PACKAGE LEAFLET

Package leaflet: Information for the patient

Nevirapine 400 mg Prolonged-release Tablets

(nevirapine anhydrous)

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 further questions, please ask your doctor or pharmacist.
- 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 are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Nevirapine is and what it is used for

Nevirapine belongs to a group of medicines called antiretrovirals, used in the treatment of Human Immunodeficiency Virus (HIV-1) infection.

The active substance of your medicine is called nevirapine. Nevirapine belongs to a class of anti-HIV medicines called non-nucleoside reverse transcriptase inhibitors (NNRTIs). Reverse transcriptase is an enzyme that HIV needs in order to multiply. Nevirapine stops reverse transcriptase from working. By stopping reverse transcriptase from working, Nevirapine helps control HIV-1 infection.

Nevirapine is indicated for the treatment of HIV-1 infected adults, adolescents and children three years and above and able to swallow tablets. You must take Nevirapine together with other antiretroviral medicines. Your doctor will recommend the best medicines for you.

Nevirapine prolonged-release tablets should only be used after a two-week treatment with another type of nevirapine (immediate-release tablets or suspension) unless you are currently on nevirapine and are switching to the prolonged-release form.

If Nevirapine has been prescribed for your child, please note that all information in this leaflet is addressed to your child (in this case please read "your child" instead of "you").

2. What you need to know before you take Nevirapine

Do not take Nevirapine:
- if you are allergic to nevirapine or any of the other ingredients of this medicine (listed in section 6).
- if you have taken nevirapine 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
- shortness of breath
- muscle or joint pain
- general feelings of illness
- abdominal pain

- hypersensitivity (allergic) reactions
- inflammation of the liver (hepatitis)

- if you have severe liver disease
- if you have had to stop nevirapine treatment in the past because of changes in your liver function
- if you are taking a medicine containing the herbal substance St. John's Wort (*Hypericum perforatum*). This herbal substance may stop Nevirapine from working properly.

Warnings and precautions

Talk to your doctor or pharmacist before taking Nevirapine.

During the first 18 weeks of treatment with Nevirapine it is very important that you and your doctor watch out for signs of liver or skin reactions. These can become severe and even life threatening. You are at greatest risk of such a reaction during the first 6 weeks of treatment.

If you experience severe rash or hypersensitivity (allergic reactions that may appear in the form of rash) accompanied by other side effects such as
- **fever,**
- **blistering,**
- **mouth sores,**
- **inflammation of the eye,**
- **swelling of the face,**
- **general swelling,**
- **shortness of breath,**
- **muscle or joint pain,**
- **general feelings of illness,**
- **or abdominal pain**

YOU SHOULD DISCONTINUE TAKING NEVIRAPINE AND YOU MUST CONTACT your doctor IMMEDIATELY as such reactions can be potentially life-threatening or lead to death. If you ever have only mild rash symptoms without any other reaction please inform your doctor immediately, who will advise you whether you should stop taking Nevirapine.

If you experience symptoms suggesting damage of the liver, such as
- **loss of appetite,**
- **feeling sick (nausea),**
- **vomiting,**
- **yellow skin (jaundice),**
- **abdominal pain**

you should discontinue taking Nevirapine and must contact your doctor immediately.

If you develop severe liver, skin or hypersensitivity reactions whilst taking Nevirapine, NEVER TAKE NEVIRAPINE again without referring to your doctor. You must take the dose of Nevirapine as prescribed by your doctor. This is especially important within the first 14 days of treatment (see more information in "How to take Nevirapine").

The following patients are at increased risk of developing liver problems:
- women
- infected with hepatitis B or C
- abnormal liver function tests
- treatment-naïve patients with higher CD4 cell counts at the start of nevirapine therapy (women more than 250 cells/mm³, men more than 400 cells/mm³)
- pre-treated patients with detectable HIV-1 plasma viral load and higher CD4 cell counts at the start of nevirapine therapy (women more than 250 cells/mm³, men more than 400 cells/mm³).

