

Package leaflet: Information for the user

Trizivir 300 mg/150 mg/300 mg film-coated tablets *abacavir/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 side effects talk to your doctor or pharmacist immediately. This includes any possible side effects not listed in this leaflet.** See section 4.

IMPORTANT — Hypersensitivity reactions

Trizivir contains abacavir (which is also an active substance in medicines such as **Kivexa**, **Triumeq** and **Ziagen**). Some people who take abacavir may develop a **hypersensitivity reaction** (a serious allergic reaction), which can be life-threatening if they continue to take abacavir containing products . **You must carefully read all the information under ‘Hypersensitivity reactions’ in the panel in Section 4.**

The Trizivir pack includes an **Alert Card**, to remind you and medical staff about abacavir hypersensitivity. **Detach this card and keep it with you at all times.**

What is in this leaflet

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

1. What Trizivir is and what it is used for

Trizivir is used to treat HIV (human immunodeficiency virus) infection in adults.

Trizivir contains three active ingredients that are used to treat HIV infection: abacavir, lamivudine and zidovudine. All of these belong to a group of anti-retroviral medicines called *nucleoside analogue reverse transcriptase inhibitors (NRTIs)*.

Trizivir helps to control your condition. Trizivir does not cure HIV infection; it reduces the amount of virus in your body, and keeps it at a low level. This helps your body to increase the CD4 cell count in your blood. CD4 cells are a type of white blood cell that are important in helping your body to fight infection.

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

2. What you need to know before you take Trizivir

Do not take Trizivir:

- if you are **allergic** (*hypersensitive*) to abacavir (or any other medicine containing abacavir — **Kivexa, Triumeq or Ziagen**), lamivudine or zidovudine, or any of the other ingredients of this medicine (*listed in Section 6*)

Carefully read all the information about hypersensitivity reactions in Section 4.

- if you have **severe kidney problems**
- 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 Trizivir

Some people taking Trizivir are more at risk of serious side effects. You need to be aware of the extra risks:

- if you have moderate or severe liver disease
- if you have ever had **liver disease**, including hepatitis B or C (if you have hepatitis B infection, do not stop Trizivir without your doctor's advice, as your hepatitis may come back)
- if you are seriously **overweight** (especially if you are a woman)

Talk to your doctor if any of these apply to you before using Trizivir.

You may need extra check-ups, including blood tests, while you are taking your medicine. **See Section 4 for more information.**

Abacavir hypersensitivity reactions

Even patients who don't have the HLA-B*5701 gene may still develop a **hypersensitivity reaction** (a serious allergic reaction). **Carefully read all the information about hypersensitivity reactions in Section 4 of this leaflet.**

Risk of heart attack

It cannot be excluded that abacavir may increase the risk of having a heart attack.

Tell your doctor if you have heart problems, if you smoke, or have other illnesses that may increase your risk of heart disease such as high blood pressure, or diabetes. Do not stop taking Trizivir unless your doctor advises you to do so.

Look out for important symptoms

Some people taking Trizivir develop other conditions, which can be serious. You need to know about important signs and symptoms to look out for while you are taking Trizivir.

Read the information 'Other possible side effects of Trizivir' in Section 4 of this leaflet.

Protect other people

HIV infection is spread by sexual contact with someone 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 by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people.

Other medicines and Trizivir

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 Trizivir.

These medicines should not be used with Trizivir:

- stavudine or emtricitabine, to treat **HIV infection**
- other medicinal products containing lamivudine, used to treat **HIV infection** or **hepatitis B 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 will 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
- dapsone, 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're taking any of these.

Some medicines interact with Trizivir

These include:

- **clarithromycin**, an antibiotic
If you are taking clarithromycin, take your dose at least 2 hours before or after you take your Trizivir.
- **phenytoin**, for treating **epilepsy**
Tell your doctor if you are taking phenytoin. Your doctor may need to monitor you while you are taking Trizivir.
- 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 taking any of these.

