

Package leaflet: Information for the user

Norvir 100 mg film-coated tablets ritonavir

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you or your child.

- 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. 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 Norvir is and what it is used for
2. What you need to know before you or your child takes Norvir
3. How to take Norvir
4. Possible side effects
5. How to store Norvir
6. Contents of the pack and other information

1. What Norvir is and what it is used for

Norvir contains the active substance ritonavir. Norvir is a protease inhibitor used to control HIV infection. Norvir is used in combination with other anti-HIV medicines (antiretrovirals) to control your HIV infection. Your doctor will discuss with you the best combination of medicines for you.

Norvir is used by children 2 years of age or older, adolescents and adults who are infected with HIV, the virus which causes AIDS.

2. What you need to know before you or your child takes Norvir

Do not take Norvir

- if you are allergic to ritonavir or any of the other ingredients of Norvir (see section 6).
- if you have severe liver disease.
- if you are currently taking any of the following medicines:
 - astemizole or terfenadine (commonly used to treat allergy symptoms – these medicines may be available without prescription);
 - amiodarone, bepridil, dronedarone, encainide, flecainide, propafenone, quinidine (used to correct irregular heartbeats);
 - dihydroergotamine, ergotamine (used to treat migraine headache);
 - ergonovine, methylergonovine (used to stop excessive bleeding that may occur following childbirth or an abortion);
 - clorazepate, diazepam, estazolam, flurazepam, triazolam or oral (taken by mouth) midazolam (used to help you sleep and/or relieve anxiety);
 - clozapine, pimozide, (used to treat abnormal thoughts or feelings);

- quetiapine (used to treat schizophrenia, bipolar disorder and major depressive disorder);
- lurasidone (used to treat depression);
- ranolazine (used to treat chronic chest pain [angina]);
- pethidine, piroxicam, propoxyphene (used to relieve pain);
- cisapride (used to relieve certain stomach problems);
- rifabutin (used to prevent/treat certain infections)*;
- voriconazole (used to treat fungal infections)*;
- simvastatin, lovastatin (used to lower blood cholesterol);
- neratinib (used to treat breast cancer);
- lomitapide (used to lower blood cholesterol);
- alfuzosin (used to treat enlarged prostate gland);
- fusidic acid (used to treat bacterial infections);
- sildenafil if you suffer from a lung disease called pulmonary arterial hypertension that makes breathing difficult. Patients without this disease may use sildenafil for impotence (erectile dysfunction) under their doctor’s supervision (see the section on **Other medicines and Norvir**);
- avanafil or vardenafil (used to treat erectile dysfunction);
- colchicine (used to treat gout) if you have kidney and/or liver problems (see the section on **Other medicines and Norvir**);
- products containing St John’s wort (*Hypericum perforatum*) as this may stop Norvir from working properly. St John’s wort is often used in herbal medicines that you can buy yourself.

* Your doctor may decide that you can take rifabutin and/or voriconazole with a booster (lower dose) of Norvir but a full dose of Norvir must not be taken together with these two medicines.

If you are currently taking any of these medicines, ask your doctor about switching to a different medicine while you are taking Norvir.

Also read the list of medicines under ‘Other medicines and Norvir’ for use with certain other medicines which require special care.

Warnings and precautions

Talk to your doctor before taking Norvir.

Important information

- If Norvir is taken in combination with other antiretroviral medicines, it is important that you also carefully read the leaflets that are provided with these other medicines. There may be additional information in those leaflets about situations when Norvir should be avoided. If you have any further questions about Norvir (ritonavir) or the other medicines prescribed, please ask your doctor or pharmacist.
- Norvir is not a cure for HIV infection or AIDS.
- People taking Norvir may still develop infections or other illnesses associated with HIV infection or AIDS. It is therefore important that you remain under the supervision of your doctor while taking Norvir.
- You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your physician the precautions needed to avoid infecting other people.

Tell your doctor if you have/had:

- A history of **liver disease**.
- **Hepatitis B or C** and are being treated with a combination of antiretroviral agents, as you are at a greater risk of a severe and potentially life threatening reaction because of the effect on the liver. Regular blood tests may be required to check your liver is working properly.
- **Haemophilia**, as there have been reports of increased bleeding in patients with haemophilia who are taking this type of medicine (protease inhibitors). The reason for this is not known. You may need additional medicine to help your blood clot (factor VIII), in order to control any bleeding.
- **Erectile dysfunction**, as the medicines used to treat erectile dysfunction can cause hypotension and prolonged erection.
- **Diabetes**, as there have been reports of worsening of or the development of diabetes (diabetes mellitus) in some patients taking protease inhibitors.
- **Kidney (renal) disease**, since your doctor may need to check the dose of your other medicines (such as protease inhibitors).