In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection (AIDS defining illness), signs and symptoms of inflammation from 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 with no obvious symptoms. If you notice any symptoms of infection, please inform your doctor immediately.

In addition to the opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking medicines for the treatment of your 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 doctor immediately to seek necessary treatment.

Changes of body fat may occur in patients receiving combination antiretroviral therapy. Contact your doctor 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 length of combination antiretroviral therapy, corticosteroid use, alcohol consumption, severe weakness of the immune system and higher body mass index may be some of the many risk factors for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms please inform your doctor.

If you are taking nevirapine and zidovudine concomitantly please inform your doctor since he might need to check your white blood cells.

Do not take nevirapine after an exposure to HIV unless you have been diagnosed with HIV and instructed to do so by your doctor.

Prednisone should not be used to treat a rash related to nevirapine.

If you are taking oral contraceptives (e.g. "pill") or other hormonal methods of birth control during treatment with nevirapine, you should use a barrier contraception (e.g. condoms) in addition to prevent pregnancy and further HIV transmission.

If you are receiving post-menopausal hormone therapy, ask your doctor for advice before taking this medicine.

If you are taking or are prescribed rifampicin to treat tuberculosis please inform your doctor before taking this medicine with nevirapine.

Nevirapine prolonged-release tablets or parts of tablets may occasionally be passed and seen in the stool (faeces). These may look like whole tablets, but will not been found to affect the efficacy of nevirapine way your medicine works. Inform your doctor if you find tablet pieces in your faeces.

Children and adolescents

Nevirapine 400 mg prolonged-release tablets can be taken by children if they:
- are ≥ 8 years of age and weigh 43.8 kg or more
- are older than 3 years of age and below 8 years of age and weigh 25 kg or more
- have a body surface area of 1.17 square metres or above.

For smaller children smaller prolonged-release tablets or pharmacistan oral suspension liquid form are available

Other medicines and Nevirapine
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines Inform your doctor about all other medicines you are taking before you start taking Nevirapine.

Your doctor might need to monitor whether your other medicines are still working and adjust doses. Carefully read the package leaflet of all other HIV medicines you are taking in combination with Nevirapine.

It is particularly important that you tell your doctor if you are taking or have recently taken:
- St John's wort (Hypericum perforatum, a medicine to treat depression)
- rifampicin (medicine to treat tuberculosis)
- rifabutin (medicine to treat tuberculosis)
- macrolides e.g. clarithromycin (medicine to treat bacterial infections)
- fluconazole (medicine to treat fungal infections)
- ketoconazole (medicine to treat fungal infections)
- itraconazole (medicine to treat fungal infections)
- methadone (medicine used for treatment of opiate addicts)
- warfarin (medicine to reduce blood clotting)
- hormonal contraceptives (e.g. the "pill")
- atazanavir (another medicine to treat HIV-infection)
- lopinavir/ritonavir (another medicine to treat HIV-infection)
- fosamprenavir (another medicine to treat HIV-infection)
- efavirenz (another medicine to treat HIV-infection)
- etravirine (another medicine to treat HIV-infection)
- rilpivirine (another medicine to treat HIV-infection)
- zidovudine (another medicine to treat HIV-infection)
- elvitegravir/cobicistat (another medicine to treat HIV-infection)

Your doctor will carefully monitor the effect of Nevirapine and any of these medicines if you are taking them together.

Taking Nevirapine with food and drink
There are no restrictions on taking Nevirapine with food and drink.

Pregnancy, and breast-feeding

If you are pregnant or think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Breast-feeding is **not recommended** in women living with HIV because HIV infection can be passed on to the baby in breast milk.
If you are breast-feeding, or thinking about breast-feeding, you **should discuss it with** your doctor **as soon as possible**.

Driving and using machines
You may experience fatigue when taking Nevirapine. Use caution when engaging in activities such as driving, using any tools or machines. If you experience fatigue you should avoid potentially hazardous tasks such as driving or using any tools or machines.

Nevirapine contains lactose and sodium
Nevirapine prolonged-release tablets contain lactose (milk sugar).

