

**Patient leaflet in accordance with the  
Pharmacists' Regulations (Preparations) - 1986**

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

## **ZIAGEN ORAL SOLUTION**

**Each ml of Ziagen Oral Solution contains:  
abacavir (as sulfate) 20 mg.**

List of the additional ingredients is detailed in Section 6.

**Read the entire leaflet carefully before using the medicine.** This leaflet contains concise information about the medicine. If you have any other questions, refer to the physician or the pharmacist.

This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them even if it seems to you that their illness is similar.

### **IMPORTANT - Hypersensitivity reactions**

**Ziagen contains abacavir** (which is also an active substance in medicines such as **Kivexa, Triumeq** and **Trizivir**). 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 Ziagen pack includes an **Alert Card**, to remind you and the medical staff about abacavir hypersensitivity.

**Detach this card and keep it with you at all times.**

This card contains important safety information that you must know and abide by before starting treatment and during the course of treatment with Ziagen. Read the Alert Card and patient leaflet before starting to use the preparation.

### **1. What is the medicine intended for?**

**Ziagen is used to treat HIV (Human Immunodeficiency Virus) infection.**

**Therapeutic group:** Ziagen contains the active ingredient abacavir. Abacavir belongs to a group of anti-retroviral medicines called *nucleoside analogue reverse transcriptase inhibitors (NRTIs)*.

Ziagen 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 Ziagen in the same way. Your physician will monitor the effectiveness of your treatment.

## 2. Before using the medicine

### **Do not use the medicine if:**

- you are **sensitive** (allergic) to abacavir (or any other medicine containing abacavir, such as **Trizivir**, **Triumeq** or **Kivexa**) or any of the additional ingredients of this medicine (listed in Section 6).

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

**Check with your physician** if you think this applies to you.

### **Special warnings regarding the use of the medicine**

Some people taking Ziagen for HIV 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 are seriously **overweight** (especially if you are a woman)
- if you have **severe kidney disease**.

**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.**

### **Abacavir hypersensitivity reactions**

Even patients who do not 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 physician** 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 Ziagen unless your physician advises you to do so.

### **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 Ziagen.

**Read the information 'Other possible side effects of combination therapy for HIV' 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 infection when taking this medicine, although the risk is lowered by effective anti-retroviral therapy. Discuss with your physician the precautions needed to avoid infecting other people.

**If you are taking or have recently taken other medicines including non-prescription medicines and food supplements, tell the physician or the pharmacist.** Remember to tell your physician or pharmacist if you begin taking a new medicine while you are taking Ziagen.

**There are medicines that interact with Ziagen,** these include:

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

**Tell your physician** if you are taking phenytoin. Your physician may need to monitor your condition while you are taking Ziagen.

- **methadone** used as a **heroin substitute**. Abacavir increases the rate at which methadone is removed from the body. If you are taking methadone, you will be checked for withdrawal symptoms. Your methadone dose may need to be changed.

**Tell your physician** if you are taking methadone.

### **Pregnancy, breast-feeding and fertility**

#### **Pregnancy**

**Ziagen is not recommended for use during pregnancy.** Ziagen and similar medicines may cause side effects in unborn babies.

If you have taken Ziagen during your pregnancy, your physician 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 Ziagen can also pass into your breast milk.

If you are breast-feeding, or thinking about breast-feeding: **Talk to your physician immediately.**

#### **Driving and using machines**

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

#### **Important information about some of the additional ingredients of Ziagen Oral Solution**

This medicine contains the sweetener sorbitol (approximately 5 grams in each 15 ml dose), which may have a mild laxative effect. Do not take medicines containing sorbitol if you have hereditary fructose intolerance. The calorific value of sorbitol is 2.6 kcal/g.

Ziagen also contains preservatives (*parahydroxybenzoates*) which may cause allergic reactions (possibly delayed reaction).

### 3. How should you use the medicine?

Always use according to the physician's instructions. You should check with the physician or the pharmacist if you are unsure about the preparation dosage and treatment regimen.

The dosage and treatment will be determined only by the physician.

Ziagen can be taken with or without food.

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

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

**Keep in touch with your physician, and do not stop taking Ziagen** without consulting your physician.

#### **The usual dosage is:**

##### **Adults, adolescents and children weighing at least 25 kg**

**The usual dosage of Ziagen is 600 mg (30 ml) a day.** Can be taken either as 300 mg (15 ml) twice a day or 600 mg (30 ml) once a day.

##### **Children from three months of age weighing less than 25 kg**

The dosage depends on the child's body weight. The usual dosage is 8 mg/kg twice a day or 16 mg/kg once a day, up to a maximum of 600 mg daily.

#### **How to measure the dose and take the medicine**

Use the measuring syringe supplied with the pack to measure your dose accurately. When the syringe is full, it contains 10 ml of solution.