Tell your doctor if you experience:

- **Diarrhoea or vomiting** that is not improving (persistent), as this may reduce how well the medicines you are taking work.
- **Feeling sick** (nausea), **vomiting** or have **stomach pain**, because these may be signs of inflammation of the pancreas (pancreatitis). Some patients taking Norvir can develop serious problems with their pancreas. Tell your doctor as soon as possible if this applies to you.
- **Symptoms of infection** – inform your doctor immediately. Some patients with advanced HIV infection (AIDS) who then start anti-HIV treatment may develop the symptoms of infections they have had in the past even if they didn't know they had had them. It is believed that this happens because the body's immune response improves and helps the body to fight these infections.
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.
- **Joint stiffness, aches and pains** (especially of the hip, knee and shoulder) and difficulty moving, tell your doctor, as this may be a sign of a problem that can destroy bone (osteonecrosis). Some patients taking a number of antiretroviral medicines may develop this disease.
- **Muscle pain, tenderness or weakness**, particularly in combination with antiretroviral therapy including protease inhibitors and nucleoside analogues. On rare occasions these muscle disorders have been serious. (See section 4 **Possible side effects**)
- **Dizziness, lightheadedness, fainting spells or abnormal heartbeat**. Some patients taking Norvir may experience changes in the electrocardiogram (ECG). Tell your doctor if you have a heart defect or conduction defect.
- If you have any other health concerns, discuss these with your doctor as soon as you can.

Children and adolescents

Norvir is not recommended in children below 2 years of age.

Other medicines and Norvir

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines, including medicines obtained without a prescription. There are some medicines you cannot

take at all with Norvir. These are listed earlier in section 2, under ‘**Do not take Norvir**’. There are some other medicines that can only be used under certain circumstances as described below.

The following warnings apply when Norvir is taken as a full dose. However, these warnings may also apply when Norvir is used in lower doses (a booster) with other medicines.

Tell your doctor if you are taking any of the medicines listed below, as special care should be taken.

- **Sildenafil or tadalafil** for impotence (erectile dysfunction).
The dose and/or frequency of use of these medicines may need to be reduced to avoid hypotension and prolonged erection. You must not take Norvir with sildenafil if you suffer from pulmonary arterial hypertension (see also section 2. **What you need to know before you or your child takes Norvir**). Tell your doctor if you are taking tadalafil for pulmonary arterial hypertension.
- **Colchicine** (for gout) as Norvir may raise the blood levels of this medicine. You must not take Norvir with colchicine if you have kidney and/or liver problems (see also ‘**Do not take Norvir**’ above).
- **Digoxin** (heart medicine). Your doctor may need to adjust the dose of digoxin and monitor you while you are taking digoxin and Norvir in order to avoid heart problems.
- **Hormonal contraceptives** containing ethinyl oestradiol as Norvir may reduce the effectiveness of these medicines. It is recommended that a condom or other non-hormonal method of contraception is used instead. You may also notice irregular uterine bleeding if you are taking this type of hormonal contraceptive with Norvir.
- **Atorvastatin or rosuvastatin** (for high cholesterol) as Norvir may raise the blood levels of these medicines. Talk to your doctor before you take any cholesterol-reducing medicines with Norvir (see also ‘**Do not take Norvir**’ above).
- **Steroids** (e.g. dexamethasone, fluticasone propionate, prednisolone, triamcinolone) as Norvir may raise the blood levels of these medicines which may lead to Cushing’s syndrome (development of a rounded face) and reduce production of the hormone cortisol. Your doctor may wish to reduce the steroid dose or monitor your side effects more closely.
- **Trazodone** (a medicine for depression) as, unwanted effects like nausea, dizziness, low blood pressure and fainting can occur when taken with Norvir.
- **Rifampicin and saquinavir** (used for tuberculosis and HIV, respectively) as serious liver damage can occur when taken with Norvir.
- **Bosentan, riociguat** (used for pulmonary arterial hypertension) as Norvir may increase the blood levels of this medicine.

