Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Viramune®
Tablets

Name and quantity of active ingredient:
Each Viramune tablet contains 200 mg nevirapine.

Inactive ingredients and allergens in this medicine: See section 2 'Important information about some of this medicine's ingredients' and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?

For the treatment of HIV-1 (human immunodeficiency virus) infections in combination with other antiretroviral medicines.

Therapeutic group: antiretrovirals (anti-HIV - human immunodeficiency virus).

The active ingredient, 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. By stopping the enzyme from working, nevirapine helps control HIV-1 infection.

If Viramune 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. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients this medicine contains (for a list of inactive ingredients, see section 6 'Additional information').
- You have taken Viramune 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)
    - changes in your liver function.
- You have severe liver disease.

- You are taking a medicine containing the herbal substance St. John's Wort (*Hypericum perforatum*). This herbal substance may stop Viramune from working properly.

Special warnings about using this medicine

Talk to your doctor or pharmacist before taking Viramune. During the first 18 weeks of treatment with Viramune it is very important that you and your doctor watch out for signs of liver or skin reactions, because these can become severe and even life threatening. You are at greater risk of such reactions 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
<u>You should discontinue taking Viramune and you must contact your doctor immediately</u> 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 Viramune.**

If you experience symptoms suggesting damage of the liver, such as loss of appetite, nausea, vomiting, yellow skin (jaundice), abdominal pain, you should discontinue taking the medicine and must contact your doctor immediately.

If you develop severe liver, skin or hypersensitivity reactions whilst taking Viramune, <u>never take Viramune again</u> without referring to your doctor.

You must take the dose of Viramune as prescribed by your doctor. This is especially important within the first 14 days of treatment (see more information in section 3 'How to use this medicine').

The following patients are at increased risk of developing liver problems:
- women
- patients infected with hepatitis B or C
- patients with abnormal liver function tests
- treatment-naive patients with higher CD4 cell counts in the blood at the start of Viramune 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 Viramune 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 infections (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 symptom 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 in order to receive the necessary treatment.

Changes of body fat may occur in patients receiving combination antiretroviral therapy. Contact your doctor if you notice changes in your body fat (see section 4 '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 (BMI) 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 (Viramune) and zidovudine concomitantly please inform your doctor since he might need to check your white blood cell count.

Do not take Viramune after an exposure to HIV unless you have been diagnosed with HIV and instructed to take Viramune by your doctor. Viramune 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. Discuss with your doctor the precautions needed to avoid infecting other people.

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

If you are taking oral contraceptives (e.g. contraceptive pills) or other hormonal methods of birth control during treatment with Viramune, 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 replacement 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 Viramune.

Children and adolescents
Viramune 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 meters.

For smaller children an oral suspension liquid form is available.

Tests and follow-up
Your doctor will monitor your condition using liver function tests and by monitoring undesirable side effects such as rash (see also section 2 'Special warnings about using this medicine'). Depending on the results of your follow-up, your doctor may decide to change or stop your Viramune treatment. Your doctor may then decide to renew your treatment at a lower dose.

Other medicines and Viramune
If you are taking, may be taking, or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Inform your doctor about all other medicines you are taking before you start taking Viramune. Your doctor might need to monitor whether your other medicines are still efficiently working and adjust their doses. Carefully read the package leaflets in all other HIV medicinal products you are taking in combination with Viramune.

It is particularly important that you tell your doctor if you are taking or have recently taken:
- St. John's Wort (*Hypericum perforatum)* (medicine to treat depression)
- rifampicin, rifabutin (medicine to treat tuberculosis)
- macrolides e.g. clarithromycin (medicine to treat bacterial infections)
- fluconazole, ketoconazole, itraconazole (medicines to treat fungal infections)
- methadone (medicine used to treat opiate addiction)
- warfarin (medicine to reduce blood clotting)
- hormonal contraceptives (e.g. contraceptive pills)
- atazanavir, lopinavir/ritonavir, fosamprenavir, efavirenz, etravirine, rilpivirine, delavirdine, zidovudine, elvitegravir/cobicistat (other medicines to treat HIV)
- boceprevir, telaprevir (medicine to treat hepatitis C).

Your doctor will carefully monitor the effect of Viramune 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 Viramune. This is because Viramune can be partly washed out of your blood by dialysis.

Using this medicine and food
You can take this medicine with or without food.

