

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

*This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities (term to be revised).
The medicine may be authorised for additional or different uses by national medicines regulatory authorities.*

Information for the patient

[HA 392 trade name]¹
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 questions about the medicine, ask your health care provider.
- 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 seem to be the same as yours.
- If you get any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [HA 392 trade name] is and what it is used for
2. What you need to know before you take [HA 392 trade name]
3. How to take [HA 392 trade name]
4. Possible side effects
5. How to store [HA 392 trade name]
6. Contents of the pack and other information

1. What [HA 392 trade name] is and what it is used for

[HA392 trade name] is used for the treatment of human immunodeficiency virus (HIV-1) in infected patients weighing 25 kg or more.

[HA392 trade name] contains the active substances *lamivudine* and *zidovudine*. Both are *antiviral* medicines also known as antiretrovirals, called nucleoside analogue reverse transcriptase inhibitors (NRTIs). Both substances interfere with enzymes used by HIV for making copies of itself and thereby block the reproduction of the virus.

[HA392 trade name] reduces the amount of HIV 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 for a healthy immune system and for helping your body to fight infection.

To prevent the virus from becoming resistant, [HA392 trade name] should always be given in combination with another antiretroviral medicine.

[HA392 trade name] may improve your condition, but it is not a cure for HIV infection.

2. What you need to know before you take [HA 392 trade name]

Do not take [HA392 trade name]:

- if you are allergic (hypersensitive) to lamivudine, zidovudine or to any of the other ingredients of [HA392 trade name] (listed in section 6, below).

¹Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

- if you have a very low red blood cell count (severe anaemia) or a very low white blood cell count (neutropenia or leucopenia).

Check with your health care provider if you think any of these apply to you.

Take special care with [HA392 trade name]

Some people taking [HA392 trade name] 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 [HA392 trade name] without your health care provider'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 health care provider if any of these apply to you. Your health care provider will decide if the active substances are suitable for you. You may need extra check-ups.

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 [HA392 trade name].

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 when taking this medicine, although the risk is lowered by effective antiretroviral therapy.

Discuss with your health care provider the precautions needed to avoid infecting other people.

Other medicines and [HA392 trade name]

Tell your health care provider 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 health care provider if you begin taking a new medicine while you are taking [HA392 trade name].

These medicines should not be used with [HA392 trade name]:

- 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 health care provider 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
- 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 **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 health care provider if you are taking any of these.

Some medicines interact with [HA392 trade name]

These include:

- **clarithromycin**, an antibiotic
if you are taking clarithromycin, take your dose at least 2 hours before or after you take your Lamivudine and Zidovudine Tablets 150 mg/300 mg.
- **phenytoin**, for treating **epilepsy**.

Tell your health care provider if you are taking phenytoin. Your health care provider may need to monitor you while you are taking [HA392 trade name].

Pregnancy

Ask your health care provider for advice before taking any medicine. Be sure to tell your health care provider immediately if you are or may be pregnant.

In babies born to mothers who have taken antiretroviral medicines comprising nucleoside and nucleotide analogues, the benefit of reduced risk of becoming infected with HIV outweighs the risk of side effects of these medicines.

Breast-feeding

If you want to breast-feed your baby, you should discuss the risks and benefits with your health care provider.

Driving and using machines

[HA392 trade name] may cause side effects such as dizziness, fatigue or headache, which can affect your ability to drive and to use machines. Therefore, don't drive or operate machines unless you are feeling well.

3. How to take [HA 392 trade name]

Always take [HA392 trade name] exactly as your health care provider has told you. This is to make sure that your medicine is fully effective, and to reduce the risk of developing resistance to the treatment. You should check with your health care provider if you are not sure. Always take the dose recommended by your health care provider. Do not change the dose unless your health care provider tells you to.

Taking [HA392 trade name]

[HA392 trade name] may be taken with food or between meals, swallowed with some water or another drink. If you cannot swallow the tablets, you may crush and take them immediately with a small amount of semi-solid food or drink. You must make sure that you take the whole dose.

How much to take

Adults, adolescents and children who weigh at least 25 kg:

The usual dose is one tablet [HA392 trade name] twice a day, leaving approximately 12 hours between each dose.

Children weighing less than 25 kg:

This product should not be used in children weighing less than 25 kg since appropriate dose adjustments cannot be made. For these patients other formulations should be used, e.g. a tablet which can be used to give smaller doses of lamivudine and zidovudine.

