

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/prequal/sites/default/files/documents/75%20SRA%20clarification_February2017_0.pdf

Information for the patient

[HA510 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 [HA510 trade name] is and what it is used for
2. What you need to know before you give [HA510 trade name] to your child
3. How to give [HA510 trade name]
4. Possible side effects
5. How to store [HA510 trade name]
6. Contents of the pack and other information

1. What [HA510 trade name] is and what it is used for

[HA510 trade name] contains the active ingredient nevirapine.

Nevirapine belongs to a group of medicines called antiretrovirals, which are used for the treatment of human immunodeficiency virus (HIV-1) infection.

Nevirapine helps to control HIV-1 infection by preventing the multiplication of HIV in the blood. Specifically, nevirapine interferes with the virus enzyme called reverse transcriptase, which is needed for making copies of the virus. Because of the way it works, nevirapine is called non-nucleoside reverse transcriptase inhibitor (often abbreviated NNRTI).

To prevent the virus becoming resistant to nevirapine, your child must take [HA510 trade name] with other antiretroviral medicines. Your health care provider will recommend the best medicines for your child.

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 [HA510 trade name] to your child

Do not give your child [HA510 trade name]

- if your child is allergic to nevirapine or to any of the other ingredients of this medicine (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:
 - o severe skin rash
 - o skin rash with other symptoms, for example:
 - fever
 - blistering
 - mouth sores
 - inflammation of the eye
 - swelling of the face
 - general swelling

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

- 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 has had to stop nevirapine treatment in the past because of changes in liver function
- if your child is taking St John's wort (*Hypericum perforatum*, herbal remedy against depression). This herbal substance may stop [HA510 trade name] from working properly

Take special care with [HA510 trade name]

During treatment with [HA510 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 the highest risk of such reactions in the first 6 weeks of treatment.

Your child **should stop taking** [HA510 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 reactions tell your health care provider at once. The health care provider will advise you whether your child should stop taking [HA510 trade name].

Your child should stop taking [HA510 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 [HA510 trade name], your child should never take nevirapine again without checking with your health care provider

Your child must take the dose of [HA510 trade name] as prescribed. This is especially important in the first 2 weeks of treatment (see more information in 'How to administer [HA510 trade name]').

The following patients are at higher risk of liver problems while taking [HA510 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. Therefore, your child 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.

Use in children

[HA510 trade name] can be taken by children of all age groups. Always follow the exact instructions given by your child's health care provider.

Taking other medicines

Before your child starts nevirapine treatment, tell your health care provider if your child is taking or has taken any 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 with [HA510 trade name].

If your child is taking or is prescribed a medicine which contains rifampicin to treat tuberculosis, you must tell your health care provider before taking this medicine with [HA510 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 and telaprevir (medicines to treat hepatitis C)

Your health care provider will carefully check the effect of [HA510 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 [HA510 trade name] with food and drink

There are no restrictions on taking [HA510 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.

[HA510 trade name] contains lactose

If a health care provider has told you that your child has an intolerance to some sugars, contact your health care provider before giving this medicine to your child.

[HA510 trade name] contains aspartame

Aspartame is a source of phenylalanine. It may be harmful if your child has phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

3. How to give [HA510 trade name]

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

Your child should not take [HA510 trade name] on its own. Your child must take it with at least two other antiretroviral medicines. Your health care provider will recommend the best medicines for your child.

Give [HA510 trade name] by mouth only. Your child may take [HA510 trade name] with food or between meals.

Dose

The dose of nevirapine for a child is calculated according to the child's body weight. [HA510 trade name] is intended for children weighing less than 25 kg. For children weighing more than 25 kg, other products, with larger amount of nevirapine, are available.

At the start of treatment, give the dose once a day usually for 2 weeks. This is called the 'lead-in' dose. If your child has any rash during this period, do not increase the dose but see your health care provider. The 2-week 'lead-in' period lowers the risk of skin rash.

If all is well, your health care provider will then ask you to give the dose twice daily to continue treatment.

