

Package leaflet: Information for the user

Combivir 150 mg/300 mg film-coated tablets *lamivudine/zidovudine*

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them even if their signs of illness are the same as yours.
- If you get any of the side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Combivir is and what it is used for
2. What you need to know before you take Combivir
3. How to take Combivir
4. Possible side effects
5. How to store Combivir
6. Contents of the pack and other information

1. What Combivir is and what it is used for

Combivir is used to treat HIV (human immunodeficiency virus) infection in adults and children.

Combivir contains two active ingredients that are used to treat HIV infection: lamivudine and zidovudine. Both of these belong to a group of antiretroviral medicines called *nucleoside analogue reverse transcriptase inhibitors (NRTIs)*.

Combivir does not completely cure HIV infection; it reduces the amount of virus in your body, and keeps it at a low level. It also 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.

Not everyone responds to treatment with Combivir in the same way. Your doctor will monitor the effectiveness of your treatment.

2. What you need to know before you take Combivir

Do not take Combivir:

- if you are **allergic** to lamivudine or zidovudine, or any of the other ingredients of this medicine (listed in section 6)
- if you have a **very low red blood cell count** (*anaemia*) or a **very low white blood cell count** (*neutropenia*).

Check with your doctor if you think any of these apply to you.

Take special care with Combivir

Some people taking Combivir or other combination treatments for HIV are more at 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 have hepatitis B infection, do not stop Combivir without your doctor's advice, as your hepatitis may come back)
- if you have **kidney disease**
- if you are seriously **overweight** (especially if you are a woman)

Talk to your doctor if any of these apply to you. Your doctor will decide if the active substances are suitable for you. You may need extra check-ups, including blood tests, while you are taking your medicine. See Section 4 for more information.

Look out for 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 Combivir.

Read the information 'Other possible side effects of combination therapy for HIV' in Section 4 of this leaflet.

Other medicines and Combivir

Tell your doctor or pharmacist if you are taking any other medicines, or if you have taken any recently, including herbal medicines or other medicines you bought without a prescription.

Remember to tell your doctor or pharmacist if you begin taking a new medicine while you are taking Combivir.

These medicines should not be used with Combivir:

- other medicinal products containing lamivudine, to treat **HIV infection or hepatitis B infection**
- emtricitabine, to treat **HIV infection**
- stavudine, to treat **HIV infection**
- ribavirin or injections of ganciclovir to treat **viral infections**
- high doses of **co-trimoxazole**, an antibiotic
- cladribine, used to treat **hairy cell leukaemia**

Tell your doctor if you are being treated with any of these.

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

These include:

- sodium valproate, to treat **epilepsy**
- interferon, to treat **viral infections**
- pyrimethamine, to treat **malaria** and other parasitic infections
- dapson, to prevent **pneumonia** and treat skin infections
- fluconazole or flucytosine, to treat **fungal infections** such as **candida**
- pentamidine or atovaquone to treat parasitic infections such as *Pneumocystis jirovecii* pneumonia (often referred to as **PCP**)
- amphotericin or co-trimoxazole, to treat **fungal and bacterial infections**
- probenecid, to treat **gout** and similar conditions, and given with some antibiotics to make them more effective
- **methadone**, used as a **heroin substitute**
- vincristine, vinblastine or doxorubicin, to treat **cancer**.

Tell your doctor if you are taking any of these.

Some medicines interact with Combivir

These include:

- **clarithromycin**, an antibiotic

if you are taking clarithromycin, take your dose at least 2 hours before or after you take your Combivir.

- **phenytoin**, for treating **epilepsy**.

Tell your doctor if you are taking phenytoin. Your doctor may need to monitor you while you are taking Combivir.

- medicines (usually liquids) containing **sorbitol and other sugar alcohols** (such as xylitol, mannitol, lactitol or maltitol), if taken regularly.

Tell your doctor or pharmacist if you are being treated with any of these.

Pregnancy

If you are pregnant, if you become pregnant or if you are planning to become pregnant talk to your doctor about the risks and benefits to you and your baby of taking Combivir.

Combivir and similar medicines may cause side effects in unborn babies. If you have taken Combivir during your pregnancy, your doctor may request 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 the protection against HIV outweighed the risk of side effects.

Breast-feeding

Breast-feeding is **not recommended** in women living with HIV because HIV infection can be passed on to the baby in breast milk.

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

If you're breast-feeding, or thinking about breast-feeding, you should **discuss it with your doctor as soon as possible**.

Driving and using machines

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

Do not drive or operate machines unless you are feeling well.

Combivir contains sodium

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

3. How to take Combivir

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

Swallow Combivir tablets, with some water. Combivir can be taken with or without food.

If you cannot swallow the tablets whole, you may crush and combine them with a small amount of food or drink, and take all the dose immediately.

Stay in regular contact with your doctor

Combivir helps to control your condition. You need to keep taking it every day to stop your illness getting worse. You may still develop other infections and illnesses linked to HIV infection.

Keep in touch with your doctor, and do not stop taking Combivir without your doctor's advice.

How much to take

Adults and adolescents 30 kg or more

The usual dose of Combivir is one tablet twice a day.

