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

[HA569 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 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 [HA569 trade name] is and what it is used for

[HA569 trade name] belongs to a group of medicines called antiretrovirals, which are used for the treatment of human immunodeficiency virus (HIV-1) infection.

The active ingredient of [HA569 trade name] is called nevirapine. 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, you must take [HA569 trade name] together with other antiretroviral medicines. Your health care provider will recommend the best medicines for you.

2. What you need to know before you take [HA569 trade name]

Do not take [HA569 trade name]

- if you are allergic (hypersensitive) to nevirapine or any of the other ingredients of [HA569 trade name] (listed in section 6)
- if you have taken [HA569 trade name] before and had to stop the treatment because you suffered from:
  - severe skin rash
  - 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 you have severe liver disease
- if you had to stop nevirapine treatment in the past because of changes in your liver function
- if you are taking St John's wort (*Hypericum perforatum*, herbal remedy against depression). This herbal substance may stop [HA569 trade name] from working properly

Take special care with [HA569 trade name]

During the first 18 weeks of treatment with [HA569 trade name] you and your health care provider must watch out for signs of liver or skin reactions. The reactions can become severe and even life-threatening. You are at highest risk of such reactions in the first 6 weeks of treatment.

If you have severe rash or you develop allergic reactions (hypersensitivity) accompanied by other side effects such as: 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.

you **should stop taking** [HA569 trade name]and contact your health care provider **immediately** as such reactions can become life threatening.

If you get mild rash without any other reaction please tell your health care provider **immediately**, who will advise you whether you should stop taking [HA569 trade name]

If you experience symptoms suggesting damage of the liver, such as
- loss of appetite
- feeling sick (nausea)
- vomiting
- yellow skin and eyes (jaundice)
- dark urine
- discoloured stool
- abdominal (belly) pain
-

you should stop taking [HA569 trade name] and you must contact your health care provider **immediately**.

If you develop severe liver, skin or allergic (hypersensitivity) reactions whilst taking [HA569 trade name], never take nevirapine again without checking with your health care provider. You must take the dose of [HA569 trade name] as prescribed. This is especially important in the first 14 days of treatment (see more information in 'How to take [HA569 trade name]).

Your child must take the dose of [HA569 trade name] as prescribed. This is especially important in the first 2 weeks of treatment (see more information in 'How to administer [HA569 trade name]').

The following patients are at increased risk of liver problems while taking [HA569 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 you are taking zidovudine, tell your health care provider because it may be necessary to check your white blood cells.

Nevirapine is not a cure for HIV infection. Therefore, you 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

Tell your health care provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Tell your health care provider about all other medicines you are taking before you start taking [HA569 trade name]. Carefully read the package leaflet of all other HIV medicines you are taking in combination with [HA569 trade name].

Tell your health care provider if you are taking or have 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 [HA569 trade name] and any of these medicines if you are 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.

If you are undergoing kidney dialysis, your health care provider may adjust the dose of [HA569 trade name]. This is because [HA569 trade name] can be partly removed from your blood by dialysis.

Taking [HA569 trade name] with food and drink

There are no restrictions on taking [HA569 trade name] with food and drink.

Pregnancy and breast-feeding

If you become pregnant, or are planning to become pregnant, you must contact your health care provider to discuss the potential benefits and risks of your antiretroviral therapy to you and your child.

If you are interested in breastfeeding your baby, you should discuss the risks and benefits with your healthcare provider.

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.

Ingredients of [HA569 trade name]

[HA569 trade name] contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take [HA569 trade name]

You should not use [HA569 trade name] on its own. You must take it with at least two other antiretroviral medicines.

Your health care provider will recommend the best medicines for you.

Always take [HA569 trade name] exactly as your health care provider has told you. You should check with your health care provider if you are not sure.

Only take [HA569 trade name] by mouth. Do not chew your tablets. You may take [HA569 trade name] with food or between meals.

Dosage:

Children and adolescents weighing less than 25 kg:

The recommended dose of [HA569 trade name] in children and adolescents weighing less than 25 kg is as shown below. The dose is taken once a day for the first 14 days of treatment ('lead-in' period). After 14 days, the dose is usually doubled and taken twice a day.

