

ZIAGEN RANGE

Patient Information Leaflet

SCHEDULING STATUS:

S4

ZIAGEN TABLETS (300 mg abacavir/tablet)

ZIAGEN ORAL SOLUTION (20 mg abacavir/ml)

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet, you may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- ZIAGEN has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

HYPERSENSITIVITY REACTION

Hypersensitivity reactions (serious allergic reaction):

ZIAGEN contains abacavir.

Abacavir can cause a serious allergic reaction known as a hypersensitivity reaction, which can be life-threatening if treatment with abacavir-containing products is not stopped.

The ZIAGEN pack includes an **Alert Card**, to remind you and medical staff about abacavir hypersensitivity. **Detach this card and always carry your Alert Card while you are taking ZIAGEN.**

Who gets these reactions?

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

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 don't have this gene). You may have been tested for this gene before ZIAGEN was prescribed for you. **If you know you have this gene, tell your doctor before you take ZIAGEN.**

What are the symptoms of a hypersensitivity reaction (serious allergic reaction)?

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, shortness of breath, cough, headache, muscle pain and discomfort.

Other less common symptoms can include:

- pains in the joints, swelling of the neck, serious breathing problems, sore throat
- occasionally, 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 ZIAGEN 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 or diarrhoea or abdominal pain
- severe tiredness or achiness or generally ill feeling.

Your doctor may advise you to stop taking ZIAGEN.

If you have stopped taking ZIAGEN:

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

If you have stopped taking ZIAGEN for any reason, particularly because you think you are having side effects or for other illness, it is important that you contact your doctor before restarting. Your doctor will check whether any symptoms you had before stopping may be related to this hypersensitivity reaction. If your doctor thinks there is a possibility that they were related, you may be told never to take ZIAGEN or any other medicine containing abacavir again. It is important that you follow this advice.

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

Reactions have developed in people who start taking abacavir again, but who had no symptoms before they stopped taking it.

If your doctor advises that you can start taking ZIAGEN 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 ZIAGEN you should return all of your unused ZIAGEN to your doctor or pharmacist for proper disposal.

What is in this leaflet:

1. What ZIAGEN is and what it is used for

2. What you need to know before you take ZIAGEN

3. How to take ZIAGEN

4. Possible side effects

5. How to store ZIAGEN

6. Contents of the pack and other information

1. WHAT ZIAGEN IS AND WHAT IT IS USED FOR:

ZIAGEN belongs to a group of antiretroviral medicines called nucleoside analogue reverse transcriptase inhibitors (NRTIs). These are used to treat Human Immunodeficiency Virus (HIV) infection.

ZIAGEN is used in combination with other antiretroviral medicines for the treatment of HIV infection.

ZIAGEN does not cure HIV infection; it reduces the amount of virus in your body and keeps it at a low level. It also increases CD4 cell count in your blood. CD4 cells play an important role in maintaining a healthy immune system to help fight infection. Response to treatment with ZIAGEN varies between patients. Your doctor will be monitoring the effectiveness of your treatment.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ZIAGEN:

Do not take ZIAGEN:

- if you are allergic (hypersensitive) to abacavir (or any other medicine containing abacavir), or any other ingredients of ZIAGEN. **Carefully read all the information about hypersensitivity in the BOXED WARNING and section 4 POSSIBLE SIDE EFFECTS**
- if you have moderate or severe liver disease
- if you have a hereditary fructose intolerance, you must not take ZIAGEN ORAL SOLUTION, as it contains sorbitol
- if you are pregnant or breastfeeding.

If you think this applies to you, don't take ZIAGEN until you have checked with your doctor.

Warnings and precautions:

Take special care with ZIAGEN:

Before you take ZIAGEN your doctor needs to know:

- if you have ever had liver disease, including hepatitis B or C.

Conditions you need to look out for:

Hypersensitivity reactions:

ZIAGEN contains abacavir. Abacavir can cause a serious allergic reaction known as a hypersensitivity reaction, which can be life-threatening if treatment with abacavir containing products is not stopped.

Carefully read all the information about hypersensitivity reactions in the BOXED WARNING.

Lactic acidosis:

A condition that is caused by build-up of lactic acid in the body. It is more likely to develop in people who have liver disease, especially in women. It can be life-threatening, causing failure of internal organs.

See “Conditions you need to look out for” in section 4 POSSIBLE SIDE EFFECTS.

Change in body shape:

People taking combination therapy for HIV may find that their body shape changes, because of changes in fat distribution.

See “Conditions you need to look out for” in section 4 POSSIBLE SIDE EFFECTS.

Infection and inflammation:

People with advanced HIV infection (AIDS) have weak immune systems and are more likely to develop serious infections (*opportunistic infections*). When they start treatment, the immune system becomes stronger, so the body starts to fight infections.

Symptoms of infection and inflammation may develop, caused by either:

- old, hidden infections flaring up again as the body fights them
- the immune system attacking healthy body tissue (*autoimmune disorders*).

