

PRODUCT INFORMATION

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

In this leaflet:

- 1. What is VIRAMUNE and what it is used for?**
- 2. Before you take VIRAMUNE**
- 3. When and how to take VIRAMUNE**
- 4. Possible side effects**
- 5. Storing VIRAMUNE**

VIRAMUNE 200 mg tablets and VIRAMUNE oral suspension 50 mg/5 ml
Nevirapine

- The active substance is nevirapine.
- The other ingredients **of the tablets** are: microcrystalline cellulose, lactose monohydrate, povidone, sodium starch glycolate, colloidal silicon dioxide and magnesium stearate
- The other ingredients **of the oral suspension** are: carbomer, methyl parahydroxybenzoate, propyl parahydroxybenzoate, sorbitol, sucrose, polysorbate 80, sodium hydroxide and water.

The marketing authorisation holder for VIRAMUNE is:

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Germany

1. WHAT IS VIRAMUNE AND WHAT IT IS USED FOR?

The active substance nevirapine belongs to a group of medicines called antiretrovirals, used in the treatment of Human Immunodeficiency Virus (HIV) infection. VIRAMUNE tablets are supplied in blisters as tablets for oral use, with 60 tablets per carton; VIRAMUNE oral suspension is supplied in plastic bottles of suspension for oral use (50 mg / 5 ml), with 240 ml or 20 ml suspension per bottle. Each VIRAMUNE tablet contains 200 mg of the active substance nevirapine, and each ml of VIRAMUNE oral suspension contains 10 mg of the active substance nevirapine (as nevirapine hemihydrate).

VIRAMUNE oral suspension is particularly suitable for children (patients under 16 years of age) or for adults unable to swallow tablets. It should be noted that VIRAMUNE tablets can be used in adult patients (16 years or older) or in patients under 16 years of age, weighing 50 kg or more.

HIV infection is a disease spread by contact with blood or sexual contact with an infected individual.

It is important to realise that VIRAMUNE is not a cure for HIV infection and that you or your child may continue to develop infections or other illnesses associated with HIV infection. It is also important to realise that VIRAMUNE has not been shown to reduce the risk of transmission of HIV to others through sexual contact or blood contamination.

BEFORE YOU TAKE VIRAMUNE

VIRAMUNE oral suspension can be used in children of two months of age or older. Always follow the exact instructions given by your child's doctor for the use of VIRAMUNE oral suspension in your child.

Do not take VIRAMUNE:

- if you are hypersensitive (allergic) to nevirapine or any of the other ingredients of VIRAMUNE tablets or oral suspension.
- if you or your child previously experienced hepatitis, severe skin rash, or liver injury while on VIRAMUNE treatment.
- if you have permanent liver disease or changes in liver function
- if you are currently taking rifampicin (used to treat tuberculosis)
- patients taking VIRAMUNE must not take products containing *Hypericum perforatum* (St John's wort) as this may stop VIRAMUNE from working properly.

Take special care with VIRAMUNE :

The first 18 weeks of treatment with VIRAMUNE are an important period which requires a close surveillance to discover the occurrence of severe and life threatening cutaneous reactions and serious hepatic injuries. During this period the dosage of VIRAMUNE prescribed by your or your child's doctor must be strictly adhered to, especially during the first 14 days of treatment, so called 'lead-in' period (see more information in "How to take VIRAMUNE").

Please be sure to inform your doctor if you or your child are suffering from, or have ever suffered from, kidney or liver disease. Also, because VIRAMUNE has been shown to cause variations in liver function, your doctor may wish to monitor the function of your or your child's liver by blood tests before and during VIRAMUNE treatment, especially during the first weeks of treatment. If your doctor is worried about the effects of VIRAMUNE on your liver function he or she may decide to perform additional blood tests to monitor the functions of your liver and according to the results he or she may decide to discontinue your treatment. It is important to realise that VIRAMUNE can result in liver toxicity, which in the worst cases can be serious and life-threatening and which has resulted in fatalities (see more information in 'Possible side effects', below). Patients with higher liver function tests and patients with hepatitis B or C infection are at increased risk for severe and potentially fatal liver damage while taking antiretroviral therapy in general, including VIRAMUNE. Women and patients with higher CD4 cell counts seem to be at increased risk for developing a rash with associated liver damage while taking VIRAMUNE.