Methadone and Trizivir

Abacavir increases the rate at which methadone is removed from the body. If you are taking methadone, you will be checked for any withdrawal symptoms. Your methadone dose may need to be changed.

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 Trizivir during your pregnancy.

Trizivir and similar medicines may cause side effects in unborn babies.

If you have taken Trizivir 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

Women who are HIV-positive must not breast-feed, because HIV infection can be passed on to the baby in breast milk. A small amount of the ingredients in Trizivir can also pass into your breast milk. If you are breast-feeding, or thinking about breast-feeding:

Talk to your doctor immediately.

Driving and using machines

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

Don't drive or operate machines unless you're feeling well.

3. How to take Trizivir

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

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

How much to take

The usual dose of Trizivir for adults is one tablet twice a day.

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

Swallow the tablets whole, with some water. Trizivir can be taken with or without food.

If you take more Trizivir than you should

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

If you forget to take Trizivir

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.

It is important to take Trizivir regularly, because if you take it at irregular intervals it may not continue to work against the HIV infection, and you may be more likely to have a hypersensitivity reaction.

If you have stopped taking Trizivir

If you have stopped taking Trizivir for any reason — especially because you think you are having side effects, or because you have other illness:

Talk to your doctor before you start taking it again. Your doctor will check whether your symptoms were related to a hypersensitivity reaction. If the doctor thinks they may have been related, **you will be told never again to take Trizivir, or any other medicine containing abacavir (Kivexa, Triumeq or Ziagen).** It is important that you follow this advice.

If your doctor advises that you can start taking Trizivir again, you may be asked to take your first doses in a place where you will have ready access to medical care if you need it.

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 Trizivir 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, Trizivir should be stopped and your HIV treatment changed.

Like all medicines, this medicine can cause side effects, although 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 Trizivir or other medicines you are taking, or an effect of the HIV infection itself. **So it is very important to talk to your doctor about any changes in your health.**

Even patients who don't have the HLA-B*5701 gene may still develop a **hypersensitivity reaction** (a serious allergic reaction), described in this leaflet in the panel headed 'Hypersensitivity reactions'. **It is very important that you read and understand the information about this serious reaction.**

As well as the side effects listed below for Trizivir, other conditions can develop during treatment. It is important to read the information on the other side of this leaflet under 'Other possible side effects of Trizivir'.

Hypersensitivity reactions

Trizivir contains **abacavir** (which is also an active substance in **Kivexa, Triumeq** and **Ziagen**). Abacavir can cause a serious allergic reaction known as a hypersensitivity reaction. These hypersensitivity reactions have been seen more frequently in people taking medicines that contain abacavir.

Who gets these reactions?

Anyone taking Trizivir could develop a hypersensitivity reaction to abacavir, which could be life threatening if they continue to take Trizivir.

You are more likely to develop such a reaction if you have a gene called **HLA-B*5701** (but you can get a reaction even if you do not have this gene). You should have been tested for this gene before Trizivir was prescribed for you. **If you know you have this gene, tell your doctor before you take Trizivir.**

About 3 to 4 in every 100 patients treated with abacavir in a clinical trial who did not have the HLA-B*5701 gene developed a hypersensitivity reaction.

What are the symptoms?

The most common symptoms are:

- **fever** (high temperature) and **skin rash**

Other common symptoms are:

- nausea (feeling sick), vomiting (being sick), diarrhoea, abdominal (stomach) pain, severe tiredness

Other symptoms include:

Pains in the joints or muscles, swelling of the neck, shortness of breath, sore throat, cough, occasional headaches, inflammation of the eye (conjunctivitis), mouth ulcers, low blood pressure, tingling or numbness of the hands or feet.

When do these reactions happen?

Hypersensitivity reactions can start at any time during treatment with Trizivir, but are more likely during the first 6 weeks of treatment.