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Nevirapine

You should not use Nevirapine on its own. You must take it with at least two other antiretroviral medicines. Your doctor will recommend the best medicines for you.

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Dosage:

Adults:
The recommended dose is one 200 mg nevirapine tablet per day for the first 14 days of treatment ("lead-in" period). A separate treatment initiation pack with 200 mg nevirapine tablets is available for this lead-in period. After 14 days, the usual dose is one Nevirapine 400 mg prolonged-release tablet once a day.

It is very important that you take only one nevirapine tablet a day for the first 14 days ("lead-in" period). If you have any rash during this period, do not start taking Nevirapine prolonged-release tablets but consult your doctor.

The 14-day "lead-in" period has been shown to lower the risk of skin rash.

Patients who are already on immediate-release tablets or oral suspension can switch to prolonged-release tablets without a lead-in period.

As Nevirapine must always be taken together 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.

Use in children and adolescents:
Nevirapine may also be available as smaller prolonged-release tablets (for children 3 years of age and above after the lead-in period) or as an oral suspension for all age groups (not marketed by the marketing authorisation holder, but may be available from other companies for all age groups).

You should continue to take Nevirapine for as long as instructed by your doctor.

As explained in 'Warnings and precautions', above, your doctor will monitor you with liver tests or for undesirable effects such as rash. Depending on the outcome your doctor may decide to interrupt or stop your Nevirapine treatment. Your doctor might then decide to restart you on a lower dose.

If you have kidney or liver problems of any degree please use only nevirapine 200 mg tablets or nevirapine 50 mg/5 ml oral suspension.

Only take Nevirapine prolonged-release tablets by mouth with a liquid. Do not chew or break your prolonged-release tablets. You may take Nevirapine with or without food.

If you take more Nevirapine than you should
Do not take more Nevirapine than prescribed by your doctor and described in this leaflet. There is at present little information on the effects of nevirapine overdose. Consult your doctor if you have taken more Nevirapine than you should.

If you forget to take Nevirapine
Try not to miss a dose. If you notice you missed a dose within 12 hours of when it was due, take the missed dose as soon as possible. If it has been more than 12 hours since the dose was due only take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Nevirapine
Taking all doses at the appropriate times:
- greatly increases the effectiveness of your combination antiretroviral medicines
- reduces the chances of your HIV infection becoming resistant to your antiretroviral medicines.

It is important that you continue taking Nevirapine correctly, as described above, unless your doctor instructs you to stop.

If you stop taking Nevirapine for more than 7 days your doctor will instruct you to start the 14 day 'lead-in' period with Nevirapine tablets (described above) once again, before returning to the once daily dose with Nevirapine prolonged-release tablets.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

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 doctor will test for these changes.

Like all medicines, this medicine can cause side effects, although not everybody gets them.

As mentioned in 'Warnings and precautions', above, 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 nevirapine. This is therefore an important period which requires close monitoring by your doctor.

If you ever observe any rash symptoms, inform your doctor immediately.

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 or life-threatening (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.

If rash occurs and you also feel sick, you must stop treatment and visit your doctor immediately.

Hypersensitivity (allergic) reactions can occur. Such reactions may appear in the form of anaphylaxis (a severe form of allergic reaction) with symptoms such as:

- rash
- swelling of the face
- difficulty breathing (bronchial spasm)
- anaphylactic shock

Hypersensitivity reactions can also occur as rash with other side effects such as:
- fever
- blistering of your skin
- mouth sores
- inflammation of the eye
- swelling of the face
- general swelling
- shortness of breath
- muscle or joint pain
- a reduction in the numbers of your white blood cells (granulocytopenia)
- general feelings of illness
- severe problems with liver or kidneys (liver or kidney failure).

Tell your doctor immediately if you experience rash and any of the other side effects of a hypersensitivity (allergic) reaction. Such reactions can be life-threatening.

Abnormal liver functioning has been reported with the use of nevirapine. This includes some cases of inflammation of the liver (hepatitis), which can be sudden and intense (fulminant hepatitis), and liver failure, which can both be fatal.

