up to 1 in 100 people:

- 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 affect **up to 1 in 1,000** people:

- lactic acidosis (excess lactic acid in the blood; see “Other possible side effects of combination therapy for HIV” below)
- 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 of 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 certain type of red blood cell (*pure red cell aplasia*).

## **Very rare side effects**

A very rare side effect that may affect **up to 1 in 10,000** people, and may show up in your 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 disease, 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 any other symptoms that worry you:

→ **See your physician as soon as possible.**

### **You may have problems with your bones**

Some people taking 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 system is 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.**

### 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](http://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 30°C. Keep the bottle in the outer carton. Can be used for one month after 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:  
Maltitol solution, glycerol, citric acid, E211 sodium benzoate, saccharin sodium, flavour strawberry (contains propylene glycol (E1520)), flavour white sugar (contains propylene glycol (E1520)), and purified water.
- What the medicine looks like and the contents of the package:  
**Retrovir oral solution** is a clear, pale yellow, strawberry-flavored, sugar-free solution containing **100 mg** of the active ingredient zidovudine per 10 ml.  
**Retrovir oral solution** is supplied in bottles of 200 ml. An oral-dosing syringe of 1 ml or 10 ml is included in the pack, with an adaptor, which should be fitted to the bottle before use. The bottle is closed with a child-resistant cap.

- License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer: ViiV Healthcare UK Ltd., Brentford, England.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 062-69-27513

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