1. **Remove the bottle cap.** Keep it safely. Opening instructions - to remove the cap, press down, while simultaneously twisting to the left (turning counterclockwise).
2. Hold the bottle firmly. **Push the plastic adapter into the neck of the bottle.**
3. **Insert the syringe** firmly into the adapter.
4. Turn the bottle upside down.
5. **Pull out the syringe plunger** until the syringe contains the first part of the full dose.
6. Turn the bottle the right way up. **Remove the syringe** from the adapter.
7. **Put the syringe into your mouth**, placing the tip of the syringe against the inside of your cheek. **Slowly push the plunger in**, allowing time to swallow. **Do not** push too hard and squirt the liquid into the back of your throat, or you may choke.
8. **Repeat steps 3 to 7** in the same way until you have taken the whole dose. For example, if the dose is 30 ml, you need to take 3 syringe-fulls of medicine.
9. **Take the syringe out of the bottle** and **wash** it thoroughly in clean water.

Let it dry completely before you use it again.

10. Close the bottle tightly with the cap, leaving the adapter in place. Closing instructions - replace cap on top of open end of the bottle and twist to the right (turning clockwise) until it locks tight enough.

**Do not exceed the recommended dose.**

**If you accidentally have taken a higher dosage** or if a child has accidentally swallowed the medicine, refer immediately to a physician or 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 it as soon as you remember. Then continue your treatment as usual. Do not take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by the physician.

Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting the physician or the pharmacist.

It is important to take Ziagen regularly, because if you take it at irregular intervals, you may be more likely to have a hypersensitivity reaction.

**If you stop taking the medicine**

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

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

If your physician 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.

**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 any other questions regarding the use of the medicine, consult the physician or the 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 health and life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your physician will test for these changes.

As with any medicine, use of Ziagen Oral Solution may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

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

Even patients who do not 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.**

**In addition to the side effects listed below for Ziagen,** 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'.

### **Hypersensitivity reactions**

**Ziagen** contains **abacavir** (which is also an active substance in **Kivexa, Triumeq** and **Trizivir**). 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 Ziagen could develop a hypersensitivity reaction to abacavir, which could be life-threatening if they continue to take Ziagen.

You are more likely to develop such a reaction if you have the **HLA-B\*5701** gene (but you can get a reaction even if you do not have this gene). You should have been tested for this gene before Ziagen was prescribed for you.

**If you know you have this gene, tell your physician before you take Ziagen.**

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, vomiting, 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 headache, inflammation of the eye (*conjunctivitis*), mouth ulcers, low blood pressure, tingling or numbness of the feet or palms of your hands.

#### **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.

**If you are caring for a child who is being treated with Ziagen, it is important that you understand the information about this hypersensitivity reaction. If your child gets the symptoms described below it is essential that you follow the instructions given.**

**Talk to your physician immediately:**

- 1. if you have a skin rash, OR**
- 2. if you have 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 physician 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 (e.g. Trizivir, Triumeq or Kivexa).** If you take, within hours, your blood pressure could fall dangerously low, which could result in death.

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

**Talk to your physician before you start again.** Your physician will check whether your symptoms were related to a hypersensitivity reaction. If the physician thinks they may have been related, **you will then be told never again to take Ziagen, or any other medicine containing abacavir (e.g. Trizivir, Triumeq or Kivexa).** 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 them.

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 physician 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, return all your remaining unused Ziagen Oral Solution for safe disposal.** Consult your physician or pharmacist.

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

### **Common side effects**

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

- hypersensitivity reaction
- nausea
- headache
- vomiting (*being sick*)
- diarrhoea
- loss of appetite
- tiredness, lack of energy
- fever (high temperature)
- skin rash.

### **Rare side effects**

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

- inflammation of the pancreas (*pancreatitis*).

### **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*)
- lactic acidosis (excess lactic acid in the blood).

**If you notice any of these symptoms talk to a physician urgently.**

### **Other possible side effects of combination therapy for HIV**

Combination therapy including Ziagen may cause other medical 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 are taking Ziagen:

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

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

Some people taking combination therapy for HIV develop a condition called *osteonecrosis* (necrosis of the bone). 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
- they are also taking anti-inflammatory medicines called corticosteroids
- they drink alcohol
- their immune systems are very weak
- 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.**

**If a side effect occurs, if one of the side effects worsens or when you suffer from a side effect not mentioned in the leaflet, consult 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](http://www.health.gov.il)) that directs you to the online form for reporting side effects, or by entering the link:

<https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdverseEffectMedic@moh.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 sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

- Do not store above 30°C.
- Use within 60 days after first opening.

## **6. Additional information**

- In addition to the active ingredient the medicine also contains - sorbitol 70% (E420), propylene glycol (E1520), sodium citrate, citric acid anhydrous, artificial strawberry and banana flavour, methyl parahydroxybenzoate (E218), saccharin sodium, propyl parahydroxybenzoate (E216), maltodextrin, lactic acid, glyceryl triacetate, purified water, sodium hydroxide and/or hydrochloric acid for pH adjustment.
- What the medicine looks like and the contents of the package - Ziagen Oral Solution is clear to yellowish in colour with strawberry/banana flavouring. It is supplied in cartons containing a white polyethylene bottle, with a child resistant cap. The bottle contains 240 ml (20 mg abacavir/ml) of solution. A 10 ml oral dosing syringe and a plastic adapter for the bottle are included in the pack.
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