Weight	**'Lead-in' dose for 2 weeks**		**Maintenance dose**	
3–5.9 kg	½ tablet once daily	50 mg once daily	½ tablet twice daily	50 mg twice daily
6–9.9 kg	Use alternative formulation	75 mg once daily	Use alternative formulation	75 mg twice daily
10–13.9 kg	1 tablet once daily	100 mg once daily	1 tablet twice daily	100 mg twice daily
14–19.9 kg	Use alternative formulation	125 mg once daily	Use alternative formulation	125 mg twice daily
20–24.9 kg	1½ tablets once daily	150 mg once daily	1½ tablets once daily	150 mg twice daily

Children weighing 25 kg or more, adolescents and adults:

The recommended dose is 200 mg (two 100-mg tablets) daily for the first 14 days, followed by 200 mg (two 100-mg tablets) twice daily.

Alternative formulations such as nevirapine tablets 200 mg are more suitable for patients weighing over 25 kg.

At the start of treatment, the dose is taken once a day usually for 14 days. This is called the 'lead-in' dose. If you have any rash during this period, do not increase the dose but see your health care provider. The 14-days 'lead-in' period lowers the risk of skin rash.

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

As [HA569 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.

You should continue to take [HA569 trade name] for as long as instructed by your health care provider.

As explained in 'Take special care with [HA569 trade name]', above, your health care provider will monitor you with liver tests or for unwanted effects such as rash. Depending on the outcome your health care provider may decide to interrupt or stop [HA569 trade name] treatment. Your health care provider might then decide to restart nevirapine at a lower dose.

If you take more [HA569 trade name] than you should

Do not take more [HA569 trade name] than prescribed by your health care provider and described in this leaflet. There is little information on the effects of [HA569 trade name] overdose. See your health care provider if you have taken more [HA569 trade name] than you should.

If you forget to take [HA569 trade name]

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

If you stop taking [HA569 trade name]

Taking all doses at the right time:

- ensures that the combination of antiretroviral medicines work as well as possible

- reduces the chances of the HIV infection becoming resistant to the antiretroviral medicines you are taking.

It is important that you continue taking [HA569 trade name] correctly, as described above, unless your health care provider instructs you to stop.
If you stop taking [HA569 trade name] for more than 7 days your health care provider will instruct you to start the 14-day 'lead-in' period (described above) once again, before returning to the twice-daily dose.
If you have any questions about your treatment, ask your health care provider.

Making [HA569 trade name] mixture

If your child cannot swallow the tablet(s), then make a mixture of the tablet(s) in some water.

To make the mixture you will need:
- [HA569 trade name] tablets
- A small cup or bowl
- Drinking water
- A teaspoon
- A 10-mL oral syringe

Make the medicine mixture as follows:
1. Clean and dry your hands before making up the medicine
2. Add the required number of [HA569 trade name] tablets to a bowl
3. Using a syringe, add a small amount of clean drinking water to the bowl. The tablet(s) should be mixed in a minimum of 10 mL water; the maximum volume of water recommended for dispersion of a dose is 50 mL.
4. Stir gently until the medicine is mixed well.
5. Give all of the medicine mixture to the child using teaspoon.
6. You may give the child a little milk/juice/water after giving the medicine. This will help to take away the taste of the medicine.
7. Repeat these steps every time you need to give the medicine.

4. Possible side effects

Like all medicines, [HA569 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 [HA569 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 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 [HA569 trade name]

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

Do not use [HA569 trade name] after the expiry date stated on the bottle and on the blister card after "EXP". The expiry date refers to the last day of that month.

This product should be stored below 30°C.

Do not use this medicine if you notice that it is different from the description below.

To protect the environment, medicines should not be disposed of in wastewater or household waste. Ask your health care provider or pharmacist how to dispose of medicines no longer required.

6. Contents of the pack and other information

What [HA569 trade name] contains

- The active ingredient is nevirapine 100 mg.
- The other ingredients of [HA569 trade name] are lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, povidone, colloidal silicon dioxide and magnesium stearate.

What [HA569 trade name] looks like and contents of the pack

White to off-white, oval-shaped, uncoated tablet, debossed with '100' on one side and scored on the other side. The tablet can be divided into equal doses.

HDPE bottle
Round, opaque, white-coloured HDPE bottle, with a polypropylene child-resistant cap.
Pack sizes: 30, 60 and 90 tablets.

Blisters
PVC/PVDC-Al blisters. Pack sizes:10 tablets per blister card. 3 or 6 cards in a carton.

Supplier
Micro Labs Limited
31, Race Course Road
Bangalore - 560001
Karnataka
India
Tel: + 91 80 2237 0451 to 2237 0456
Fax: + 91 80 2237 0463
Email: exp@microlabs.in

Manufacturer
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Verna Industrial Estate
Verna Salcette- 403722, Goa
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For any information about this medicine, contact the local representative of 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