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

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

Abacavir-Lamivudine Taro

Film-coated tablets

Active ingredients:
Each film-coated tablet contains:
600 mg abacavir
300 mg lamivudine

Inactive ingredients and allergens: see section 2 under 'Important information about some of the ingredients of the medicine' and section 6 'Additional information'.

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

IMPORTANT - Hypersensitivity reactions
Abacavir-Lamivudine Taro contains abacavir (which is also an active ingredient in medicines such as **Trizivir, 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 products containing abacavir.
You must carefully read al l the information under 'Hypersensitivity reactions' in the panel in section 4.

The Abacavir-Lamivudine Taro 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 Abacavir-Lamivudine Taro. Read the alert card and patient leaflet before starting to use the medicine.

1. What is the medicine intended for?

Abacavir-Lamivudine Taro is used to treat HIV (human immunodeficiency syndrome) infection in adults, adolescents and in children weighing at least 25 kg.

Therapeutic group:
Abacavir-Lamivudine Taro contains two active ingredients that are used to treat HIV infection: abacavir and lamivudine. These belong to a group of anti-retroviral medicines called nucleoside analogue reverse transcriptase inhibitors (NRTIs).

Abacavir-Lamivudine Taro 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 fight infection.

Not everyone responds to treatment with Abacavir-Lamivudine Taro 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 (e.g., **Trizivir**, **Triumeq** or **Ziagen**), lamivudine or any of the additional ingredients that this medicine contains (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. Do not take Abacavir-Lamivudine Taro.

Special warnings regarding the use of the medicine

Some people taking Abacavir-Lamivudine Taro or other combination therapy 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** in the past, including hepatitis B or C (if you have hepatitis B infection, do not stop taking Abacavir-Lamivudine Taro without your physician's advice, as your hepatitis may come back)
- if you are seriously **overweight** (especially if you are a woman)
- if you have a **kidney problem**

→ **If any of these apply to you, talk to your physician before using Abacavir-Lamivudine Taro.** You may need extra check-ups, including blood tests, while you are taking your medicine. **See section 4 for more information.**

<u>Abacavir hypersensitivity reactions</u>

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 Abacavir-Lamivudine Taro unless your physician advises you to do so.

Look out for important symptoms
Some people taking medicines for HIV infection develop other medical conditions, which can be serious. You need to know about important signs and symptoms to look out for while you are taking Abacavir-Lamivudine Taro.
→ **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 a person who has the infection, or by transfer of infected blood (for example, by sharing injection needles). You can still transmit HIV when taking this medicine, although the risk is lowered by effective anti-retroviral therapy. Discuss with your physician the precautions necessary to avoid infecting other people.

Other medicines and Abacavir-Lamivudine Taro
If you are taking, or have recently taken, other medicines, including non-prescription medicines and dietary supplements, tell the physician or pharmacist.
Remember to tell your physician or pharmacist if you begin taking a new medicine while you are taking Abacavir-Lamivudine Taro.

Avoid taking these medicines with Abacavir-Lamivudine Taro:
- emtricitabine, to treat **HIV infection**
- other medicinal products containing lamivudine, used to treat **HIV infection** or **hepatitis B infection**
- high doses of **trimethoprim/sulfamethoxazole**, an antibiotic
- cladribine, used to treat **hairy cell leukaemia**

→ **Tell your physician** if you are being treated with any of these medicines.

Some medicines interact with Abacavir-Lamivudine Taro
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 Abacavir-Lamivudine Taro.

- **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 any withdrawal symptoms. Your methadone dose may need to be changed.
→ **Tell your physician** if you are taking methadone.

- medicines (usually liquids) containing **sorbitol and other sugar alcohols** (such as xylitol, mannitol, lactitol or maltitol), if taken regularly.
  Tell your physician or pharmacist if you are taking any of these.

- Riociguat, for treating high blood pressure in the blood vessels (pulmonary arteries) that carry blood from the heart to the lungs. Your physician may need to reduce your riociguat dose, as abacavir may increase riociguat blood levels.

