

Package leaflet: Information for the patient
Vonaday 600 mg/300 mg/300 mg film-coated tablets
Efavirenz/Lamivudine/tenofovir disoproxil

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

1. What Vonaday is and what it is used for

Vonaday contains three active substances that are used to treat human immunodeficiency virus

(HIV) infection in adults.

- Efavirenz is a non-nucleoside reverse transcriptase inhibitor (NNRTI)
- Lamivudine is a nucleoside reverse transcriptase inhibitor (NRTI)
- Tenofovir is a nucleotide reverse transcriptase inhibitor (NRTI)

Each of these active substances are antiretroviral medicines that fight human immunodeficiency virus (HIV-1) infection, which work by interfering with an enzyme (reverse transcriptase) that is essential for the virus to multiply.

2. What you need to know before you take Vonaday

Do not take Vonaday

- **If you are allergic** to efavirenz, lamivudine, tenofovir, tenofovir disoproxil fumarate or any of the other ingredients of this medicine (listed in section 6).
- **Elbasvir and grazoprevir** (used to treat of hepatitis C)

Warnings and precautions

Talk to your doctor or pharmacist before taking Vonaday.

- **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. This medicine is not a cure for HIV infection. While taking Vonaday you may still develop infections or other illnesses associated with HIV infection.
- You must remain under the care of your doctor while taking Vonaday.

Tell your doctor:

- **Build-up of lactate in your blood (lactic acidosis).** Lactic acidosis may occur in few people on Vonaday. Lactic acidosis is a serious medical emergency that can cause death. You may be more likely to get lactic acidosis or serious liver problems if you are female, very overweight (obese), or have been taking nucleoside analog medicines for a long time. Serious liver problems can happen in people who take this medicine. In some cases, these serious liver problems can lead to death. Your liver may become large (hepatomegaly) and you may develop fat in your liver (steatosis).
- **if you have a history of heart ailment**
- **if you have a history of Nervous System Symptoms** such as signs of dizziness, difficulty sleeping, drowsiness, difficulty concentrating or abnormal dreaming.
- **if you are taking other medicines** that contain efavirenz, lamivudine, tenofovir disoproxil fumarate, tenofovir alafenamide, emtricitabine or adefovir dipivoxil. Vonaday should not be taken with any of these medicines.
- **Any signs of skin rash.** If you see any signs of a severe rash with blistering or fever, stop taking this medicine and tell your doctor at once. If you had a rash while taking another NNRTI, you may be at a higher risk of getting a rash with Vonaday.
- **if you have a history of liver disease, including chronic active hepatitis.** Patients with liver disease including chronic hepatitis B or C, who are treated with combination antiretrovirals, have a higher risk of severe and potentially life-threatening liver problems. Your doctor may conduct blood tests in order to check how well your liver is working or may switch you to another medicine. **If you have severe liver disease, do not take Vonaday.**
- **if you have a history of mental illness,** including depression. Tell your doctor immediately if you feel depressed, have suicidal thoughts or have strange thoughts.
- **any signs of inflammation or infection.** In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, 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 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 tell your doctor at once.

- 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.
- Resistant Hepatitis B Virus (HBV). If you have HIV-1 and hepatitis B, the hepatitis B virus can change (mutate) during your treatment with Vonaday and become harder to treat (resistant).
- **Use with interferon and ribavirin-based regimens.** Worsening of liver disease that has caused death has happened in people infected with both HIV-1 and hepatitis C virus who are taking antiretroviral medicines and are also being treated for hepatitis C with interferon with or without ribavirin. If you are taking Vonaday and interferon with or without ribavirin, tell your healthcare provider if you have any new symptoms.
- Treatment with Vonaday has increases in the concentration of total cholesterol and triglycerides in blood and also Redistribution/accumulation of body fat.
- **if you have a history of convulsions (fits or seizures)** or if you are being treated with anticonvulsant therapy such as carbamazepine, phenobarbital and phenytoin. If you are taking any of these medicines, your doctor may need to check the level of anticonvulsant medicine in your blood to ensure that it is not affected while taking Vonaday. Your doctor may give you a different anticonvulsant.
- If you have hepatitis B infection, your doctor will carefully consider the best treatment regimen for you. Symptoms of your hepatitis may become worse after discontinuation of Vonaday. Your doctor may then conduct blood tests at regular intervals in order to check how well your liver is working.
- Independent of a history of liver disease, your doctor will consider regular blood tests to check how your liver is working.
- **if you have or have had kidney disease**, or if tests have shown problems with your kidneys. Vonaday is not recommended if you have moderate to severe kidney disease. Vonaday may affect your kidneys. Before starting treatment, your doctor may order blood tests to assess kidney function. Your doctor may also order blood tests during treatment to monitor your kidneys. Vonaday is not usually taken with other medicines that can damage your kidneys. If this is unavoidable, your doctor will monitor your kidney function adequately.
- **bone problems.** 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 immunosuppression, higher body mass index, among others, 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.
Bone problems (sometimes resulting in fractures) may also occur due to damage to kidney tubule cells (see section 4, Possible side effects).