The symptoms of auto-immune disorders may develop many months after you start taking medicine to treat your HIV infection.

See “Conditions you need to look out for” in section 4 POSSIBLE SIDE EFFECTS.

Heart disease:

Abacavir may increase your risk of heart attack. If you have heart problems, smoke or suffer from diseases that increase your risk of heart disease such as high blood pressure and diabetes, tell your doctor. Do not stop taking ZIAGEN unless you are advised to do so by your doctor.

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). ZIAGEN will not stop you passing HIV infection on to other people. To protect other people from becoming infected with HIV:

- **Use a condom** when you have oral or penetrative sex.
- **Do not risk blood transfer** – for example, don't share needles.

You will need regular blood tests:

For as long as you are taking ZIAGEN, your doctor will arrange regular blood tests to check for side effects. There is more information about these side effects in this leaflet. See section 4 POSSIBLE SIDE EFFECTS.

Stay in regular contact with your doctor:

ZIAGEN 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.

Other medicines and ZIAGEN:

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

If you are taking methadone, your doctor may need to adjust your methadone dose, as abacavir increases the rate at which methadone is cleared from your body. This change is unlikely to affect most patients.

Alcohol increases the amount of abacavir in your blood, however this is not considered to be a safety concern.

ZIAGEN with food and drink and alcohol:

ZIAGEN does not have to be taken with food.

Pregnancy, breastfeeding and fertility:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking ZIAGEN.

Pregnancy:

The safe use of ZIAGEN in human pregnancy has not been established. Your doctor will advise whether you should continue to take ZIAGEN.

Breastfeeding:

Where possible, women who are HIV-positive should not breastfeed. This is because HIV infection can be passed on to the baby in breast milk. If formula feeding is not possible, you should

get advice from your doctor. A small amount of the ingredients in ZIAGEN can also pass into your breast-milk.

Driving and using machines:

ZIAGEN is unlikely to affect your ability to drive or operate machinery. If you have any concerns consult your doctor.

ZIAGEN ORAL SOLUTION contains sorbitol and maltodextrin.

ZIAGEN ORAL SOLUTION contains the sweetener sorbitol (approximately 5 g in each 15 ml dose), and may have a laxative effect. If you have been told that you have an intolerance to some sugars, you should not take ZIAGEN ORAL SOLUTION.

ZIAGEN ORAL SOLUTION contains maltodextrin which may have an effect on the control of your blood sugar if you have diabetes mellitus.

3. HOW TO TAKE ZIAGEN:

Do not share medicines prescribed for you with any other person.

Take ZIAGEN as your doctor has advised you. If you are unsure about how to take it, ask your doctor or pharmacist.

How much to take:

The usual dose in adults, adolescents and children weighing at least 25 kg is 600 mg daily. This may be administered as either 300 mg (one tablet) twice daily, approximately 12 hours apart, or 600 mg (two tablets) once a day, as advised by your doctor.

The usual dose in children weighing at least 14 kg and less than 20 kg is 300 mg a day. This can be taken as 150 mg (half a tablet) twice daily or 300 mg (one whole tablet) once a day, as advised by your doctor.

The usual dose in children weighing at least 20 kg and less than 25 kg is 450 mg a day. This can be taken as 150 mg (half a tablet) in the morning and 300 mg (one whole tablet) in the evening, or 450 mg (one and a half tablets) once a day as advised by your doctor.

If you have liver disease the daily dose of ZIAGEN may need to be reduced to 200 mg twice daily.

An oral solution (20 mg abacavir/ml) is available for patients who require a dose reduction or who are unable to take tablets.

How to take ZIAGEN oral solution:

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

1. Remove the bottle cap.
2. Push the plastic adapter into the neck of the bottle, while holding the bottle firmly.
3. Insert the syringe firmly into the adapter.
4. Turn bottle upside down
5. Pull out syringe plunger until the correct amount is withdrawn.
6. Turn the bottle the correct way up and remove the syringe from the adapter.
7. Replace and tighten the bottle cap.
8. Administer the dose into the mouth by placing the tip of the syringe against the inside of the cheek. Slowly depress the plunger, allowing time to swallow. Forceful squirting to the back of the throat may cause choking.

After use the syringe must not be left in the bottle and should be washed thoroughly in clean water.

If you take more ZIAGEN than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take a dose of ZIAGEN:

If you forget to take a dose of your medicine, take it as soon as you remember, and then continue as before. Do not take a double dose to make up for forgotten individual doses.

If you stop taking ZIAGEN:

If you have stopped taking ZIAGEN for any reason, particularly because you think you are having side effects or for other illness, it is important that you contact your doctor before restarting. In some cases, your doctor will ask you to restart ZIAGEN under direct medical supervision or where medical care can be readily accessed by yourself or others.