If you have a kidney problem, your dose may need to be altered. Talk to your health care provider if this applies to you.

If you take more [HA392 trade name] than you should

Accidentally taking too much [HA392 trade name] is unlikely to cause any serious problems. If you take too much, tell your health care provider, or contact your nearest hospital emergency department for further advice.

If you forget to take [HA392 trade name]

If you forget to take a dose and there are more than 6 hours till your next dose, take the missed dose as soon as possible. Then continue your treatment as before. If there are less than 6 hours till your next dose, skip the missed dose. Don't take a double dose to make up for a missed dose.

If you stop taking [HA392 trade name]

Because your medicine controls and does not cure your condition, you will normally need to take it continuously.

You should not stop treatment unless your health care provider tells you to.

If you have any further questions on the use of this product, ask your health care provider.

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 health care provider will test for these changes.

Treatment with [HA392 trade name] 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 health care provider should monitor for signs of lipoatrophy. Tell your health care provider if you notice any loss of fat from your legs, arms, and face. When these signs occur, [HA392 trade name] 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 [HA392 trade name] or other medicines you are taking, or an effect of the HIV disease itself. **So it is very important to talk to your health care provider about any changes in your health.**

As well as the side effects listed below for [HA392 trade name], 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 *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 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 health care provider 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 [HA392 trade name] 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 health care provider immediately to seek necessary treatment.

If you get any symptoms of infection while you are taking [HA392 trade name]:

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

Lactic acidosis is a rare but serious side effect

Some people taking [HA392 trade name] develop a condition called lactic acidosis, together with an enlarged liver.

Lactic acidosis is caused by a buildup 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 health care provider 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 health care provider 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 health care provider.**

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 health care provider. This includes unwanted effects not listed in this leaflet. If available, you can also report side effects directly through the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store [HA 392 trade name]

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

Do not store above 30°C. Store in the original package.

Do not use [HA392 trade name] after the expiry date which is stated on the blister card / container label. The expiry date refers to the last day of that month.

Do not use [HA392 trade name] if you notice any change from the description of the tablet below

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

6. Contents of the pack and other information

What [HA392 trade name] contains

- The active ingredients are lamivudine and zidovudine.
- The other ingredients are microcrystalline cellulose, colloidal anhydrous silica, sodium starch glycolate, magnesium stearate, hypromellose, titanium dioxide and propylene glycol.

What [HA392 trade name] looks like and contents of the pack

White to off-white, film-coated, capsule shaped, biconvex tablet debossed with 'M' on one side of the score and '2' on other side of score on one side of the tablet and 'L' on one side of the score and 'Z' on other side of the score on the other side.

Blister pack

Blister pack comprises clear transparent PVdC coated PVC film with backing of aluminium foil coated with heat seal lacquer. Pack of 60s.

HDPE bottle pack

HDPE bottle pack comprises white opaque HDPE bottle with screw cap. Seal made of aluminium foil is used in the samples. Bottle of 60s.

HDPE bottle pack comprises white opaque HDPE bottle with screw cap and silica gel desiccant. Seal made of aluminium foil is used in the samples. Bottle of 60s.

Supplier	Manufacturer
<p>Mylan Laboratories Limited Plot No. 564/A/22, Road No.92 Jubilee Hills Hyderabad – 500 034 Telangana India Tel No: +91 40 39258109 Email: imtiyaz.basade@mylan.in</p>	<p>Mylan Laboratories Limited F-4, F-12, Malegaon M.I.D.C Sinnar Nashik – 422 113 Maharashtra India</p> <p>Mission Vivacare Limited Plot No. 14, Indore SEZ Phase II Pharma Zone, Sector III, Pithampur Dhar, Madhya Pradesh India</p> <p>Mylan Laboratories Limited, H-12 & H-13, M.I.D.C, Waluj Aurangabad – 431 136 Maharashtra India</p> <p>Mylan Laboratories Limited, Plot No. 11,12 & 13 Indore special economic zone, Phase II, Sector III Pithampur – 454775 Dhar, Madhya Pradesh India</p>

This leaflet was last revised on December 2019

Detailed information on this medicine is available on the World Health Organization (WHO) web site:
<https://extranet.who.int/prequal/>.