Take the tablets at regular times, leaving approximately 12 hours between each tablet.

Children who weigh between 21 and 30 kg

The usual starting dose of Combivir is one half tablet ($\frac{1}{2}$) taken in the morning and one whole tablet taken in the evening.

Children who weigh between 14 and 21 kg

The usual starting dose of Combivir is one half tablet ($\frac{1}{2}$) taken in the morning and one half tablet ($\frac{1}{2}$) taken in the evening.

For children who weigh less than 14 kg lamivudine and zidovudine (the ingredients of Combivir) should be taken separately.

If you take more Combivir than you should

If you accidentally take too much Combivir, tell your doctor or your pharmacist, or contact your nearest hospital emergency department for further advice.

If you forget to take Combivir

If you forget to take a dose, take it as soon as you remember. Then continue your treatment as before. Do not take a double dose to make up for a forgotten dose.

4. Possible 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 doctor will test for these changes.

Treatment with Combivir 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 doctor should monitor for signs of lipoatrophy. Tell your doctor if you notice any loss of fat from your legs, arms, and face. When these signs occur, Combivir should be stopped and your HIV treatment changed.

Like all medicines, this medicine can cause side effects, but not everyone gets them.

When you are being treated for HIV, it can be hard to tell whether a symptom is a side effect of Combivir or other medicines you are taking, or an effect of the HIV disease itself. **So it is very important to talk to your doctor about any changes in your health.**

As well as the side effects listed below for Combivir, other conditions can develop during combination therapy for HIV.

It is important to read the information later in this section under 'Other possible side effects of combination therapy for HIV'.

Very common side effects

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

- headache
- feeling sick (*nausea*).

Common side effects

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

- being sick (*vomiting*)

- diarrhoea
- stomach pains
- loss of appetite
- feeling dizzy
- tiredness, lack of energy
- fever (high temperature)
- general feeling of being unwell
- difficulty in sleeping (*insomnia*)
- muscle pain and discomfort
- joint pain
- cough
- irritated or runny nose
- skin rash
- hair loss (*alopecia*).

Common side effects that might show up in blood tests are:

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

Uncommon side effects

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

- feeling breathless
- wind (*flatulence*)
- itching
- muscle weakness.

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

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

Rare side effects

These may affect **up to 1 in 1000** people:

- serious allergic reaction causing swelling of the face, tongue or throat which may cause difficulty in swallowing or breathing
- liver disorders, such as jaundice, enlarged liver or fatty liver, inflammation (*hepatitis*)
- lactic acidosis (excess lactic acid in the blood; see the next section, ‘Other possible side effects of combination therapy for HIV’)
- inflammation of the pancreas (*pancreatitis*)
- chest pain; disease of the heart muscle (*cardiomyopathy*)
- fits (*convulsions*)
- feeling depressed or anxious, not being able to concentrate, feeling drowsy
- indigestion, taste disturbance
- changes in the colour of your nails, your skin or the skin inside your mouth
- a flu-like feeling – chills and sweating
- tingly feelings in the skin (pins and needles)
- sensation of weakness in the limbs
- breakdown of muscle tissue
- numbness
- passing urine more often
- enlarged breasts in men.

Rare side effects that may show up in blood tests are:

- an increase in an enzyme called amylase
- a failure of the bone marrow to produce new red blood cells (*pure red cell aplasia*).

Very rare side effects

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

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

- a failure of the bone marrow to produce new red or white blood cells (*aplastic anaemia*).

If you get side effects

Tell your doctor or pharmacist if any of the side effects get severe or troublesome, or if you notice any side effects not listed in this leaflet.

Other possible side effects of combination therapy for HIV

Combination therapy such as Combivir may cause other conditions to 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 moving up towards the trunk of the body, palpitations, tremor or hyperactivity, please inform your doctor immediately to seek necessary treatment.

If you get any symptoms of infection while you are taking Combivir:

Tell your doctor immediately. Do not take other medicines for the infection without your doctor's advice.

Lactic acidosis is a rare but serious side effect

Some people taking Combivir 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
- feeling sick (nausea), being sick (vomiting)
- stomach pain.

During your treatment, your doctor 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 doctor 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 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 doctor.

Other effects may show up in blood 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

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Combivir

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton.

Do not store above 30°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Combivir contains

The active substances are lamivudine and zidovudine. The other ingredients are

- *tablet core*; microcrystalline cellulose, sodium starch glycollate (gluten free), magnesium stearate, colloidal silicon dioxide
- *tablet film-coat*; hypromellose, titanium dioxide, macrogol 400 and polysorbate 80.

What Combivir looks like and contents of the pack

Combivir film-coated tablets are provided in cartons, containing blister packs or bottles with a child resistant-closure. Each pack type contains 60 film-coated tablets. They are white to off-white, capsule-shaped scored tablets marked with the code GXFC3 on both sides.

Marketing Authorisation Holder

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Other formats

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK Only)

Please be ready to give the following information:

| | |
|---------------------|---|
| Product name | Combivir 150 mg/300 mg film-coated tablets |
| Reference number | 35728/0030 |

This is a service provided by the Royal National Institute of Blind People.

This leaflet was last revised in November 2022

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