

Package leaflet: Information for the user

Noxafil® 300 mg gastro-resistant powder and solvent for oral suspension posaconazole

Read all of this leaflet carefully before you start taking or giving this medicine to your child 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, pharmacist, or nurse.
- This medicine has been prescribed for you or your child 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Noxafil is and what it is used for

Noxafil contains a medicine called posaconazole. This belongs to a group of medicines called “antifungals”. It is used to prevent and treat many different fungal infections.

This medicine works by killing or stopping the growth of some types of fungi that can cause infections.

Noxafil can be used in children from 2 years of age to treat the following types of fungal infections when other antifungal medicines have not worked or you have had to stop taking them:

- infections caused by fungi of the *Aspergillus* family that have not improved during treatment with the antifungal medicines amphotericin B or itraconazole or when these medicines have had to be stopped;
- infections caused by fungi of the *Fusarium* family that have not improved during treatment with amphotericin B or when amphotericin B has had to be stopped;
- infections caused by fungi that cause the conditions known as “chromoblastomycosis” and “mycetoma” that have not improved during treatment with itraconazole or when itraconazole has had to be stopped;
- infections caused by a fungus called *Coccidioides* that have not improved during treatment with one or more of amphotericin B, itraconazole or fluconazole or when these medicines have had to be stopped.

This medicine can also be used to prevent fungal infections in children from 2 years of age who are at high-risk of getting a fungal infection, such as:

- patients who have a weak immune system due to having chemotherapy for “acute myelogenous leukaemia” (AML) or “myelodysplastic syndromes” (MDS).
- patients having “high-dose immunosuppressive therapy” after “hematopoietic stem cell transplant” (HSCT).

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

Do not take Noxafil

- if you or your child is allergic to posaconazole or any of the other ingredients of this medicine (listed in section 6).
- if you or your child is taking: terfenadine, astemizole, cisapride, pimozone, halofantrine, quinidine, any medicines that contain “ergot alkaloids” such as ergotamine or dihydroergotamine, or a “statin” such as simvastatin, atorvastatin or lovastatin.
- if you have just started taking venetoclax or your venetoclax dose is being slowly increased for treatment of chronic lymphocytic leukaemia (CLL)

Do not take Noxafil if any of the above apply to you or your child. If you are not sure, talk to your doctor or pharmacist before taking Noxafil.

See “Other medicines and Noxafil” below for more information including information on other medicines which may interact with Noxafil.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Noxafil if you or your child:

- has had an allergic reaction to another antifungal medicine such as ketoconazole, fluconazole, itraconazole or voriconazole.
- has or have ever had liver problems. You may need to have blood tests while you are taking this medicine.
- develops severe diarrhoea or vomiting, as these conditions may limit the effectiveness of this medicine.
- has an abnormal heart rhythm tracing (ECG) that shows a problem called long QTc interval
- has a weakness of the heart muscle or heart failure
- has a very slow heartbeat
- has heart rhythm disturbance
- has any problem with potassium, magnesium or calcium levels in your blood
- is taking vincristine, vinblastine and other “vinca alkaloids” (medicines used to treat cancer).
- are taking venetoclax (a medicine used to treat cancer).

You should avoid sun exposure while being treated. It is important to cover sun exposed areas of skin with protective clothing and use sunscreen with a high sun protection factor (SPF), as an increased sensitivity of skin to the sun’s UV rays may occur.

If any of the above apply to you or your child (or you are not sure), talk to your doctor, pharmacist or nurse before taking Noxafil.

If you develop severe diarrhoea or vomiting (being sick) while taking Noxafil, talk to your doctor, pharmacist or nurse straight away, as this may stop it from working properly. See section 4 for more information.

Noxafil gastro-resistant powder and solvent for oral suspension with food and drink

This medicine can be taken with or without food.

Alcohol may affect the absorption of this medicine.

Children

Noxafil should not be given to children younger than 2 years of age.

Other medicines and Noxafil

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

Do not take Noxafil if you or your child is taking any of the following:

- terfenadine (used to treat allergies)
- astemizole (used to treat allergies)
- cisapride (used to treat stomach problems)
- pimozide (used to treat symptoms of Tourette's and mental illness)
- halofantrine (used to treat malaria)
- quinidine (used to treat abnormal heart rhythms).