Tell your doctor if you experience any of the following clinical symptoms of liver damage:
- loss of appetite
- feeling sick (nausea)
- vomiting
- yellow skin (jaundice)
- abdominal pain

The side effects described below have been experienced by patients given nevirapine 200 mg tablets during the 14 day lead-in phase:

Common (may affect up to 1 in 10 people):
- rash
- fever
- headache
- abdominal pain
- feeling sick (nausea)
- loose stools (diarrhoea)
- feeling tired (fatigue)

Uncommon (may affect up to 1 in 100 people):
- allergic reactions (hypersensitivity)
- allergic reaction characterized by rash, swelling of the face, difficulty breathing (bronchial spasm) or anaphylactic shock
- drug reaction with systemic symptoms (drug reaction with eosinophilia and systemic symptoms)
- sudden and intense inflammation of the liver (fulminant hepatitis)
- severe and life-threatening skin rashes (Stevens Johnson Syndrome/toxic epidermal necrolysis)
- yellow skin (jaundice)
- hives (urticaria)
- fluid under the skin (angioneurotic oedema)

- vomiting
- muscle pain (myalgia)
- joint pain (arthralgia)
- decreased numbers of white blood cells (granulocytopenia)
- abnormal liver function tests
- decreased blood phosphorus
- increased blood pressure

Rare (may affect up to 1 in 1000 people):

- inflammation of the liver (hepatitis)
- decreased numbers of red blood cells (anaemia)

The side effects described below have been experienced by patients given nevirapine prolonged-release tablets once daily in the maintenance phase:

Common (may affect up to 1 in 10 people):
- rash
- headache
- abdominal pain
- feeling sick (nausea)
- inflammation of the liver (hepatitis)
- feeling tired (fatigue)
- abnormal liver function tests
- fever
- vomiting
- loose stools (diarrhoea)

Uncommon (may affect up to 1 in 100 people):
- allergic reactions (hypersensitivity)
- allergic reaction characterized by rash, swelling of the face, difficulty breathing (bronchial spasm) or anaphylactic shock
- drug reaction with systemic symptoms (drug reaction with eosinophilia and systemic symptoms)
- sudden and intense inflammation of the liver (fulminant hepatitis)
- severe and life-threatening skin rashes (Stevens Johnson Syndrome/toxic epidermal necrolysis)
- decreased numbers of red blood cells (anaemia)
- decreased numbers of white blood cells (granulocytopenia)
- yellow skin (jaundice)
- hives (urticaria)
- fluid under the skin (angioneurotic oedema)
- muscle pain (myalgia)
- joint pain (arthralgia)
- decreased blood phosphorus
- increased blood pressure

The following events have also been reported when nevirapine have been used in combination with other antiretroviral agents:
- 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 agents and may be expected to occur when Nevirapine is used in combination with other agents; however, it is unlikely that these events are due to treatment with Nevirapine.

Additional side effects in children and adolescents
A reduction in white blood cells (granulocytopenia) can occur, which is more common in children. A reduction in red blood cells (anaemia), which may be related to nevirapine therapy, is also more commonly observed in children. As with rash symptoms, please inform your doctor of any side effects.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nevirapine

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

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

This medicine does not require any special storage conditions.

For bottle packs. Once opened, use within 100 days.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist 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 Nevirapine contains

- The active substance is nevirapine. Each prolonged-release tablet contains 400 mg nevirapine.
- The other ingredients are lactose monohydrate (see section 2 Nevirapine contains lactose and sodium), hypromellose, and sodium stearylfumarate.

What Nevirapine looks like and contents of the pack

Nevirapine is a white to off-white, oval shaped prolonged-release tablet, debossed with **M** on one side of the tablet and **N403** on the other side.

Nevirapine is packed in PVC/Aluminium foil blisters containing 14, 30, 30 x 1 (unit dose blister), 60, 90, 100 and 120 prolonged-release tablets and white HDPE bottles with white opaque polypropylene screw caps containing 30, 90, 250, and 500 prolonged-release tablets. The bottles also contain cotton wool.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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