- **if you are over 65.** Insufficient numbers of patients over 65 years of age have been studied. If you are over 65 years of age and are prescribed Vonaday, your doctor will monitor you carefully.

Children and adolescents

- **Do not give Vonaday to children and adolescents** under 18 years of age. The use of Vonaday in children and adolescents has not been studied.

Other medicines and Vonaday

You must not take Vonaday with certain medicines. These are listed under Do not take Vonaday, at the start of section 2. They include some common medicines which can cause serious interactions.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Also, Vonaday should not be taken with any other medicines that contain efavirenz (unless recommended by your doctor), emtricitabine, tenofovir disoproxil fumarate, tenofovir alafenamide, or lamivudine or adefovir dipivoxil.

Tell your doctor if you are taking other medicines which may damage your kidneys. Some examples include:

- Aminoglycosides (medicines for bacterial infections)
- Ganciclovir, cidofovir (medicines for viral infections)
- Non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains)

It is important to tell your doctor or pharmacist if you are taking any of the following:

- **Medicines containing didanosine (for HIV infection):** Taking Vonaday with other antiviral medicines that contain didanosine can raise the levels of didanosine in your blood and may reduce CD4 cell counts. Inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), which sometimes caused death, have been reported rarely when medicines containing tenofovir disoproxil fumarate and didanosine were taken together. Your doctor will carefully consider whether to treat you with medicines containing tenofovir and didanosine.
- **Other medicines used for HIV infection:** The following protease inhibitors: darunavir, indinavir, lopinavir/ritonavir, ritonavir, or ritonavir boosted atazanavir or saquinavir. Your doctor may consider giving you an alternative medicine or changing the dose of the protease inhibitors. Also, tell your doctor if you are taking Maraviroc.
- **Medicines used to treat infection with the hepatitis C virus:** boceprevir, telaprevir, simeprevir, sofosbuvir/velpatasvir.
- **Medicines used to lower blood fats (also called statins):** Atorvastatin, pravastatin, simvastatin. Vonaday can reduce the amount of statins in your blood. Your doctor will check your cholesterol levels and will consider changing the dose of your statin, if needed.
- **Medicines used to treat convulsions/seizures (anticonvulsants):** Carbamazepine, phenytoin, phenobarbital. Vonaday can reduce the amount of the anticonvulsant in

your blood. Carbamazepine can reduce the amount of efavirenz, one of the components of Vonaday, in your blood. Your doctor may need to consider giving you a different anticonvulsant.

- **Medicines used to treat bacterial infections**, including tuberculosis and AIDS-related *Mycobacterium avium* complex: Clarithromycin, rifabutin, rifampicin. Your doctor may need to consider changing your dose or giving you an alternative antibiotic. In addition, your doctor may consider giving you an additional dose of efavirenz to treat your HIV infection.
- **Medicines used to treat fungal infections (antifungals)**: Itraconazole or posaconazole. Vonaday can reduce the amount of itraconazole or posaconazole in your blood. Your doctor may need to consider giving you a different antifungal.
- **Medicines used to treat malaria**: Atovaquone/proguanil or artemether/lumefantrine. Vonaday may reduce the amount of atovaquone/proguanil or artemether/lumefantrine in your blood.
- **Hormonal contraceptive, such as birth control pills, an injected contraceptive (for example, Depo-Provera), or a contraceptive implant**: You must also use a reliable barrier method of contraception (see Pregnancy and breast-feeding). Vonaday may make hormonal contraceptives less likely to work. Pregnancies have occurred in women taking efavirenz, a component of Vonaday, while using a contraceptive implant, although it has not been established that the efavirenz therapy caused the contraceptive to fail.
- **Methadone**, a medicine used to treat opiate addiction, as your doctor may need to change your methadone dose.
- **Sertraline**, a medicine used to treat depression, as your doctor may need to change your dose of sertraline.
- **Bupropion**, a medicine used to treat depression or to help you stop smoking, as your doctor may need to change your dose of bupropion.
- **Diltiazem or similar medicines (called calcium channel blockers)**: When you start taking Vonaday, your doctor may need to adjust your dose of the calcium channel blocker.
- **Medicines used to prevent organ transplant rejection (also called immunosuppressants)**, such as cyclosporine, sirolimus or tacrolimus. When you start or stop taking Vonaday your doctor will closely monitor your plasma levels of the immunosuppressant and may need to adjust its dose.
- **Warfarin or acenocoumarol (medicines used to reduce clotting of the blood)**: Your doctor may need to adjust your dose of warfarin or acenocoumarol.