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

You should stop breastfeeding if you are taking Viramune. It is in general recommended that you do not breastfeed 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
Using Viramune may cause fatigue. Use caution when engaging in activities such as driving, using any tools, or operating machines. If you experience fatigue you should avoid such hazardous activities. Caution children against riding a bicycle, playing near a road, and similar activities.

Important information about some of this medicine's ingredients
Viramune tablets contain lactose and sodium.
Viramune 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.
Each tablet contains 318 mg lactose.
Viramune tablets contain less than 1 millimole (mmol) (23 mg) sodium per tablet which means that this medicine is essentially 'sodium free'.

3. How to use this medicine?
You should not use Viramune on its own. You must take it with at least one other antiretroviral medicine. Your doctor will recommend the best medicines for you.

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
Only your doctor will determine your dose and how you should take this medicine.

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.

Do not exceed the recommended dose.

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

As Viramune must always be taken together with other HIV medicines, you should follow the instructions for your other medicines carefully. You will find the instructions in the patient information leaflets of each of these medicines.
Viramune is also available in liquid form as an oral suspension. This is particularly suitable if:

- you have problems swallowing tablets
- the patient is a child weighing less than 50 kg
- the patient is a child with a body surface area smaller than 1.25 square meters (your doctor will work out this information).

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

Swallow the tablets whole, with water. Do not crush, split, or chew the tablets. You can take Viramune with or without food.

The score line is not intended for breaking the tablet.

If you have accidentally taken a higher dose
Do not take more Viramune than prescribed by your doctor and described in this leaflet. There is at present little information on the effects of Viramune overdose. Consult your doctor if you have taken more Viramune than you should.
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine
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 missed dose as soon as possible. If it has been more than 8 hours since the dose was due only take the next dose at the usual time.
Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.

If you stop taking this medicine
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 Viramune correctly, as described above, unless your doctor instructs you to stop.

If you stop taking Viramune 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.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. <u>Side effects</u>

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 with all medicines, using Viramune tablets may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

As mentioned in section 2 'Special warnings about using this medicine', the most important side effects of Viramune are life threatening skin reactions and serious liver damage. These reactions occur mainly in the first 18 weeks of treatment with Viramune. 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 to moderate rash occur in the first 6 weeks of treatment.
If rash occurs and you also feel nausea, 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).

Contact 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 Viramune. 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, nausea, vomiting, yellow skin (jaundice), abdominal pain.

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

<u>Very common side effects (may affect more than 1 in 10 people):</u>
- rash.

<u>Common side effects (may affect up to 1 in 10 people):</u>

- decreased numbers of white blood cells (granulocytopenia)
- allergic reactions (hypersensitivity)
- headache
- nausea
- vomiting
- abdominal pain
- loose stools (diarrhoea)
- inflammation of the liver (hepatitis)
- feeling tired (fatigue)
- fever
- abnormal liver function tests.

Uncommon side effects (may affect up to 1 in 100 people):
- allergic reaction characterized 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)
- fluid under the skin (angioedema)
- joint pain
- muscle pain
- decreased blood phosphorus
- increased blood pressure.

Rare side effects (may affect up to 1 in 1000 people):
- sudden and intense inflammation of the liver (fulminant hepatitis)
- reaction to the medicine with systemic symptoms (reaction to the medicine with increased numbers of white blood cells [eosinophilia] and other systemic symptoms).

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

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 (Viramune) therapy, is also more commonly observed in children. As with rash symptoms, please inform your doctor of any side effects.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment ' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il/

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:
No special storage conditions. Storing at room temperature is recommended.

6. Additional information

- In addition to the active ingredient, this medicine also contains - Lactose monohydrate, microcrystalline cellulose, povidone, sodium starch glycolate, colloidal silicon dioxide, magnesium stearate.

- What the medicine looks like and contents of the pack: white, oval, biconvex tablet with a score line. One side is marked with the code "54 193", with a single bisect separating the "54" and "193". The opposite side is marked with the Boehringer Ingelheim company symbol.

- Each package contains 60 tablets.

- Registration holder: Boehringer Ingelheim Israel, 89 Medinat Heyehudim St., POB 4124, Herzlia Pituah 4676672.

- Manufacturer: Boehringer Ingelheim Pharma KG, Ingelheim am Rhein, Germany.

- This leaflet was revised in April 2020.

- Registration number of the medicine in the Ministry of Health National Drug Registry: 119-78-30052-00