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.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

Information for the patient

[HA483 trade name][†]
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 are concerned about 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 [HA483 trade name] is and what it is used for
2. What you need to know before you take [HA483 trade name]
3. How to take [HA483 trade name]
4. Possible side effects
5. How to store [HA483 trade name]
6. Contents of the pack and other information

1. What [HA483 trade name] is and what it is used for

[HA483 trade name], which contains zidovudine as the active ingredient, belongs to a group of antiviral medicines called nucleoside analogue reverse transcriptase inhibitors (NRTIs). These are used to treat human immunodeficiency virus (HIV) infection.

[HA483 trade name] is used:

- in antiretroviral combination therapy for the treatment of HIV infection in children
- in newborns and infants, for the prevention of mother-to-child transmission of HIV

Treatment with [HA483 trade name] reduces the amount of virus in your child's body and keeps it at a low level. It also increases CD4 cell counts. CD4 cells are a type of white blood cell that are important to help fight infection. Your health care provider will be monitoring the effectiveness of your child's treatment.

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. This medicine is not a cure for HIV infection. While taking [HA483 trade name], you may still develop infections or other illnesses associated with HIV infection.

2. What you need to know before you take [HA483 trade name]

Do not use [HA483 trade name] if your child:

- Is allergic (*hypersensitive*) to zidovudine or to any of the other ingredients of [HA483 trade name];
- Has a very low red blood cell count (severe anaemia) or very low white blood cell count (neutropenia).

Do not use [HA483 trade name] if a newborn baby has certain liver problems:

- Some cases of increased amount of bilirubin in the blood (hyperbilirubinaemia), a condition which might make the baby's skin look yellow;
- Excessive amount of certain liver enzymes in the blood.

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

Take special care with [HA483 trade name]

Before using this medicine, you should tell your health care provider if your child:

- suffers from liver disease (such as hepatitis) or severe kidney disease,
- has diabetes and is using insulin.

It is important that your child's health care provider knows about all your child's symptoms even if you think they are not related to HIV infection.

Blood disorders

Anaemia (low red blood cell count) and neutropenia/leukopenia (low white blood cell count) may occur within 4–6 weeks after starting treatment with [HA483 trade name]. If severe, the health care provider may stop treatment with [HA483 trade name]. This occurs more commonly in patients with advanced HIV disease and with higher doses of zidovudine. Regular blood tests will be arranged to check whether there is a problem. This adverse reaction is infrequent in patients with early HIV disease and blood tests may be performed less frequently.

Lactic acidosis

The class of medicines to which [HA483 trade name] belongs (NRTIs) can cause a condition called lactic acidosis, together with an enlarged liver. Lactic acidosis, if it occurs, usually develops after a few months of treatment. Lactic acidosis is a build-up of lactic acid in the body, which can cause dehydration and coma. Deep, rapid breathing, drowsiness, and non-specific symptoms such as nausea, vomiting and stomach pain, may indicate the development of lactic acidosis. Lactic acidosis may rarely lead to liver failure, kidney failure or fatal hepatitis. This rare, but serious side effect occurs more often in women, particularly if very overweight. If your child has liver disease, he or she may also be more at risk of getting this condition. While taking [HA483 trade name], the health care provider will monitor your child closely for any signs that he or she may be developing lactic acidosis.

Liver disease

Patients with chronic hepatitis B or C who are treated with antiretroviral agents are at increased risk for severe and potentially fatal liver adverse events and may require blood tests for monitoring of liver function.

In patients with a chronic hepatitis B infection, the treatment should not be stopped without instructions from the health care provider, as he or she may have a recurrence of the hepatitis. This recurrence may be more severe if the patient has serious liver disease.

Additionally, patients receiving zidovudine with ribavirin in combination with alpha interferons could be at increased risk of developing anaemia (low number of red blood cells). Therefore, the use of zidovudine and ribavirin in combination with alpha interferons is not recommended.

Immune Reactivation Syndrome

In some patients with advanced HIV infection (AIDS) and a history of AIDS-associated (opportunistic) infection, signs and symptoms of inflammation from such previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present without obvious symptoms. In addition, autoimmune disorders (the immune system attacking healthy body tissue) may also occur after you start taking medicines for the treatment of your HIV infection. These may occur many months after the start of treatment. If you notice any symptoms of infection or other symptoms in your child 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 the health care provider immediately to seek necessary treatment.

