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.

[*] https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[HA200 trade name] †
Nevirapine

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 your child's.
- 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 [HA200 trade name] is and what it is used for

[HA200 trade name] is an HIV medicine (antiretroviral) that contains the active ingredient nevirapine.

It is used with other HIV medicines for the treatment of human immunodeficiency virus (HIV-1) infection in children weighing up to 25 kg.

[HA200 trade name] can also be given to newborn babies to protect them against HIV-1 infection passed from mother to baby at birth and during breast-feeding.

The active ingredient of [HA200 trade name], nevirapine, helps to control HIV-1 infection by blocking an enzyme in the virus called *reverse transcriptase,* which is needed for making copies of the virus. It does not cure HIV infection but reduces the amount of the virus in the body and helps keep it at a low level. Because of the way it works, nevirapine is called a *non-nucleoside reverse transcriptase inhibitor* (often abbreviated NNRTI).

To prevent the virus becoming resistant to nevirapine, [HA200 trade name] treatment is given together with other antiretroviral medicines. Your health care provider will recommend the best medicines for your child.

Although this medicine is intended for use in children, safety information based on nevirapine use in adults is also provided for completeness.

2. What you need to know before you give [HA200 trade name] to your child

Do not give your child [HA200 trade name]

- if your child is allergic (hypersensitive) to nevirapine or any of the other ingredients of [HA200 trade name] (listed in section 6)
- if your child has taken a medicine containing nevirapine before and had to stop the treatment because your child suffered from:
  - severe skin rash
  - skin rash with other symptoms, for example:
    - fever

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

  - blistering
  - mouth sores
  - inflammation of the eye
  - swelling of the face
  - general swelling
  - shortness of breath
  - muscle or joint pain
  - general feeling of illness
  - abdominal pain
  - allergic (hypersensitivity) reactions
  - inflammation of the liver (hepatitis)
- if your child has severe liver disease
- if your child had to stop nevirapine treatment in the past because of changes in liver function
- if your child is taking rifampicin (a medicine for tuberculosis) or St John's wort (Hypericum perforatum, herbal remedy against depression). These medicines may stop [HA200 trade name] from working properly

Take special care with [HA200 trade name]

During the first 18 weeks of treatment with [HA200 trade name] you and your health care provider must watch out for signs of liver or skin reactions in your child. The reactions can become severe and even life-threatening. Your child is at highest risk of such reactions in the first 6 weeks of treatment.

Your child **should stop taking** [HA200 trade name] and you **must contact** your health care provider at once if your child has severe rash or develops allergic reactions (hypersensitivity) together with other side effects such as:
- fever
- blistering
- mouth sores
- redness and swelling of the eye
- swelling of the face
- swelling in various parts of the body
- shortness of breath
- muscle or joint pain
- general feeling of illness
- abdominal (belly) pain.

If your child has a mild rash without any other reaction tell your health care provider **immediately**. The health care provider will advise you whether your child should stop taking [HA200 trade name].

Your child should stop taking [HA200 trade name] and you must contact your health care provider at once if your child has symptoms of liver damage. The following symptoms can suggest liver damage:
- loss of appetite
- feeling sick (nausea)
- vomiting
- yellow skin and eyes (jaundice)
- dark urine
- discoloured stool
- abdominal (belly) pain
-

If your child develops severe liver, skin or allergic (hypersensitivity) reactions whilst taking [HA200 trade name], your child should never take nevirapine again without checking with your health care provider.

Your child must take the dose of [HA200 trade name] as prescribed. This is especially important in the first 2 weeks of treatment (see more information in 'How to give [HA200 trade name]').

The following patients are at increased risk of liver problems while taking [HA200 trade name]:

- women
- people who have hepatitis B or C infection
- people whose liver function tests are abnormal
- people with higher CD4 cell count at the start of nevirapine therapy (women more than 250 CD4-cells per cubic millimetre, men more than 400 CD4-cells per cubic millimetre)

In some patients with advanced HIV infection (AIDS) who have had other infections, signs and symptoms of these previous infection may occur soon after starting antiretroviral treatment ('immune reactivation syndrome'). These symptoms probably result from improvement in the body's immune response, enabling the body once again to fight infections that may be present but caused no obvious symptoms. If you notice any symptoms of infection, tell your health care provider immediately.

Also, autoimmune disorders (involving the immune system attacking healthy body tissue) may occur after starting treatment with HIV medicines. Autoimmune disorders may occur many months after the start of treatment. Tell your health care provider immediately if you notice any infection or other symptoms such as muscle weakness, weakness starting in the hands and feet and moving towards the trunk of the body, palpitations, tremor or hyperactivity.

