PACKAGE LEAFLET

Package leaflet: Information for the patient

Nevirapine 200 mg Tablets

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 any further questions, 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 ingredient 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 used for the treatment of HIV-1 infected adults, adolescents and children of any age. You must take Nevirapine together with other antiretroviral medicines. Your doctor will recommend the best medicines for you.

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 stop 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.

Potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis) have been reported with the use of nevirapine, appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk.

Additional signs to look for include ulcers in the mouth, throat, nose, genitals, swelling of the face and conjunctivitis (red and swollen eyes). These potentially life-threatening skin rashes are often accompanied by flu-like symptoms (fever, muscle or joint aches and general fatigue). The rash may progress to widespread blistering or peeling of the skin.

If you have developed Stevens-Johnson syndrome or toxic epidermal necrolysis with the use of nevirapine, you must not be re-started on nevirapine at any time. If you develop a rash or these skin symptoms, stop taking Nevirapine, seek urgent advice from a doctor and tell him that you are taking this medicine.

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

- abdominal pain

you **should stop taking Nevirapine** and you **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 dosage of Nevirapine as prescribed by your doctor. This is especially important within the first 14 days of treatment (see section 3 "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/mm^3, men more than 400 cells/mm^3)
- 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/mm^3, men more than 400 cells/mm^3).

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 together 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 told to do so by your doctor.

Nevirapine is not a cure for HIV infection. Therefore, you may continue to develop infections and other illnesses associated with HIV infection. You should therefore remain in regular contact with your doctor. You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Talk to your doctor the precautions needed to prevent passing on HIV to other people.

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.

Children and adolescents
Nevirapine tablets can be taken by:
- children 16 years of age or older
- children under 16 years of age who weigh 50 kg or more or have a body surface area above 1.25 square metres (your doctor will work out your surface area).

For children weighing less than 50 kg or who have a body surface area less than 1.25 square metres (your doctor will work out body surface area) an oral suspension liquid form is available.

Other medicines and Nevirapine
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription 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 medicinal products you are taking in combination with Nevirapine.

Do not take Nevirapine if you are taking or have recently taken:
- St John's Wort (*Hypericum perforatum*, medicine to treat depression)

It is particularly important that you tell your doctor if you are taking or have recently taken:
- 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"). Nevirapine might reduce their effectiveness. When used for birth control, you must also use a reliable barrier method of contraception (for example, a condom).
- other medicines to treat HIV infection (e.g. atazanavir, lopinavir/ritonavir, fosamprenavir, efavirenz, etravirine, rilpivirine, delavirdine, zidovudine, elvitegravir/cobicistat)
- boceprevir or telaprevir (medicines used to treat hepatitis C).

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

If you are undergoing kidney dialysis, your doctor may consider a dose adjustment of Nevirapine. This is because Nevirapine can be partly washed out of your blood by dialysis.

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

If you become pregnant or are planning to become pregnant, you must contact your doctor to discuss the potential adverse effects and the benefits and risks of your antiretroviral therapy to you and your child.

You should stop breast-feeding if you are taking Nevirapine. It is generally recommended that you do not breast-feed if you have HIV infection because it is possible that your baby can become infected with HIV through your breast milk.

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
Nevirapine 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 medicine.

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 or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Only take Nevirapine tablets by mouth with liquid. Do not chew or crush your tablets. You may take Nevirapine with or without food.

If you have problems swallowing tablets, an oral suspension liquid form is available.

Dosage
The recommended dose is one 200 mg tablet per day for the first 14 days of treatment ("lead-in" period). After 14 days, the recommended dose is one 200 mg tablet twice a day.

It is very important that you take only one Nevirapine for the first 14-days. If you have a rash during this period do not increase the dose but tell your doctor.

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

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.

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

As explained in section 2, 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.

Use in children and adolescents
Nevirapine tablets can be taken by:
- children 16 years of age or older
- children under 16 years of age who weigh 50 kg or more or have a body surface area above 1.25 square metres(your doctor will work out your surface area).

For children weighing less than 50 kg or who have a body surface area less than 1.25 square metres (your doctor will work out body surface area) an oral suspension liquid form is recommended.

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, but you may feel tired, sick, be sick, or have a spinning sensation (vertigo), a fever, headache, skin rashes or notice weight loss, fluid retention or lung problems. Consult your doctor if you have taken more Nevirapine than you should for further advice.

If you forget to take Nevirapine
Try not to miss a dose. If you notice that you have missed a dose within 8 hours of when it was due, take the next dose as soon as possible. If it has been more than 8hours 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 (described above) once again, before returning to the twice daily dose.

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 fats (lipids) and sugar (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. Drug rash with eosinophilia and systemic

symptoms (DRESS) has also been rarely reported. 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
- hives (urticaria)
- swelling of the face
- difficulty breathing (bronchial spasm)
- anaphylactic shock (sudden wheezing, swelling of your lips, tongue and throat or body, rash, fainting or difficulties in swallowing)

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, including swollen or enlarged lymph nodes
- shortness of breath
- muscle or joint pain
- inflammation of internal organs
- changes in your blood including a reduction in the numbers of your white blood cells (granulocytopenia), your blood platelets (thrombocytopenia) or an increase in the number of a certain type of white blood cell (eosinophils)
- 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 be both fatal.

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

The side effects described below have been experienced by patients given nevirapine:

Very Common (may affect more than 1 in 10 people):
- rash

Common (may affect up to 1 in 10 people):
- headache
- feeling sick (nausea)
- vomiting (being sick)
- abdominal pain

- loose stools (diarrhoea)
- feeling tired (fatigue)
- fever
- abnormal liver function tests

Uncommon (may affect up to 1 in 100 people)
- decreased numbers of red blood cells (anaemia)
- fluid under the skin (angioedema)
- joint pain (arthralgia)
- muscle pain (myalgia)
- decreased blood phosphorus
- increased blood pressure

The following events have also been reported when nevirapine has been used in combination with other antiretroviral agents:
- decreased numbers of red blood cells or platelets
- inflammation of the pancreas (symptoms can include severe upper stomach pain, often with nausea (feeling sick) and vomiting (being sick)
- 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. Pay special attention to any rashes your child develops. Although these may appear normal (for example nappy rash), they might be rashes due to Nevirapine. If in doubt ask your child's doctor.

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
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 after "EXP". The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

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 to protect the environment.

6. Contents of the pack and other information

What Nevirapine contains

- The active substance is nevirapine. Each tablet contains 200 mg nevirapine.
- The other ingredients are Lactose Monohydrate, Microcrystalline Cellulose (E460), Povidone (E1201), Sodium Starch Glycolate (Type A), Silica Colloidal Anhydrous (E551), and Magnesium Stearate (E572).

What Nevirapine looks like and contents of the pack

The 200 mg tablet is a white to off-white, oval shaped tablet, debossed with "NE 200" on one side with a score line separating the NE and 200 and debossed with "M" on the other side with a score line.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

Nevirapine is packed in PVC/Aluminium blisters, of 14, 14 x 1 (unit dose blister), 30, 60, 60 x 1 (unit dose blister), 100, 120, 200 and HDPE bottle pack comprises of white coloured HDPE bottle with white opaque polypropylene (PP) screw cap containing 60 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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