If you or your child experience clinical symptoms suggesting an injury of the liver, such as loss of appetite, nausea, vomiting, jaundice, you should promptly inform your or your child's doctor.
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Because VIRAMUNE may interact with other medicinal products, please inform your doctor of any other medicinal products you or your child are taking. If you normally take oral contraceptives then it will be necessary to change your form of contraception upon starting treatment with VIRAMUNE.

You should carefully read the package leaflet of the other HIV medicinal products which you or your child will be taking in combination with VIRAMUNE.

It is important to realise that VIRAMUNE can result in skin reactions and hypersensitivity reactions, which in the worst cases can be serious and life-threatening and which have resulted in fatalities (see more detailed information in 'Possible side effects', below).

Hypersensitivity (allergic) reactions can occur. Such reactions may appear in the form of rash accompanied by other side effects such as fever, blistering, mouth sores, eye inflammation, facial swelling, general swelling, muscle or joint aches, a reduction in white blood cells (granulocytopenia), general feelings of illness or severe problems with liver or kidneys.

If you or your child experience rash and any of the other side effects of a hypersensitivity reaction, **YOU MUST CONTACT** your or your child's doctor **IMMEDIATELY** as such reactions can be potentially life-threatening.

If you or your child ever have any rash symptoms please inform your or your child's doctor immediately, who will advise you whether you or your child should stop taking VIRAMUNE.

If you or your child develop a severe rash whilst taking VIRAMUNE, **NEVER TAKE VIRAMUNE** again without referring to your or your child's doctor.

The following events have also been reported when VIRAMUNE has been used in combination with other antiretroviral agents: a reduction in red blood cells or in platelets, inflammation of pancreas and decrease in or abnormal skin sensations. These events are commonly associated with other antiretroviral agents and may be expected to occur when VIRAMUNE is used in combination with other agents; however it is unlikely that these events are due to a treatment with VIRAMUNE.

Redistribution, accumulation or loss of body fat may occur in patients receiving combination antiretroviral therapy. Contact your doctor if you notice changes in body fat.

Taking VIRAMUNE with food and drink:

There are no restrictions on taking VIRAMUNE oral suspension and food and drink.

Pregnancy

Ask your doctor or pharmacist for advice before taking any medicine.

There is limited experience of the use of VIRAMUNE for the treatment of HIV-infected pregnant woman. VIRAMUNE should be used during pregnancy only if the potential benefit justifies the potential risk to the child, in particular in order to prevent the transmission of HIV-infection from the mother to the child during delivery.

Breast-feeding

You should discontinue breast feeding if you are taking VIRAMUNE. Some health experts anyway recommend that you discontinue breast-feeding if you have HIV infection in order to lower the chances of passing the infection on to your baby.

Driving and using machines:

There are no specific studies on the ability to drive vehicles and use machinery.

Important information about some of the ingredients of VIRAMUNE :

You must not take VIRAMUNE if you are hypersensitive (allergic) to nevirapine or any of the other ingredients of these two drug products.

VIRAMUNE oral suspension contains sucrose and sorbitol. When taken according to the dosage recommendations, each dose can supply up to 3 g of sucrose and up to 3.2 g of sorbitol. VIRAMUNE oral suspension is therefore unsuitable in hereditary fructose intolerance, glucose-galactose malabsorption syndrome or sucrase-isomaltase deficiency. VIRAMUNE oral suspension can cause stomach upset and diarrhoea.

Taking other medicines:

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed. You should inform your doctor of all other medicines you or your child are

taking before you start taking VIRAMUNE because he or she might need to monitor whether the other medicines are still having their desired effects and make necessary dose-adjustments.

The antibiotics rifabutin and rifampicin have been shown to reduce the blood concentration of VIRAMUNE whilst cimetidine and macrolides (e.g. clarithromycin) and the antifungal drug fluconazole have been shown to increase concentrations. Your doctor will carefully monitor the effect of VIRAMUNE and any of these medicines if you are taking VIRAMUNE and any of these medicines together. See Section 2, BEFORE YOU TAKE VIRAMUNE, for further information.

It is possible that VIRAMUNE can affect oral contraceptives and therefore you should employ an alternative contraceptive method such as barrier contraception (eg condoms) if you are taking VIRAMUNE oral suspension.