Changes of body fat may occur in patients receiving combination antiretroviral therapy. Contact your health care provider if you notice changes in body fat (see section 4, Possible side effects).

Some patients taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The condition is more likely with long-term combination antiretroviral therapy, corticosteroid use, excessive use of alcohol, very weak immune system, and being overweight. Osteonecrosis causes joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms tell your health care provider.

If your child is also taking zidovudine, tell your health care provider because it may be necessary to check your child's white blood cells.

Nevirapine is not a cure for HIV infection. Therefore, your child may continue to develop infections and other illnesses associated with HIV infection. You should be in regular contact with the health care provider.

Nevirapine does not prevent the risk of passing on HIV to others through blood or sexual contact and precautions are needed to prevent passing on HIV to other people. Ask your health care provider for more information.

Taking other medicines

Before your child starts nevirapine treatment, tell your health care provider if your child is taking or has taken any other medicines, including medicines obtained without a prescription. Your health care provider might need to check if your child's other medicines are still needed and if any doses need to be changed. Carefully read the package leaflet of all other HIV medicines your child is taking in combination with [HA200 trade name].

Tell your health care provider if your child is taking or has recently taken:

- St John's wort (Hypericum perforatum, medicine to treat depression)
- rifabutin and rifampicin (medicines to treat tuberculosis)
- clarithromycin and other macrolides antibiotics (medicine to treat bacterial infection) fluconazole, itraconazole and ketoconazole (medicines to treat fungal infection)

- methadone (medicine for opioid addiction)
- warfarin (medicine to prevent blood clotting)
- atazanavir, delavirdine, efavirenz, elvitegravir/cobicistat, etravirine, fosamprenavir, lopinavir/ritonavir, rilpivirine, and zidovudine (medicines to treat HIV-infection)
- boceprevir, telaprevir, daclatasvir, elbasvir/grazoprevir, glecaprevir/pibrentasvir, sofosbuvir/velpatasvir (medicines to treat hepatitis C)

Your health care provider will carefully check the effect of [HA200 trade name] and any of these medicines if your child is taking them together.

A contraceptive (birth control) pill or other types of hormonal contraception may not be suitable for a woman starting nevirapine treatment. The woman should ask her health care provider for advice on an alternative method of contraception. Barrier methods of contraception (e.g. condoms) are suitable and they prevent passing on of HIV to another person.

A woman using post-menopausal hormone replacement therapy should take advice from her health care provider before starting nevirapine treatment.

Taking [HA200 trade name] with food and drink

There are no restrictions on taking [HA200 trade name] with food and drink.

Pregnancy and breast-feeding

A woman who is pregnant or thinks she may be pregnant should ask her health care provider before taking any medicine.

If a mother wants to breast-feed her baby, she should ask her health care provider for advice on the risks and benefits. Treatment with medicines of mother or child or both may be needed.

Driving and using machines

The effect of nevirapine on a person's ability to drive vehicles and use machinery has not been specifically studied. Nevirapine may make a person feel tired. If the person feels tired or feels that the ability to drive or use machines may be affected then the person should not drive or use machines.

Important information about some of the ingredients of [HA200 trade name]

[HA200 trade name] contains 250 mg of sorbitol in each 5 ml of the medicine. Sorbitol is a source of fructose. If a health care provider has told you that your child has an intolerance to some sugars or if your child has been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your child's health care provider before giving this medicine to your child.

[HA200 trade name] also contains methyl parahydroxybenzoate and propyl parahydroxybenzoate. These ingredients can cause allergic reactions (possibly delayed).

This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially 'sodium-free'.

3. How to give [HA200 trade name]

Always give this medicine exactly as the health care provider has told you. Check with your health care provider if you are not sure.

The health care provider will work out the right dose for your child, taking into account their age and weight. They will also explain any other medicines that must be taken. Make sure that you understand what doses your child must be given.

[HA200 trade name] should only be given by mouth (see 'How to give [HA200 trade name]', below). Your child may take [HA200 trade name] with food or between meals.

If you have any questions about [HA200 trade name] treatment, ask your health care provider.

Treatment of HIV infection (in combination with other antiretroviral drugs)

For treating HIV infection, your child should be given the selected dose once a day for the first 14 days of treatment ('lead-in period'). After this they will switch to getting the dose twice daily.

It is very important that your child takes [HA200 trade name] only once a day for the first 14 days ('lead-in' period). If your child develops any rash during this period, do not increase the dose but see the health care provider. The 14-day 'lead-in' period can lower the risk of skin rash.