There are medicines that may not mix with Norvir because their effects could increase or decrease when taken together. In some cases your doctor may need to perform certain tests, change the dose or monitor you regularly. This is why you should tell your doctor if you are taking any medicines, including those you have bought yourself or herbal products, but it is especially important to mention these:

- amphetamine or amphetamine derivatives;
- antibiotics (e.g. erythromycin, clarithromycin);
- anticancer treatments (e.g. abemaciclib; afatinib, apalutamide, ceritinib, encorafenib, dasatinib, ibrutinib, nilotinib, venetoclax, vincristine, vinblastine);
- anticoagulants (e.g. rivaroxaban, vorapaxar, warfarin);
- antidepressants (e.g. amitriptyline, desipramine, fluoxetine, imipramine, nefazodone, nortriptyline, paroxetine, sertraline, trazodone);
- antifungals (e.g. ketoconazole, itraconazole);
- antihistamines (e.g. loratidine, fexofenadine);
- antiretroviral medicines including HIV-protease inhibitors (amprenavir, atazanavir, darunavir, fosamprenavir, indinavir, nelfinavir, saquinavir, tipranavir) non-nucleoside reverse transcriptase

- inhibitors(NNRTI) (delavirdine, efavirenz, nevirapine), and others (didanosine, maraviroc, raltegravir, zidovudine);
- anti-tuberculosis medicine (bedaquiline and delamanid);
 - antiviral medicine used to treat chronic hepatitis C virus (HCV) infection in adults (e.g. glecaprevir/pibrentasvir and simeprevir);
 - anxiety medicine, buspirone;
 - asthma medicine, theophylline, salmeterol;
 - atovaquone, a medicine used to treat a certain type of pneumonia and malaria;
 - buprenorphine, a medicine used for the treatment of chronic pain;
 - bupropion, a medicine used to help you stop smoking;
 - epilepsy medicines (e.g. carbamazepine, divalproex, lamotrigine, phenytoin);
 - heart medicines (e.g. disopyramide, mexiletine and calcium channel antagonists such as amlodipine, diltiazem and nifedipine);
 - immune system (e.g. cyclosporine, tacrolimus, everolimus);
 - levothyroxine (used to treat thyroid problems);
 - morphine and morphine-like medicines used to treat severe pain (e.g. methadone, fentanyl);
 - sleeping pills (e.g. alprazolam, zolpidem) and also midazolam administered by injection;
 - tranquillisers (e.g. haloperidol, risperidone, thioridazine);
 - colchicine, a treatment for gout.

There are some medicines you cannot take at all with Norvir. These are listed earlier in section 2, under ‘**Do not take Norvir**’.

Taking Norvir with food and drink

Norvir tablets should be taken with food.

Pregnancy and breast-feeding

If you think you are pregnant or you are planning to become pregnant, it is very important that you discuss this with your doctor.

There is a large amount of information on the use of ritonavir (the active ingredient in Norvir) during pregnancy. In general, pregnant mothers received ritonavir after the first three months of pregnancy at a lower dose (booster) along with other protease inhibitors. Norvir did not appear to increase the chance of developing birth defects compared to the general population.

Norvir can pass into breast milk. To avoid transmitting the infection, mothers with HIV must not breast feed their babies.

Driving and using machines

Norvir can cause dizziness. If you are affected do not drive or use machinery.

3. How to take Norvir

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Take this medicine one or two times a day every day with food.

It is important that Norvir tablets are swallowed whole and not chewed, broken or crushed.

Recommended doses of Norvir are:

- if Norvir is used to boost the effects of certain other anti-HIV medicines the typical dose for adults is 1 to 2 tablets once or twice daily. For more detailed dose recommendations, including

those for children, see the Package Leaflet of the anti-HIV medicines Norvir is given in combination with.

- if your doctor prescribes a full dose, adults may be started on a dose of 3 tablets in the morning and 3 tablets 12 hours later, gradually increasing over a period of up to 14 days to the full dose of 6 tablets twice daily (totaling 1,200mg per day). Children (2 – 12 years of age) will start with a dose smaller than this and continue up to the maximum allowed for their size.

Your doctor will advise you on the dosage to be taken.

Norvir should be taken every day to help control your HIV, no matter how much better you feel. If a side effect is preventing you from taking Norvir as directed, tell your doctor straight away. During episodes of diarrhoea your doctor may decide that extra monitoring is needed.

Always keep enough Norvir on hand so you don't run out. When you travel or need to stay in the hospital, make sure you have enough Norvir to last until you can get a new supply.

If you take more Norvir than you should

Numbness, tingling, or a “pins and needles” sensation may occur if you take too much Norvir. If you realise you have taken more Norvir than you were supposed to, contact your doctor or the Accident and Emergency Department of your nearest hospital straight away.

If you forget to take Norvir

If you miss a dose, take the missed dose as soon as possible. If it is nearly time for the next dose, just take that one. Do not take a double dose to make up for a forgotten dose.

If you stop taking Norvir

Even if you feel better, do not stop taking Norvir without talking to your doctor. Taking Norvir as recommended should give you the best chance of delaying resistance to the medicines.