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.

Women should not get pregnant during treatment with Vonaday and for 12 weeks thereafter. Your doctor may require you to take a pregnancy test to ensure you are not pregnant before starting treatment with Vonaday.

If you could get pregnant while receiving Vonaday, you need to use a reliable form of barrier contraception (for example, a condom) with other methods of contraception including oral (pill) or other hormonal contraceptives (for example, implants, injection). Efavirenz, one of the active components of Vonaday, may remain in your blood for a time after therapy is stopped. Therefore, you should continue to use contraceptive measures, as above, for 12 weeks after you stop taking Vonaday.

Tell your doctor immediately if you are pregnant or intend to become pregnant. If you are pregnant, you should take Vonaday only if you and your doctor decide it is clearly needed. If you have taken Vonaday during your pregnancy, your doctor may request regular blood tests and other diagnostic tests to monitor the development of your child. In children whose mothers took NRTIs during pregnancy, the benefit from the protection against HIV outweighed the risk of side effects.

Serious birth defects have been seen in unborn animals and in the babies of women treated with efavirenz during pregnancy.

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

Do not breast-feed during treatment with Vonaday. Both HIV and the ingredients of Vonaday may pass through breast milk and cause serious harm to your baby.

Driving and using machines

Vonaday may cause dizziness, impaired concentration and drowsiness. If you are affected, do not drive and do not use any tools or machines.

Vonaday contains sodium

This medicine contains sodium in each tablet which should be taken into consideration if you are on a controlled sodium diet.

3. How to take Vonaday

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

The recommended dose is:

One tablet taken each day by mouth. Vonaday should be taken on an empty stomach (commonly defined as 1 hour before or 2 hours after a meal) preferably at bedtime. This may make some side effects (for example, dizziness, drowsiness) less troublesome. Swallow Vonaday whole with water.

Vonaday must be taken every day.

If your doctor decides to stop one of the components of Vonaday, you may be given efavirenz, lamivudine and/or tenofovir disoproxil separately or with other medicines for the treatment of your HIV infection.

If you take more Vonaday than you should

If you accidentally take too many Vonaday tablets you may be at increased risk of experiencing possible side effects with this medicine. Contact your doctor or nearest emergency department for advice. Keep the tablet bottle with you so that you can easily describe what you have taken.

If you forget to take Vonaday

It is important not to miss a dose of Vonaday.

If you do miss a dose of Vonaday within 12 hours of when it is usually taken, take it as soon as you can, and then take your next dose at its regular time.

If it is almost time (less than 12 hours) for your next dose anyway, do not take the missed dose. Wait and take the next dose at the regular time. Do not take a double dose to make up for a forgotten tablet.

If you throw up the tablet (within 1 hour after taking Vonaday), you should take another tablet. Do not wait until your next dose is due. You do not need to take another tablet if you were sick more than 1 hour after taking Vonaday.

If you stop taking Vonaday

Don't stop taking Vonaday without talking to your doctor. Stopping Vonaday can seriously affect your response to future treatment. If Vonaday is stopped, speak to your doctor before you restart taking Vonaday tablets. Your doctor may consider giving you the components of Vonaday separately if you are having problems or need your dose adjusted.

When your supply of Vonaday starts to run low, get more from your doctor or pharmacist. This is very important because the amount of virus may start to increase if the medicine is stopped for even a short time. The virus may then become harder to treat.

If you have both HIV infection and hepatitis B, it is especially important not to stop your Vonaday treatment without talking to your doctor first. Some patients have had blood tests or symptoms indicating that their hepatitis has got worse after stopping tenofovir disoproxil fumarate (one of the component of Vonaday). If Vonaday is stopped your doctor may recommend that you resume hepatitis B treatment. You may require blood tests to check how your liver is working for 4 months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to worsening of your hepatitis, which may be life-threatening.

- Tell your doctor immediately about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

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

4. Possible side effects

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

The following side effects are **very common** (these may affect more than 1 in 10 patients)

- Weakness, feeling sick (nausea), dizziness
- Being sick (vomiting)
- Decreases in phosphate levels in the blood
- Rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions

The following side effects are **common** (these may affect up to 1 in 10 patients)

- Headache
- Pain in the abdomen (stomach)
- Wind (flatulence)
- Fever
- Pain in a joint (arthralgia)
- Cough
- Baldness
- Severe itching of the skin
- Feeling worried or depressed
- Difficulty sleeping
- Nervousness
- Tiredness
- Abnormal dreams
- Drowsiness
- Disturbances of coordination and balance
- Fitting (seizures)

The following side effects are **uncommon** (these may affect up to 1 in every 100 patients):