The recommended lead-in and maintenance doses are shown below:

Weight	'Lead-in' dose for 2 weeks ¹	Maintenance dose
3–5.9 kg	1 tablet once daily	1 tablet twice daily
6–9.9 kg	1½ tablets once daily	1½ tablets twice daily
10–13.9 kg	2 tablets once daily	2 tablets twice daily
14–19.9 kg	2½ tablets once daily	2½ tablets twice daily
20–24.9 kg	3 tablets once daily	3 tablets twice daily

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 [HA510 trade name] treatment if necessary. The health care provider might then restart nevirapine treatment at a lower dose.

For patients on kidney dialysis, the health care provider may adjust the dose of [HA510 trade name] because dialysis removes nevirapine from blood.

Your child should continue to take [HA510 trade name] for as long as instructed by your health care provider.

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

If your child takes more [HA510 trade name] than your child should

Your child must not take more [HA510 trade name] than prescribed by your health care provider. There is little information on the effects of nevirapine overdose. See your health care provider if your child has taken more [HA510 trade name] than your child should.

If your child forgets to take [HA510 trade name]

Try not to miss a dose. If you notice that your child has missed a dose within 8 hours, take the missed dose as soon as possible. If more than 8 hours have passed since your child's dose was missed, omit the missed dose and give the next dose at the usual time.

If your child stops taking [HA510 trade name]

It is important to give HIV medicines, including [HA510 trade name], regularly and at the right time to:

- ensure that the combination of antiretroviral medicines works as well as possible
- reduce the chances of the HIV becoming resistant to the antiretroviral medicines your child is taking

It is important that your child continues taking [HA510 trade name] correctly, unless your health care provider stops the medicine.

If your child has not taken [HA510 trade name] for more than 7 days, your health care provider will ask that your child starts the 2-week 'lead-in' period once again, before returning to the twice-daily dose.

If you have any questions about your treatment, ask your health care provider.

How to give [HA510 trade name]

Ask your child to swallow [HA510 trade name] with water. If your child cannot swallow the tablet, you can mix the tablets in a small quantity of water as described below.

1. Using dry hands, put the recommended dose in a clean tumbler (or cup).
2. Add a small amount of clean drinking water to the tumbler. The amount of water depends on how much is needed to mix the dose properly (see table, below) and how much your child will drink.

3. Swirl or stir the tumbler to mix the tablets completely in water.
4. The child should drink all the mixture.
5. To make sure that your child gets the full dose, rinse the tumbler with more water and the child should drink this also.

Recommended dose	Amount of clean drinking water to use for mixing the dose
1 or 1½ tablets	2 teaspoonfuls (10 ml)
2 or 2½ tablets	3 teaspoonfuls (15 ml)
3 tablets	4 teaspoonfuls (20 ml)

4. Possible side effects

Like all medicines, [HA510 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 [HA510 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.

Please inform your health care provider of any side effects; if any side effects get serious, or if you notice any side effects not listed in this leaflet.

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 [HA510 trade name]

Do not store above 30°C.

Keep out of the reach and sight of children.

Do not use [HA510 trade name] after the expiry date which is stated on the bottle and on the blister after "EXP". The expiry date refers to the last day of that month.

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 [HA510 trade name] contains

The active substance is nevirapine. Each dispersible tablet contains 50 mg nevirapine.

The other ingredients are: aspartame, corn starch, lactose monohydrate, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, strawberry cream flavour (containing natural flavouring substance, maltodextrin, propylene glycol and modified starch).

What [HA510 trade name] looks like and contents of the pack

White to off-white coloured, circular shaped, biconvex, uncoated dispersible tablet with central break line on one side and 'L' debossed on the other side. The tablet can be divided into equal doses.

Blister pack:

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

Bottle pack:

The tablets are also packaged in HDPE bottles with non-CRC HDPE screw cap, containing a 1g silica gel bag as desiccant and rayon sani coil as filler. Each HDPE bottle contains 60 tablets.

Supplier and Manufacturer

Supplier

Cipla Limited
Cipla House, Peninsula Business Park
Ganpatrao Kadam Marg, Lower Parel
Mumbai 400013, India
Phone : 9122 24826000
Fax: 9122 24826120
E-mail: globalra@cipla.com

Manufacturer

Cipla Limited
Unit II, A-42, MIDC
Patalganga, District: Raigad
410220, Maharashtra, India

Cipla Limited
Unit I, A-33 & A-37/2/2, MIDC
Patalganga, District: Raigad
410220, Maharashtra, India

For any information about this medicine, contact the supplier.

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