VIRAMUNE may decrease blood concentrations of the HIV protease inhibitors, saquinavir, indinavir, ritonavir or lopinavir. Your doctor, or your child's doctor, will consider the necessity of appropriate dose adjustments with indinavir or lopinavir but a dose adjustment is not necessary for combination of VIRAMUNE with ritonavir or with saquinavir soft gel capsules when used with a low dose of ritonavir (100mg). VIRAMUNE does not have any important interactions with nelfinavir and therefore no dosage adjustments are necessary for combination of VIRAMUNE with nelfinavir.

VIRAMUNE does not have any interaction with the HIV nucleoside reverse transcriptase inhibitors zidovudine, didanosine, zalcitabine, stavudine or lamivudine and therefore no dose-adjustment of any of these medicinal products is necessary.

If you or your baby are taking VIRAMUNE together with efavirenz it is possible that your doctor will consider a dose increase of efavirenz.

If you are undergoing dialysis, your doctor may consider a dose increase of VIRAMUNE.

VIRAMUNE may affect blood concentrations of methadone and warfarin. Therefore if you are undergoing methadone or warfarin treatment it is possible that your doctor will consider methadone dosage adjustments.

Ketoconazole and VIRAMUNE should not be taken at the same time.

3. WHEN AND HOW TO TAKE VIRAMUNE

VIRAMUNE is in a tablet or a liquid suspension form and should only be taken by mouth.

- VIRAMUNE is indicated **for the prevention of mother to child transmission of HIV-1** in pregnant women who are not taking antiretroviral therapy at the time of labour, VIRAMUNE is indicated and may be used alone, as a single oral dose to the mother during labour and a single oral dose to the infant within 72 hours after birth.

The recommended dose **for the prevention of mother to child transmission of HIV-1** is :

- **Single oral dose of 200 mg (one 200 mg tablet or 20 ml oral suspension) to the pregnant woman during labour,**
- **Single oral dose of 2 mg / kg or 0.2 ml / kg (oral suspension) to the infant within 72 hours after birth.**

If the mother received her VIRAMUNE dose less than two hours prior to delivery, the infant should be administered the single 2 mg / kg or 0.2 ml / kg dose of VIRAMUNE oral suspension immediately after birth and the second 2 mg / kg or 0.2 ml / kg dose within 24-72 hours after the first dose.

It is essential to follow the above mentioned dosing recommendations and not to exceed the recommended doses of VIRAMUNE.

Instructions for use of the oral suspension

Shake the bottle gently before use. The required dosage is the same for all adults (20 ml). The required dosage for children is calculated according to your child's body weight. The exact dosage should be measured using the supplied measuring syringe and adapter as follows:

1. First, shake the bottle gently.
2. Open the bottle and fit (by first pressing and then screwing) the plastic adapter onto the open bottle neck. Make sure the adapter is tightly fitted.
3. Insert the syringe into the adapter. Make sure the syringe is tightly inserted.
4. Turn the bottle upside down and gently withdraw the required amount of VIRAMUNE oral suspension.
5. The maximum volume you can withdraw is 5 ml at a time. If you require a higher dose please repeat steps 3-4 above.

The bottle can be kept sealed with the lid of the plastic adapter.

If you are an adult and choose to use another measuring device (e.g. cup or teaspoon) please be sure that the entire dose is taken as some VIRAMUNE oral suspension can remain in the cup or spoon.

- VIRAMUNE is also used **in combination with other HIV antiretrovirals for the treatment of HIV infection in both children and adults.**

The recommended dose **for the chronic treatment of HIV-infection** is :

The required dosage for all adults is 20 ml oral suspension **or** one 200 mg tablet per dose. The required dosage for children is calculated according to your child's age and body weight. Be sure that your child's doctor clearly informs you what the correct dosage for your child should be.

For adults

The normal dosage for adults is **20 ml oral suspension or one 200 mg tablet once a day for the first 14 days** (this 'lead in' period has been shown to lower the incidence of skin rash) followed by **20 ml oral suspension or one 200 mg tablet twice daily**. It should be noted that VIRAMUNE tablet should only be used in patients aged 16 years or more or patients weighing 50 kg or more.