Fat distribution

Loss of body fat may occur in patients receiving zidovudine. Contact the doctor or health care provider if you notice changes in your child's body fat.

Bone problems

Some patients taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue). The risk of developing this disease may be higher if the immune system is severely

weakened, or if one drinks alcohol regularly. So far, this disease has been reported mainly in adults. However, if your child suffers from joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement, inform the health care provider.

Other

Your child will need to take [HA483 trade name] every day. This medicine helps to control your child's condition, but it is not a cure for HIV infection. Your child may continue to develop other infections (opportunistic infection) and other illnesses associated with HIV disease. You should keep in regular contact with your child's health care provider. Do not stop your child's medicine without first talking to the health care provider.

Taking other medicines

Please tell the health care provider if your child is taking or has recently taken any other medicines, including herbal medicines and medicines obtained without a prescription. These may affect the action of zidovudine, or zidovudine may affect their action.

[HA483 trade name] should not be taken with either stavudine or ribavirin.

Do not take [HA483 trade name] with rifampicin (an antibiotic).

[HA483 trade name] may also interact with valproic acid, fluconazole, methadone and probenecid making side effects worse; these medicines should be used with caution.

Taking [HA483 trade name] at the same time as other medicines that are potentially toxic to the kidneys or bone marrow may increase the risk of adverse reactions to [HA483 trade name]. Such medicines include, for instance, pentamidine, dapsone, pyrimethamine, sulfamethoxazole + trimethoprim, amphotericin, flucytosine, ganciclovir, valganciclovir, interferon, vincristine, vinblastine and doxorubicin. If your child requires any of these medications with [HA483 trade name], then the health care provider may need to monitor his or her kidney function and blood parameters more closely and, if required, the dosage of one or more of the drugs may be reduced.

Taking [HA483 trade name] with food and drink

[HA483 trade name] may be taken with or without food.

Pregnancy

If a woman becomes pregnant, or is planning to become pregnant, she should contact the health care provider to discuss the potential adverse effects and the benefits and risks of the antiretroviral therapy to the pregnant woman and her child.

Breast-feeding

Zidovudine, the active ingredient in this medicine, is found in human breast milk.

A woman with HIV who wants to breastfeed her baby should discuss the risks and benefits with her healthcare provider.

Driving and using machines

No studies on the effects of zidovudine on the ability to drive and use machines have been performed. However, one should consider the state of the person's health and the possible side effects of zidovudine before one considers driving or using machines.

3. How to take [HA483 trade name]

Always take [HA483 trade name] exactly as your health care provider has instructed you. You should check with your health care provider if you are unsure.

The usual dose of [HA483 trade name] for patients weighing 25 kg or more is one tablet of 300 mg zidovudine twice a day. Each dose of [HA483 trade name] should be taken approximately 12 hours apart. Swallow [HA483 trade name] whole with water or another drink.
[HA483 trade name] can be taken with or without food.

Other formulations containing less zidovudine are available for dosing in children weighing less than 25kg.

[HA483 trade name] will always be taken in combination with other antiretroviral medication; please make sure to follow the instructions within the supplied package leaflets.

If you take more [HA483 trade name] than you should
If you have taken too many tablets or if someone accidentally swallows some, there is no immediate danger. However, you should contact your health care provider, or the nearest hospital emergency department for further advice.

If you forget to take [HA483 trade name]
If you forget to take a dose of your medicine, take it as soon as you remember, and then continue as before. If your next dose is due in less than 6 hours, do not take the forgotten dose, but take the next regular dose when it is due. Do not take a double dose to make up for forgotten individual doses.

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

4. Possible side effects

Like all medicines, [HA483 trade name] can cause side effects, although not everybody gets them. When treating HIV infection, it is not always possible to differentiate between unwanted effects caused by [HA483 trade name], or those caused by any other medicines your child may be taking at the same time, or by the HIV disease. For this reason, it is important that you inform the health care provider of any change in your child's health.

The most serious adverse reactions include anaemia (low red blood cell count), low white blood cell count and lactic acidosis (a build-up of lactic acid in the body that can cause dehydration and coma). These are more common in patients with advanced HIV infection.

Anaemia has not been serious during [HA483 trade name] use for prevention of mother-to-child transmission.

Zidovudine may cause loss of body fat, particularly in the arms, legs and face.