If you have hepatitis B infection, don't stop ZIAGEN without your doctor's advice, as your hepatitis may come back.

4. POSSIBLE SIDE EFFECTS:

ZIAGEN can have side effects.

Not all side effects reported for ZIAGEN are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking ZIAGEN, please consult your doctor, pharmacist or health care professional for advice.

Conditions to look out for:

Hypersensitivity reactions:

ZIAGEN can cause a hypersensitivity reaction (serious allergic reaction) which can be life-threatening. This is described in the BOXED WARNING at the beginning of the leaflet. It is important that you read and understand the information about this serious reaction.

Symptoms of infection and inflammation:

Symptoms of infection and inflammation may develop and include:

- muscle weakness and/or muscle pain
- joint pain or swelling
- weakness beginning in the hands and feet and moving up towards the trunk of the body
- palpitations or tremor
- hyperactivity (excessive restlessness and movement).

If you get any symptoms of infection while you're taking ZIAGEN, tell your doctor immediately. Don't take other medicines for the infection without your doctor's advice.

See "Take special care with ZIAGEN".

Your body shape may change:

People taking combination therapy for HIV may find that their body shape changes, because of changes in fat distribution:

- Fat may be lost from the legs, arms or face.
- Extra fat may build up around the stomach, or on the breasts or internal organs.
- Fatty lumps (sometimes called buffalo hump) may appear on the back of the neck.

If you notice changes in your body shape, tell your doctor immediately.

Lactic acidosis is a serious side effect:

Some people taking ZIAGEN develop a condition called lactic acidosis, together with an enlarged liver.

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 immediately**.

As well as the conditions listed above, other side effects can develop:

Frequently reported side effects:

- feeling sick (*nausea*)
- being sick (*vomiting*)
- hypersensitivity reaction (see BOXED WARNING)
- diarrhoea
- headache
- high temperature (*fever*)
- lack of energy (*lethargy*)
- fatigue
- loss of appetite
- skin rash (without any other illness).

Less frequently reported side effects:

- inflammation of the pancreas (*pancreatitis*)
- lactic acidosis (see “Conditions you need to look out for”)
- 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.

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
- increased levels of sugar and fats (triglycerides and cholesterol) in the blood.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects:

If you get side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the '6.04 Adverse Drug Reaction Reporting Form', found on-line under SAHPRA'S publications: <http://www.sahpra.org.za/Publications/Index/8>. By reporting side effects, you can help provide more information on the safety of ZIAGEN.

5. HOW TO STORE ZIAGEN:

Store all medicines out of reach of children.

Store at or below 30 °C.

Discard oral solution two months after first opening.

Do not take the medicine after the expiry date stated on the packaging.

6. CONTENTS OF THE PACK AND OTHER INFORMATION:

What ZIAGEN contains:

Tablets:

Each ZIAGEN film-coated tablet contains 300 mg of the active ingredient abacavir (as abacavir sulfate).

The tablet core contains colloidal anhydrous silica, magnesium stearate, microcrystalline cellulose and sodium starch glycollate. The tablet coating contains iron oxide yellow, methylhydroxypropylcellulose, polysorbate 80, titanium dioxide and triacetin.
Sugar-free.

Oral Solution:

ZIAGEN ORAL SOLUTION contains 20 mg of the active ingredient abacavir (as abacavir sulfate) in each ml of the solution.

Preservatives: methyl hydroxybenzoate 0,15 % *m/v*, propyl hydroxybenzoate 0,018 % *m/v*.

Other ingredients: citric acid anhydrous, methyl parahydroxybenzoate (E218), natural and artificial strawberry and banana flavour, propyl parahydroxybenzoate (E216), propylene glycol, purified water, saccharin sodium, sodium citrate, sorbitol.

Contains sugar (sorbitol 70 %: 492 mg/ml).

Contains sweetener (saccharin sodium: 0,3 mg/ml).

What ZIAGEN looks like and contents of the pack:

ZIAGEN TABLETS:

The scored tablets are biconvex, capsule-shaped, yellow tablets, engraved with 'GX 623' on both sides.

Available in polyvinyl chloride/foil blister packs or polyvinyl chloride/child resistant foil blister packs containing 60 tablets.

ZIAGEN ORAL SOLUTION:

A clear to slightly opalescent yellowish solution with a fruity odour.

Note from SAHPRA: The updated format of this PIL (dated 05 August 2019) is deemed implementable once the final Regulation 11 amendments required to support this change have been published in the Government Gazette.

Supplied in high density polyethylene bottles with child-resistant closures, containing 240 ml of oral solution. A 10 ml polypropylene oral dosing syringe and a polyethylene adaptor are also included in the pack.

Registration Numbers:

ZIAGEN TABLETS: 33/20.2.8/0464

ZIAGEN ORAL SOLUTION: 33/20.2.8/0465

Holder of Certificate of Registration and Manufacturer:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

The leaflet was last revised in 05 August 2019