Contact your doctor immediately:

- 1 if you get a skin rash, OR**
- 2 if you get symptoms from at least 2 of the following groups:**
 - fever
 - shortness of breath, sore throat or cough
 - nausea or vomiting, diarrhoea or abdominal pain
 - severe tiredness or achiness, or generally feeling ill

Your doctor may advise you to stop taking Trizivir.

If you have stopped taking Trizivir

If you have stopped taking Trizivir because of a hypersensitivity reaction, **you must NEVER AGAIN take Trizivir, or any other medicine containing abacavir (Kivexa, Triumeq or Ziagen)**. If you do, within hours, your blood pressure could fall dangerously low, which could result in death.

If you have stopped taking Trizivir for any reason — especially because you think you are having side effects, or because you have other illness:

Talk to your doctor before you start again. Your doctor will check whether your symptoms were related to a hypersensitivity reaction. If the doctor thinks they may have been, **you will then be told never again to take Trizivir, or any other medicine containing abacavir (Kivexa, Triumeq or Ziagen)**. It is important that you follow this advice.

Occasionally, hypersensitivity reactions have developed in people who start taking abacavir containing products again, but who had only one symptom on the Alert Card before they stopped taking it.

Very rarely, patients who have taken medicines containing abacavir in the past without any symptoms of hypersensitivity have developed a hypersensitivity reaction when they start taking these medicines again.

If your doctor advises that you can start taking Trizivir again, you may be asked to take your first doses in a place where you will have ready access to medical care if you need it.

If you are hypersensitive to Trizivir, return all your unused Trizivir tablets for safe disposal. Ask your doctor or pharmacist for advice.

The Trizivir pack includes an **Alert Card**, to remind you and medical staff about hypersensitivity reactions. **Detach this card and keep it with you at all times.**

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:

- hypersensitivity reaction
- 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

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

- a low red blood cell count (*anaemia*) 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 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 tests 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:

- 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 Trizivir'*)
- 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:

- 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:

- skin rash, which may form blisters and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) (*erythema multiforme*)
- a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (*Stevens–Johnson syndrome*), and a more severe form causing skin peeling in more than 30% of the body surface (*toxic epidermal necrolysis*)

If you notice any of these symptoms contact a doctor urgently.

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 gets severe or troublesome, or if you notice any side effects not listed in this leaflet.

Other possible side effects of Trizivir

Trizivir may cause other conditions to develop during HIV treatment.

Symptoms of infection and inflammation

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. Symptoms usually include **fever**, plus some of the following:

- headache
- stomach ache
- difficulty breathing

In rare cases, as the immune system becomes stronger, it can also attack healthy body tissue (*autoimmune disorders*). The symptoms of autoimmune disorders may develop many months after you start taking medicine to treat your HIV infection. Symptoms may include:

- palpitations (rapid or irregular heartbeat) or tremor
- hyperactivity (excessive restlessness and movement)
- weakness beginning in the hands and feet and moving up towards the trunk of the body

If you get any symptoms of infection while you're taking Trizivir:

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 Trizivir 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:

- feeling sick (nausea), being sick (vomiting)
- stomach pain
- generally feeling unwell
- loss of appetite, weight loss
- deep, rapid, difficult breathing
- numbness or weakness in the limbs

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

Trizivir 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 the 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 Trizivir

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

Do not take this medicine after the expiry date shown on the carton. The expiry date refers to the last day of that month.

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 help protect the environment.

6. Contents of the pack and other information

What Trizivir contains

The active substances in each Trizivir film-coated tablet are 300 mg of abacavir (as sulfate), 150 mg lamivudine and 300 mg zidovudine.

The other ingredients are microcrystalline cellulose, sodium starch glycollate and magnesium stearate in the core of the tablet. The tablet coating contains hypromellose, titanium dioxide, polyethylene glycol, indigo carmine aluminium lake, iron oxide yellow.

What Trizivir looks like and contents of the pack

Trizivir film-coated tablets are engraved with 'GX LL1' on one side. They are blue/green and capsule-shaped and are provided in blister packs containing 60 tablets or bottles containing 60 tablets with child-resistant tops.

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Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>