For children

The dosage **during the first two weeks** is 4 mg/kg **once a day** for all children. Thereafter for children aged 2 months up to 8 years the dosage is 7 mg/kg **twice daily** (up to a maximum of 400 mg per day). For children older than eight years the dosage is 4 mg/kg **twice daily** (up to a maximum of 400 mg per day). VIRAMUNE tablets can only be used in patients weighing 50 kg or more. Your child's doctor will inform you exactly of the correct dose for your child, and will continually check your child's weight to ensure the correct dose. If you are uncertain please be sure to ask your child's doctor or pharmacist.

VIRAMUNE will always be taken in combination with other HIV antiretrovirals, for which you should follow the instructions within the supplied package leaflet.

It is essential to follow strictly the once a day dosage during the 14 day 'lead in' period before rising to the twice daily dosage.

You or your child should continue to take VIRAMUNE for as long as instructed by your or your child's doctor.

As explained in '*Take special care with VIRAMUNE*', above, your doctor will monitor you or your child by liver tests or for undesirable effects such as rash. Depending on the outcome he or she may decide to interrupt or stop VIRAMUNE treatment. He or she might then decide to restart you or your child on a lower dose.

If you or your child 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.

If you take more VIRAMUNE than you should:

Do not exceed the dose 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 or your child take an overdose.

If you forget to take VIRAMUNE :

Try not to miss a dose. If you or your child do miss a dose, take the next dose, or give the next dose to your child, as soon as possible but do not try to double the next dose.

Effects when treatment with VIRAMUNE is stopped:

It has been shown that taking all doses at the appropriate times may greatly increase the effectiveness of your medicinal product combination regimen and reduce the development of viral resistance. Therefore, unless your doctor or your child's doctor, instructs you or your child to stop treatment, it is important to keep taking VIRAMUNE correctly, as described above.

4. POSSIBLE SIDE EFFECTS

Like all medicines, VIRAMUNE can have side effects.

As mentioned in '*Take special care with VIRAMUNE*', above, the major side effects of VIRAMUNE oral suspension are severe and life threatening cutaneous reactions and serious hepatic injuries. These reactions occur mainly in the first 18 weeks of treatment with VIRAMUNE. This is therefore an important period which requires a close surveillance.

When rash does occur 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 fatalities have been recorded. Most of the cases of both severe rash and mild/moderate rash occur in the first six weeks of treatment.

If you ever do observe any rash symptoms please inform your doctor immediately. If the symptoms are severe you must stop treatment and visit your doctor immediately. Please pay special attention to any rashes which your child develops. Although these may appear normal (for example nappy rash), they may in fact be rashes due to VIRAMUNE. If in doubt ask your child's doctor.

Hypersensitivity (allergic) reactions can occur. Such reactions may appear in the form of anaphylaxis (characterised by rash, facial swelling, bronchial spasm or shock), or rash accompanied by other side effects such as fever, blistering, mouth sores, eye inflammation, facial swelling, general swelling, muscle or joint aches, a reduction in white blood cells (granulocytopenia), general feelings of illness or severe problems with liver or kidneys. If you or your child experience rash and any of the other side effects of a hypersensitivity reaction, please be sure to tell your or your child's doctor immediately as such reactions can be potentially life-threatening.

Abnormal liver functioning has been reported with the use of VIRAMUNE as long term treatment of HIV-infection, including some cases of hepatitis, which have resulted in recorded fatalities.

If you or your child experience clinical symptoms suggesting an injury of the liver, such as loss of appetite, nausea, vomiting, jaundice, you should inform your doctor.

Other side effects which can occur are fever, nausea, headache, sleepiness, vomiting, diarrhoea, stomach pain muscle pain and allergic reactions. Many of these side effects can occur together with the rash side effect (hypersensitivity reaction). Joint pain has been reported as a stand-alone event in rare instances in patients receiving nevirapine containing regimens.

In addition, a reduction in white blood cells (granulocytopenia) can occur, which is more common in children. In very rare instances a reduction in red blood cells (anaemia) may be related to nevirapine therapy. As with rash symptoms, please inform your doctor of any side effects.

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 at this time. Combination antiretroviral therapy may also cause raised lactic acid and sugar in the blood, hyperlipaemia (increased fats in the blood) and resistance to insulin.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. STORING VIRAMUNE

Keep out of the reach and sight of children. There are no special storage instructions.

Do not use after the expiry date stated on the carton, blister and the bottle.