Very common side effects (greater than 1 in every 10 patients treated):

- headache
- feeling sick (nausea)

Common side effects (greater than 1 in every 100 patients treated):

- decreased red blood cell count (anaemia). If the number of red blood cells is reduced, there may be symptoms of tiredness or breathlessness.
- decreased white blood cell count. A reduction in white blood cell count can cause proneness to infection.
- vomiting, abdominal pain, diarrhoea
- dizziness
- raised blood levels of liver enzymes and of bilirubin in the blood which may make your skin look yellow.
- muscle pain

Uncommon side effects (between 1 in 1 000 and 1 in 100 patients treated):

- low platelet count. If there is a low platelet count, you may notice that the child bruises more easily.
- decrease in the number of all kinds of blood cells (pancytopenia).
- difficulties breathing
- wind (flatulence)
- skin rash
- fever
- muscle tissue disorders (myopathy), weakness
- general aches and pains

Rare side effects (between 1 in 10 000 to 1 in 1 000 patients treated):

- anxiety
- depression
- sleeplessness (insomnia)
- not being able to concentrate
- feeling drowsy
- tingling of the skin (‘pins and needles’)
- cough
- loss of appetite
- taste disturbance
- indigestion
- inflammation of the pancreas (pancreatitis)
- chest pain
- disease of the heart muscle
- fits (convulsions)
- nail and skin pigmentation
- colour change of the inside of the mouth
- hives
- flu-like feelings – chills, sweating
- sweating
- enlarged breasts in male patients
- fat accumulation in the liver
- inability to produce new red blood cells (pure red cell anaemia)
- increased urinary frequency
- lactic acidosis (a build-up of lactic acid in the body, that can cause dehydration and coma).

Deep, rapid breathing, drowsiness, and non-specific symptoms such as nausea, vomiting and stomach pain, may indicate the development of lactic acidosis.

Very rare side effects (less than 1 in 10 000 patients treated):

- loss of production of all blood cells (aplastic anaemia).

Frequency not known (frequency cannot be estimated from the available data):

Changes in body shape due to changes in fat distribution have been reported in patients treated with medications of the group NRTIs. This may include loss of fat from legs, arms and face, increased fat in the abdomen (belly) and other internal organs, breast enlargement and fatty lumps on the back of the neck ('buffalo hump'). The cause and long-term health effects of these conditions are not known at this time.

Also, osteonecrosis (death of bone tissue) and immune reconstitution syndrome have been reported in patients taking combination antiretroviral therapy (see also section 2 “Take special care with [HA483 trade name]”).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell the health care provider.

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 improve understanding about the safety of this medicine.

5. How to store [HA483 trade name]

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

Do not store above 30°C. Protect from high humidity.

Do not use this medicine after the expiry date (exp) which is stated on the carton.The expiry date refers to the last day of that month.

Do not use this medicine if you notice any description of the visible signs of deterioration that it is different from the description 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 [HA483 trade name] contains

The active ingredient is 300 mg zidovudine

The other ingredients are:
Tablet core: Hypromellose, magnesium stearate, microcrystalline cellulose and sodium starch glycolate.

Film coating (Opadry white): Hypromellose, polyethylene glycol 400, polysorbate 80 and titanium dioxide.

What [HA483 trade name] looks like and contents of the pack

White, round biconvex, film-coated tablet plain on both the sides.
The tablets should not be divided.

The primary packs are:

- PVDC/PVC–Aluminium blisters; 10 tablets per blister card and 10 blister cards per carton (pack size: 100 tablets).
- Round, white opaque HDPE bottle 40cc/33 MM SP 400 Neck Style M (heavy weight) sealed with induction seal and white round, polypropylene cap (pack size: 30 tablets).
- Round, white opaque HDPE bottle 50cc/33 MM SP 400 Neck Style M (heavy weight) sealed with induction seal and white round, polypropylene cap (pack size: 60 tablets)
- Round, white opaque HDPE bottle 75cc/38 MM SP 400 Neck Style M (heavy weight) sealed with induction seal and white round, polypropylene cap; (pack size: 90 tablets).

Supplier and Manufacturer

Supplier

Micro Labs Ltd
31, Race Course Road
Bangalore-560001
Karnataka
India
Tel : +91-80-22370451-57
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Manufacturer

Micro Labs Limited
Plot No S-155 to S-159, Verna Industrial Estate,
Phase III, Verna, Goa – 403722, India
Tel: +91-832- 6686262
Fax No. +91-832- 6686203

For any information about this medicine, contact the local representative of the supplier:

Micro Labs Ltd,
31, Race Course Road,
Bangalore-560001,
Karnataka, India.

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

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