Pregnancy, breast-feeding and fertility
Pregnancy
Abacavir-Lamivudine Taro is not recommended for use during pregnancy. Abacavir-Lamivudine Taro and similar medicines may cause side effects in unborn babies.
If you have taken Abacavir-Lamivudine Taro 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 Abacavir-Lamivudine Taro 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
Abacavir-Lamivudine Taro may cause side effects which could affect your ability to drive or use machines.
→ **Talk to your physician** about your ability to drive or operate machines while taking Abacavir-Lamivudine Taro.

Important information about some of the ingredients of the medicine
Abacavir-Lamivudine Taro contains a colouring called Sunset Yellow (E110), this may cause allergic reactions in some people.
Abacavir-Lamivudine Taro contains less than 23 mg sodium per tablet, that is to say essentially 'sodium-free'.

3. How should you use the medicine?
Always use the medicine 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 regimen will be determined by the physician only.
The usual recommended Abacavir-Lamivudine Taro dosage for adults, adolescents and children weighing 25 kg or more is one tablet, once a day.

Swallow the tablets whole, with some water. Abacavir-Lamivudine Taro can be taken with or without food.
There is no information regarding crushing/halving/chewing.

Stay in regular contact with your physician
Abacavir-Lamivudine Taro helps control your condition. You need to keep taking it every day to stop your illness from getting worse. You may still develop other illnesses and infections linked to HIV infection.
→ **Keep in touch with your physician, and do not stop taking Abacavir-Lamivudine Taro** without your physician's advice.

Do not exceed the recommended dose.

If you have accidentally taken a higher dosage
If you have taken an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a physician or to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine
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.

Adhere to the treatment as recommended by the physician.

It is important to continue taking Abacavir-Lamivudine Taro 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 Abacavir-Lamivudine Taro for any reason - especially because you think you are having side effects, or because you have another 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 Abacavir-Lamivudine Taro, or any other medicine containing abacavir (e.g., Trizivir, Triumeq or Ziagen).** It is important that you follow this advice.

If your physician advises that you can start taking Abacavir-Lamivudine Taro 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 <u>every time</u> 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. These effects are partly linked to restored health

and lifestyle, and in the case of blood lipids, there is sometimes a link to the HIV medicines themselves. Your physician will test for these changes.

As with any medicine, use of Abacavir-Lamivudine Taro may cause side effects in some of the users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

When you are being treated for HIV infection, it can be hard to tell whether a symptom is a side effect of Abacavir-Lamivudine Taro or of 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.

As well as the side effects listed below for Abacavir-Lamivudine Taro, other medical 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

Abacavir-Lamivudine Taro contains **abacavir** (which is also an active substance in medicines such as **Trizivir**, **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 Abacavir-Lamivudine Taro could develop a hypersensitivity reaction to abacavir, which could be life-threatening if they continue to take Abacavir-Lamivudine Taro.
You are more likely to develop this reaction if you have a gene called **HLA-B*5701** (but you can develop a reaction even if you do not have this gene). You should have been tested for this gene before Abacavir-Lamivudine Taro was prescribed for you. **If you know you have this gene, tell your physician before you take Abacavir-Lamivudine Taro.**

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** and **skin rash**.

Other common symptoms are:

• nausea, vomiting, diarrhoea, stomach ache, severe tiredness.

Other symptoms include:

• pain 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 symptoms occur?
Hypersensitivity reactions may start at any time during treatment with Abacavir-Lamivudine Taro, but are more likely during the first 6 weeks of treatment.

Contact your physician 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 stomach ache
- severe tiredness or pain, or generally feeling ill.

Your physician may advise you to stop taking Abacavir-Lamivudine Taro.

If you have stopped taking Abacavir-Lamivudine Taro
If you have stopped taking Abacavir-Lamivudine Taro because of a hypersensitivity reaction, you must **NEVER AGAIN take Abacavir-Lamivudine Taro, or any other medicine containing abacavir (e.g., Trizivir, Triumeq or Ziagen)**. If you take them, within hours, your blood pressure may drop dangerously low, which could result in death.