- Decreases in potassium in the blood (hypokalemia)
- Inflammation of the pancreas (pancreatitis)
- The destruction of muscle cells (rhabdomyolysis), muscular weakness
- increased creatinine
- Increased liver enzymes (most commonly AST, ALT gamma GT)
- Inflammation of the liver.
- Confusional state
- A feeling of intense excitement and happiness, upset or worried
- Loss of memory
- Loss body movements (ataxia), tremor (shaking)
- A feeling of spinning or tilting (vertigo)
- Flushing (Face become red and hot, typically as the result of illness or strong emotion)
- Mental illness
- Severe skin reactions
- Ringing or buzzing in the ears (tinnitus)

The following side effects are **rare** (these may affect up to 1 in every 1,000 patients):

- Swelling of the skin, which may be allergic reactions (Angioedema)
- Fat in your liver (hepatic steatosis)
- Osteomalacia (manifested as bone pain and which may contribute to fractures)
- Muscle tissue disease
- Death of tubular epithelial cells that form the renal tubules of the kidneys.
- Kidney problems, including kidney failure. Your doctor may do blood tests to see if your kidneys are working properly
- Inflammation of the kidney
- Diabetes insipidus due to abnormal working of the kidney
- Liver failure
- Increased amylase
- Stress or depression, a mild mental illness
- Suicide
- Light sensitized allergic reaction (Photoallergic dermatitis)
- Damage of nerves

Lactic acidosis (excess lactic acid in the blood) is a rare but serious side effect that can be fatal. The following side effects may be signs of lactic acidosis: deep rapid breathing, drowsiness, feeling sick (nausea), being sick (vomiting) and stomach pain.

The following side effects are **not known** (frequency cannot be estimated from the available data)

- Back pain
- Diarrhea, indigestion
- Lipodystrophy, is a disorder in which the body is unable to produce fat
- Muscle pain (myalgia)
- Lung inflammation due to bacterial or viral infection
- Inflammation of a nasal sinus
- Lack or loss of appetite, weight loss
- Sweating, Chills
- Difficult breathing (dyspnea)
- The presence of protein in the urine (proteinuria)
- Abnormally large volumes of dilute urine (polyuria)
- Inflammation of the liver
- Inflammation of the mucous membrane of the mouth
- Abnormal enlargement of the spleen
- Abnormal breath sounds/wheezing
- Signs or symptoms of ears, nasal discharge or congestion
- Lymphadenopathy (lymph nodes disease)
- Redistribution/accumulation of body fat
- Diabetes mellitus (Hyperglycemia)
- Deficiency of red cells or of haemoglobin in the blood (Anemia, including pure red cell aplasia and severe anemias progressing on therapy)
- Allergic reaction

- Muscle weakness
- Increased creatine phosphokinase (CPK elevation) leads to injury or stress to muscle tissue
- Seeing or hearing things that are not really there or false beliefs (hallucinations)
- Unconsciousness, abnormal thinking, impaired concentration, aggressive behaviours
- Mental disorders
- Disturbances of coordination and balance
- Reduced sense of touch or sensation (Hypoesthesia), Damage to peripheral nerves (Paraesthesia)
- Disease or dysfunction of one or more peripheral nerves, typically causing numbness or weakness (Neuropathy)
- Breast enlargement in males
- Constipation, indigestion or imperfect absorption of food material by the small intestine (malabsorption)
- Irregular heartbeat
- Increased cholesterol in the blood (hypercholesterolemia)
- Increased triglycerides in the blood (Hypertriglyceridemia)
- Changes in mood, where strong emotions or feelings (uncontrollable laughing or crying, or heightened irritability or Anger)
- Abnormality of movement and behaviour arising from a disturbed mental state

Side effects to the liver: If you are also infected with hepatitis B virus, you may experience a worsening of hepatitis after discontinuation of treatment

If you think that you may have any of these serious side effects, talk to your doctor.

5. How to store Vonaday

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 bottle and carton after {EXP}. The expiry date refers to the last day of that month.

Store at 25°C (77°F); excursions permitted 15°C to 30°C (59°F to 86°F) {See USP Controlled Room Temperature}

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 Vonaday contains

- The active substances are efavirenz, lamivudine and tenofovir disoproxil. Each Vonaday film-coated tablet contains 600 mg of efavirenz, 300 mg of lamivudine and 245 mg of tenofovir disoproxil (as fumarate).

- The other ingredients in the tablet are

Microcrystalline Cellulose, Croscarmellose Sodium, Sodium Lauryl Sulphate, Hydroxypropyl Cellulose, Colloidal Silicon dioxide, Sodium Chloride, Magnesium Stearate, Hypromellose, Polysorbate 80, Purified Water, Opadry II White 85F18422

The following pack sizes are available:

30 tablets are packed in HDPE bottle container.

90 tablets are packed in HDPE bottle container

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Emcure Pharmaceuticals Limited.

Manufacturer:

Emcure Pharmaceuticals Limited.

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