

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

[HA555 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 your child 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 [HA555 trade name] is and what it is used for
2. What you need to know before you give [HA555 trade name] to your child
3. How to take [HA555 trade name]
4. Possible side effects
5. How to store [HA555 trade name]
6. Contents of the pack and other information

1. What [HA555 trade name] is and what it is used for

[HA555 trade name] is used for the treatment of human immunodeficiency virus (HIV-1) in children aged 4 weeks and older, and weighing from 3 kg to 25 kg

[HA555 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.

[HA555 trade name] reduces the amount of HIV in the body, and keeps it at a low level. It also increases the CD4 cell count in the blood. CD4 cells are a type of white blood cells that are important for a healthy immune system and for helping the body to fight infection.

To prevent the virus from becoming resistant, [HA555 trade name] should always be given in combination with another antiretroviral medicine.

[HA555 trade name] may improve your child's condition, but it is not a cure for HIV infection.

This product is intended for use in children. Safety information on use in adults is also provided.

2. What you need to know before you give [HA555 trade name] to your child

Your child should not be given [HA555 trade name]:

- if he/she is allergic (hypersensitive) to lamivudine, zidovudine or to any of the other ingredients of [HA555 trade name] (listed in section 6, below).
- if he/she has 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 your child.

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

Take special care with [HA555 trade name]

Some people taking [HA555 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 your child has ever had **liver disease**, including hepatitis B or C (if one has hepatitis B infection, [HA555 trade name] should not be stopped without the health care provider's advice, as the hepatitis may come back)
- if your child has **kidney disease**
- if your child is seriously **overweight** (especially if a woman)

Talk to your health care provider if any of these apply to your child. Your health care provider will decide if the active substances are suitable for your child. Extra check-ups may be needed.

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 your child is taking [HA555 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). One 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 [HA555 trade name]

Tell your health care provider if your child is taking any other medicines, or if your child has taken any recently, including herbal medicines or other medicines you bought without a prescription.

Remember to tell your health care provider if your child begins taking a new medicine while taking [HA555 trade name].

These medicines should not be used with [HA555 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 your child is being treated with any of these.

Some medicines can make it more likely that your child 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 a certain lung infection (**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 to treat drug addiction (replacing **heroin**)
- vincristine, vinblastine or doxorubicin, to treat **cancer**.

Tell your health care provider if you are taking any of these.

Some medicines interact with [HA555 trade name]

These include:

- **clarithromycin**, an antibiotic
if your child is taking clarithromycin, give the dose at least 2 hours before or after you give [HA555 trade name] to your child .
- **phenytoin**, for treating **epilepsy**.

Tell your health care provider if your child is taking phenytoin. Your health care provider may need to monitor your child while taking [HA555 trade name].

Pregnancy

Ask your health care provider for advice before taking any medicine. Be sure to tell your health care provider immediately if the patient is 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 one wants to breast-feed a baby, the risks and benefits should be discuss with the health care provider.

Driving and using machines

[HA555 trade name] may cause side effects such as dizziness, fatigue or headache, which can affect one's ability to drive and to use machines. Therefore, the patient shouldn't drive or operate machines unless he/she is feeling well.

3. How to give [HA555 trade name]

Your child should always be given [HA555 trade name] exactly as the health care provider has instructed. You should check with the health care provider if you are not sure.

Children at least 4 weeks of age and weighing 3 kg to less than 25 kg

[HA555 trade name] may be given twice-daily follows:

The number of tablets to be given twice daily (approximately 12 hours apart) is shown in the table below:

Child's weight	Morning	Evening
3 – 5.9 kg	1 tablet	1 tablet
6 – 9.9 kg	1.5 tablets	1.5 tablets
10 – 13.9 kg	2 tablets	2 tablets
14 – 19.9 kg	2.5 tablets	2.5 tablets
20 – 24.9 kg	3 tablets	3 tablets

Your child can take [HA555 trade name] with food or between meals.

For very young children not able to swallow the tablets whole, the tablets may be crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately.

Children weighing 25 kg or more, adolescents and adults:

For these patient groups other fixed dose formulations with higher amounts of the active substances are available.

For situations where discontinuation of therapy with one of the active substances of [HA555 trade name], or dose reduction is necessary, separate preparations of lamivudine and zidovudine are available.

If one takes more [HA555 trade name] than one should

If your child is accidentally given too much medicine, get medical help immediately. Try to take any remaining tablets, the packaging or this leaflet with you to show the health care provider what your child has been given.

If you forget to give [HA555 trade name]

It is important not to miss doses of [HA555 trade name]. If you forget to give a dose of the medicine, and notice this within 6 hours, give the missed dose as soon as possible. Give the next regular dose as scheduled. If you notice later, give the normal dose to the child when the next one is due. Do not give a double dose to make up for forgotten doses.

If one stops taking [HA555 trade name]

Because this medicine controls and does not cure the condition, your child normally needs to take it continuously. You should not stop treatment unless the health care provider tells you to. If you have any further questions on the use of this product, ask the 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 [HA555 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 child's legs, arms, and face. When these signs occur, [HA555 trade name] should be stopped and the HIV treatment changed.

Like all medicines, this medicine can cause side effects, but not everyone gets them.

When your child is being treated for HIV, it can be hard to tell whether a symptom is a side effect of [HA555 trade name] or other medicines he/she is 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 child's health.**

As well as the side effects listed below for [HA555 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

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

- a low red blood cell count or low white blood cell count
- 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 child's 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 or in all kinds of blood cells.

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
- 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 and white blood cells (*aplastic anaemia*).

If your child gets 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 [HA555 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 one starts taking medicines for the treatment of 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 your child gets any symptoms of infection while taking [HA555 trade name]:

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

Lactic acidosis is a rare but serious side effect

Some people taking [HA555 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, being sick
- stomach pain.

During treatment, your health care provider will monitor for signs of lactic acidosis. If your child has any of the symptoms listed above, or any other symptoms that worry you:

See your health care provider as soon as possible.

One may have problems with 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 your child gets 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 [HA555 trade name]

Keep out of the reach and sight of children.

HDPE Bottles

Do not store above 30°C. Protect from light.

Blisters

Do not store above 30°C. Protect from light. Store tablets in blisters in the provided carton.

Do not use [HA555 trade name] after the expiry date which is stated on the bottle label. The expiry date refers to the last day of that month

Do not use [HA555 trade name] if you notice any change in the physical description of the tablet than what is mentioned below.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What [HA555 trade name] contains

The active ingredients are lamivudine and zidovudine.

The other ingredients are;

Core tablet: Colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, sodium starch glycolate

Film coating: Hypromellose, polyethylene glycol 400, polysorbate 80, titanium dioxide

What [HA555 trade name] looks like and contents of the pack

White, capsule shaped, beveled edged, biconvex, film coated tablet with plain surface on one side and scored on other side.

The tablet can be divided into equal doses

The tablets are packaged in round opaque white coloured HDPE bottle with PP child-resistant caps containing 60, 100 or 1000 tablets

The tablets are also packaged in clear PVC/PVDC-Al blisters. Each blister card contains 10 tablets. 6 such blisters are packed in one carton.

Supplier

Micro Labs Limited
#31, Race Course Road
Bangalore – 560001
Karnataka, India.
Tel : +91-80-2237 0451 to 2237 0457
Fax : +91-80-2237 0463
Email : jainethesh@microlabs.in

Manufacturer

Micro Labs Limited
Plot No: S-155 to S-159 & N1
Phase III & Phase IV
Verna Industrial Estate
Verna, Goa- 403722
India
Tel : +91-832-6686262

Fax : +91-832-6686203

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