If you have stopped taking Abacavir-Lamivudine Taro for any reason - especially because you think you are having side effects, or because you have another 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 are related, **you will then be told never again to take Abacavir-Lamivudine Taro, or any other medicine containing abacavir (e.g., Trizivir, 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 of the symptoms on the Alert Card before they stopped taking them.

Very rarely, patients who took medicines containing abacavir in the past, and did not have any symptoms of hypersensitivity, developed a hypersensitivity reaction when they started taking these medicines again.

If your physician advises that you can start taking Abacavir-Lamivudine Taro 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 Abacavir-Lamivudine Taro, return all your remaining unused Abacavir-Lamivudine Taro tablets for safe disposal.
Ask your physician or pharmacist for advice.

The Abacavir-Lamivudine Taro 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 occur **in up to 1 in 10** people:

- hypersensitivity reaction
- headache
- vomiting

- nausea
- diarrhoea
- stomach ache
- loss of appetite
- tiredness, lack of energy
- fever
- general feeling of being unwell
- difficulty in sleeping (insomnia)
- muscle pain and discomfort
- joint pain
- cough
- irritated or runny nose
- skin rash
- hair loss

Uncommon side effects
These may occur **in up to 1 in 100** people and may show up in blood tests:

- a low red blood cell count (anaemia) or low white blood cell count (neutropenia)
- an increase in the level of liver enzymes
- a decrease in the number of blood cells involved in blood clotting (thrombocytopenia)

Rare side effects
These may occur **in up to 1 in 1,000** people:

- liver disorders, such as jaundice, enlarged liver or fatty liver, inflammation (hepatitis)
- inflammation of the pancreas (pancreatitis)
- breakdown of muscle tissue

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

- increase in the amylase enzyme

Very rare side effects
These may occur **in up to 1 in 10,000** people:

- numbness, tingly feelings in the skin (pins and needles)
- sensation of weakness in the limbs
- skin rash, which may form blisters and look 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 that causes 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, contact a physician urgently.

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

- failure of the bone marrow to produce new red blood cells (pure red cell aplasia)

Other possible side effects of combination therapy for HIV
Combination therapy such as Abacavir-Lamivudine Taro, 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 a weak immune system, and are more likely to develop serious infections (opportunistic infections). Such infections may have been “silent” and were not detected by the weak immune system before treatment was started. After starting treatment, the immune system becomes stronger, and may attack the infections, which can cause symptoms of infection and inflammation.

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 feet and hands and moving up towards the trunk of the body

If you get any symptoms of infection and inflammation or if you notice any of the symptoms above:
→ **Tell your physician immediately.** Do not take other anti-infective medicines without your physician’s advice.

You may have bone problems
Some people receiving 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 are 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**

If you experience any side effect, if any side effect gets worse or if you experience a side effect not mentioned in this leaflet, consult your 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) and which directs you to the online form for reporting side effects, or by following the link:
https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a 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.

Storage conditions: Store below 25°C.

6. Additional information

In addition to the active ingredients, the medicine also contains:
The tablet core contains:
microcrystalline cellulose, sodium starch glycolate, povidone K90, and magnesium stearate in the core of the tablet.

The tablet coating contains:
hypromellose, titanium dioxide (E171), macrogol 400 and Sunset yellow FCF aluminium lake (E110).

What the medicine looks like and the contents of the package:
Abacavir-Lamivudine Taro tablets are film-coated. They are orange and capsule-shaped.
Each pack contains 30 tablets.

License holder's name and address: Taro International Ltd., 14 Hakitor Street, Haifa Bay 2624761

Manufacturer's name and address:
Remedica Ltd., Aharnon Street, Limassol Industrial Estate, 3056 Limassol, Cyprus

This leaflet was revised in March 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 164-76-35411