For treating children more than 4 weeks old who weigh up to 14 kg the usual recommended doses are:

Usual doses for treating HIV infection (in combination with other antiretroviral medicines)		
Child's weight	**'Lead-in' dose for first 14 days in ml of [HA200 trade name]**	**Maintenance dose in ml of [HA200 trade name]**
3–5.9 kg	5 ml once daily	5 ml twice daily
6–9.9 kg	8 ml once daily	8 ml twice daily
10–13.9 kg	10 ml once daily	10 ml twice daily

For treating children who weigh between 14 and 25 kg, nevirapine tablets that can be made into a mixture with water (dispersible tablets) are available. However, if these cannot be used, the following doses of [HA200 trade name] may be given:

Usual doses for treating HIV infection (in combination with other antiretroviral medicines)		
Child's weight	**'Lead-in' dose for first 14 days in ml of [HA200 trade name]**	**Maintenance dose in ml of [HA200 trade name]**
14-19.9 kg	15 ml once daily	15 ml twice daily
20-24.9 kg	20 ml once daily	20 ml twice daily

For children and older patients weighing more than 25 kg, tablets containing larger amounts of nevirapine are available.

Your health care provider will check your child for unwanted effects such as rash and for any problems with the liver. The health care provider may decide to stop [HA200 trade name] treatment if necessary. The health care provider might then restart nevirapine at a lower dose.

As [HA200 trade name] must always be taken with other HIV antiretroviral medicines, you should follow the instructions for your other medicines carefully. These are supplied in the package leaflets for those medicines.

Your child should continue to take [HA200 trade name] for as long as instructed by the health care provider.

Preventing passing HIV infection from mother to newborn baby

For preventing infection in a new-born baby, [HA200 trade name] is started as soon as possible after birth, preferably within the first 6 hours, together with other HIV medicines as appropriate. The medicine is usually given for 6 weeks but it can be given for another 6 weeks if the baby is breast-feeding and the mother is not taking antiretroviral medicines.

The WHO-recommended doses for the baby are shown in the table below:

Age	Dose in mL of [HA200 trade name]
Birth to 6 weeks, weighing 2 to 2.5 kg	1 ml once daily
Birth to 6 weeks, weighing over 2.5 kg	1.5 ml once daily
6 weeks – 12 weeks	2 ml once daily

If your baby weighs less than 2 kg at birth, your health care provider will work out a dose for them based on their weight.

If your child takes more [HA200 trade name] than they should

If your child accidentally takes too much medicine, you should tell the health care provider immediately or contact your nearest hospital emergency department for further advice. Your child may require medical attention. Remember to take the medicine with you, and show it to the health care provider. If you have run out of solution, take the empty packaging along with you.

If you forget to give [HA200 trade name]

It is important not to miss doses of [HA200 trade name]. If you forget to give a dose of your child's medicine, and notice this within 8 hours, give the missed dose as soon as possible. Then give the next regular dose at its proper time.

If it is longer than 8 hours since the dose should have been given, do not give it. Instead, just give your child their next dose at the usual time. Do not give a double dose to make up for forgotten doses.

If your child stops taking [HA200 trade name]

It is important that your child continues taking [HA200 trade name] correctly unless the health care provider instructs that your child should stop taking it.

Taking all doses at the right time:

- ensures that the combination of HIV medicines work as well as possible
- reduces the chances of the HIV infection becoming resistant to the medicines your child is taking.

If your child stops taking [HA200 trade name] for more than 7 days, your health care provider will ask that the child starts the 14-day 'lead-in' period (described above) once again, before returning to the twice-daily dose.

How to give [HA200 trade name]

This medicine will come with an oral dosing syringe or dosing cup to help you accurately measure the dose your health care provider has prescribed for your child. Follow the instructions given below on how to prepare and use an oral dosing syringe.

1. Shake the bottle gently before giving the medicine.
2. Open the bottle. Keep the bottle cap safely.
3. Push the tube (cannula) of the plastic adapter fully into the bottle until the white cap fits into the mouth of the bottle
4. Insert the syringe into the white cap of the adapter.
5. Draw the required volume of liquid (as prescribed by the health care provider) into the syringe ensuring that no large bubbles are present in the syringe (a few tiny bubbles will not cause problems with the dose)
6. Put the syringe into your child's mouth, placing the tip of the syringe against the inside of their cheek. Slowly push the plunger in, allowing time to swallow. Do not push too hard and squirt the liquid into the back of your child's throat or they may cough or choke.
7. The most that you can withdraw is 2 ml at a time. If you need a higher dose, repeat steps 4–6 above.
8. Close the bottle with its cap, leaving the adapter in place.

If a dosing cup is used instead of a syringe, after giving the dose to your child, add a small quantity of water to the cup and rinse it around. Give this water to your child to drink, to make sure they get the full dose of the medicine.