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, Norvir can cause side effects, although not everybody gets them. Also, the side effects of Norvir when used with other antiretroviral medicines are dependent on the other medicines. So it is important that you carefully read the side effects section of the leaflets that are provided with these other medicines.

Very common: may affect more than 1 in 10 people

- upper or lower stomach ache
- vomiting
- diarrhoea (may be severe)
- feeling sick (nausea)
- flushing, feeling hot
- headache
- dizziness
- pain in the throat
- cough
- a tingling sensation or numbness in the hands, feet or around the lips and mouth
- feeling weak/tired
- bad taste in the mouth
- damage to the nerves that can cause weakness and pain
- itching
- rash
- joint pain and back pain

- upset stomach or indigestion

Common: may affect up to 1 in 10 people

- allergic reactions including skin rashes (may be red, raised, itchy), severe swelling of the skin and other tissues
- inability to sleep (insomnia)
- anxiety
- increase in cholesterol
- increase in triglycerides
- gout
- stomach bleeding
- inflammation of the liver and yellowing of skin or whites of the eyes
- increase in urination
- reduced kidney function
- seizures (fits)
- low levels of blood platelets
- thirst (dehydration)
- abnormally heavy periods
- wind (flatulence)
- loss of appetite
- mouth ulcer
- muscle aches (pain), tenderness or weakness
- fever
- weight loss
- laboratory test results: changes in blood test results (such as blood chemistry and blood count)
- confusion
- difficulty paying attention
- fainting
- blurred vision
- swelling of the hands and feet
- high blood pressure
- low blood pressure and feeling faint when getting up
- coldness in the hands and feet
- acne

Uncommon: may affect up to 1 in 100 people

- heart attack
- diabetes
- kidney failure

Rare: may affect up to 1 in 1,000 people

- severe or life threatening skin reaction including blisters (Stevens Johnson syndrome, toxic epidermal necrolysis)
- serious allergic reaction (anaphylaxis)
- high levels of sugar in the blood

Tell your doctor if you feel sick (nauseous), are vomiting, or have stomach pain, because these may be signs of an inflamed pancreas. Also tell your doctor if you experience joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty moving, as this may be a sign of osteonecrosis. See also section 2. **What you need to know before you or your child takes Norvir.**

In patients with haemophilia type A and B, there have been reports of increased bleeding while taking this treatment or another protease inhibitor. Should this happen to you, seek immediate advice from your doctor.

Abnormal liver function tests, hepatitis (inflammation of the liver), and rarely jaundice, have been reported in patients taking Norvir. Some people had other illnesses or were taking other medicines. People with liver disease or hepatitis may have worsening of liver disease.

There have been reports of muscle pain, tenderness or weakness, particularly when taking medicines to lower cholesterol in combination with antiretroviral therapy, including protease inhibitors and nucleoside analogues. On rare occasions these muscle disorders have been serious (rhabdomyolysis). In the event of unexplained or continual muscle pain, tenderness, weakness or cramps, stop taking the

medicine, contact your doctor as soon as possible or go to the Accident and Emergency Department of your nearest hospital.

Inform your doctor as soon as possible if you experience any symptoms that suggest an allergic reaction after taking Norvir such as rash, hives or breathing difficulties.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, contact your doctor, pharmacist, Accident and Emergency department or if it is urgent get immediate medical help.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects, you can help provide more information on the safety of this medicine.

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Norvir

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

Do not use Norvir after the expiry date on the label. The expiry date refers to the last day of that month.

This medicinal product does not require any special temperature storage conditions. Store in the original bottle in order to protect from moisture.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help the environment.

6. Contents of the pack and other information

What Norvir contains

- The active substance is ritonavir. Each film-coated tablet contains 100 mg ritonavir.
- The other tablet ingredients are: copovidone, sorbitan laurate, anhydrous calcium hydrogen phosphate, colloidal anhydrous silica, sodium stearyl fumarate.
- The tablet coating is composed of: hypromellose, titanium dioxide, macrogols, hydroxypropyl cellulose, talc, colloidal anhydrous silica, polysorbate 80.

What Norvir looks like and contents of the pack

Norvir film-coated tablets are white debossed with [Abbott logo] and the code “NK”.

Three pack sizes are available for Norvir tablets:

- 1 bottle of 30 tablets
- 1 bottle of 60 tablets
- Multipacks comprising 3 bottles each containing 30 film-coated tablets (90 tablets)

Not all pack sizes may be marketed.

Norvir is also supplied as a powder for oral suspension containing 100 mg of ritonavir.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG, Knollstrasse, 67061 Ludwigshafen, Germany

Manufacturers

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Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>