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

4. Possible side effects

Like all medicines, [HA200 trade name] can cause side effects, but not everybody gets them.

The most important side effects of nevirapine are severe and life-threatening skin reactions and serious liver damage. These reactions occur mainly in the first 18 weeks of treatment with [HA200 trade name]. This is therefore an important period which requires close monitoring by your health care provider.

When rash occurs it is normally mild to moderate. However, in some patients a rash, which appears as a blistering skin reaction, can be severe (Stevens-Johnson syndrome and toxic epidermal necrolysis) and deaths have been recorded. Most of the cases of both severe rash and mild/moderate rash occur in the first six weeks of treatment.

Allergic (hypersensitivity) reactions can occur. Such reactions may appear as anaphylaxis (a severe form of allergic reaction) with symptoms such as rash, swelling of the face, difficulty breathing (bronchial spasm), anaphylactic shock.

The side effects described below have occurred in patients given nevirapine:

Very common (occurring in more than 1 in 10 patients treated):
- rash

Common (occurring in 1 in 100 to 1 in 10 patients treated):
- decreased number of white blood cells (granulocytopenia)
- allergic reactions (hypersensitivity)
- headache
- feeling sick (nausea)
- vomiting
- abdominal pain
- loose stools (diarrhoea)
- inflammation of the liver (hepatitis)
- feeling tired (fatigue)
- fever
- abnormal liver function tests

Uncommon (occurring in 1 in 1000 to 1 in 100 patients treated):
- allergic reaction characterised by rash, swelling of the face, difficulty breathing (bronchial spasm) or anaphylactic shock
- decreased numbers of red blood cells (anaemia)
- yellow skin (jaundice)
- severe and life-threatening skin rashes (Stevens-Johnson syndrome/toxic epidermal necrolysis)
- hives (urticaria)
- accumulation of fluid and swelling under the skin (angioedema)
- joint pain (arthralgia)
- muscle pain
- decreased blood phosphorus
- increased blood pressure

Rare: (occurring in 1 in 10 000 to 1 in 1000 patients treated):
- sudden and intense inflammation of the liver (fulminant hepatitis)

- drug rash with symptoms which affect the whole body (drug rash with eosinophilia and systemic symptoms)
- sudden and intense inflammation of the liver (fulminant hepatitis)
- drug rash with symptoms which affect the whole body (drug rash with eosinophilia and systemic symptoms)

Combination antiretroviral therapy may cause changes in body shape due to changes in fat distribution. These 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. Combination antiretroviral therapy may also cause raised lactic acid, resistance to insulin, raised sugar in the blood, and increased fats in the blood (hyperlipaemia).

The following events have also been reported when nevirapine has been used in combination with other antiretroviral medicines:

- decreased numbers of red blood cells or platelets
- inflammation of the pancreas
- decrease in or abnormal skin sensations

These events are commonly associated with other antiretroviral medicines and may be expected when nevirapine is used in combination with other medicines; however, it is unlikely that these events are due to treatment with nevirapine.

Use in children
Reduction in white blood cells (granulocytopenia) is more common in children. A reduction in red blood cells (anaemia), which may be related to nevirapine therapy, is also more common in children.

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 [HA200 trade name]

[HA200 trade name] should be stored below 30°C.

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

Do not use this medicine after the expiry date which is stated on the carton and on the bottle after "EXP". The expiry date refers to the last day of that month.

[HA200 trade name] should be used within 1 months of first opening the bottle.

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 [HA200 trade name] contains

- The active substance is nevirapine. Each mL contains 10 mg of nevirapine (as nevirapine hemihydrate).
- The other ingredients are:
    - methyl parahydroxybenzoate
    - propyl parahydroxybenzoate
    - polysorbate 80
    - microcrystalline cellulose
    - simeticone emulsion

- purified water
- sodium saccharin
- sorbitol solution 70% (non-crystallizing)
- carboxy methyl cellulose sodium

What [HA200 trade name] looks like and contents of the pack

[HA200 trade name] is a white to off-white uniform suspension.

It is available in the following packs:

- 100-ml or 240 ml amber-coloured PET bottle pack with a plastic pouch containing a plastic cannula, a 2-ml syringe with a dust cap and a10-mL measuring cup.
- 25-ml amber-coloured glass bottle pack with a plastic pouch containing a plastic cannula, a 2-ml syringe with a dust cap and a 10-ml measuring cup.
- 10-ml amber-coloured glass bottle pack with a plastic pouch containing a plastic cannula, a 2-ml syringe with a dust cap.

Nevirapine is also available as tablets.

Supplier and Manufacturer

Supplier

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Manufacturers

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For any information about this medicine, contact the supplier.

This leaflet was last revised in February 2021

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