Noxafil can increase the amount of these medicines in the blood which may lead to very serious changes to your heart rhythm.

- any medicines that contain “ergot alkaloids” such as ergotamine or dihydroergotamine used to treat migraines. Noxafil can increase the amount of these medicines in the blood which may lead to a severe decrease in blood flow to your fingers or toes and could cause damage to them.
- a “statin” such as simvastatin, atorvastatin or lovastatin used to treat high cholesterol.
- venetoclax when used at the start of the treatment of a type of cancer, chronic lymphocytic leukaemia (CLL)

Do not take Noxafil if any of the above apply to you or your child. If you are not sure, talk to your doctor or pharmacist before taking this medicine.

Other medicines

Look at the list of medicines given above that must not be taken while you or your child is taking Noxafil. In addition to the medicines named above there are other medicines that carry a risk of rhythm problems that may be greater when they are taken with Noxafil. Please make sure you tell your doctor about all the medicines you or your child is taking (prescribed or non-prescribed).

Certain medicines may increase the risk of side effects of Noxafil by increasing the amount of Noxafil in the blood.

The following medicines may decrease the effectiveness of Noxafil by decreasing the amount of Noxafil in the blood:

- rifabutin and rifampicin (used to treat certain infections). If you are already taking rifabutin, you will need a blood test and you will need to look out for some possible side effects of rifabutin.
- phenytoin, carbamazepine, phenobarbital or primidone (used to treat or prevent fits).
- efavirenz and fosamprenavir used to treat HIV infection.
- flucloxacillin (antibiotic used against bacterial infections).

Noxafil may possibly increase the risk of side effects of some other medicines by increasing the amount of these medicines in the blood. These medicines include:

- vincristine, vinblastine and other “vinca alkaloids” (used to treat cancer)
- venetoclax (used to treat cancer)
- ciclosporin (used during or after transplant surgery)
- tacrolimus and sirolimus (used during or after transplant surgery)
- rifabutin (used to treat certain infections)
- medicines used to treat HIV called protease inhibitors (including lopinavir and atazanavir, which are given with ritonavir)
- midazolam, triazolam, alprazolam or other “benzodiazepines” (used as sedatives or muscle relaxants)
- diltiazem, verapamil, nifedipine, nisoldipine or other “calcium channel blockers” (used to treat high blood pressure)
- digoxin (used to treat heart failure)
- glipizide or other “sulfonylureas” (used to treat high blood sugar)
- all-trans retinoic acid (ATRA), also called tretinoin (used to treat certain blood cancers).

If any of the above apply to you or your child (or you are not sure), talk to your doctor or pharmacist before taking Noxafil.

Pregnancy and breast-feeding

Tell your doctor if you are or think you are pregnant before you start to take Noxafil.

Do not take Noxafil if you are pregnant unless you are told to by your doctor.

If you are a woman who could become pregnant you should use effective contraception while you are taking this medicine. If you become pregnant while you are taking Noxafil, contact your doctor straight away.

Do not breast-feed while taking Noxafil. This is because small amounts may pass into breast milk.

Driving and using machines

You may feel dizzy, sleepy, or have blurred vision while taking Noxafil, which may affect your ability to drive or use tools or machines. If this happens, do not drive or use any tools or machines and contact your doctor.

Noxafil contains methyl parahydroxybenzoate and propyl parahydroxybenzoate

This medicine contains methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate. May cause allergic reactions (possibly delayed).

Noxafil contains sorbitol

This medicine contains 47 mg sorbitol (E420) per mL.

Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive this medicine.

Noxafil contains propylene glycol

This medicine contains 7 mg of propylene glycol (E1520) per mL.

Noxafil contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to take Noxafil

Do not switch between taking Noxafil gastro-resistant powder and solvent for oral suspension and Noxafil oral suspension.

Always give this medicine to your child exactly as their doctor or pharmacist has told you. You should check with your child's doctor or pharmacist if you are not sure.

- See the instructions for use in the booklet for how to prepare and give a dose of Noxafil. Keep the booklet and follow it each time you prepare the medicine. Bring this booklet to your child's appointments.
- Make sure the doctor or pharmacist explains how to mix and give the right dose to your child.
- The powder for oral suspension needs to be mixed with the provided solvent before use. You must give to your child within 30 minutes of mixing.
- ONLY the solvent in the kit should be used to prepare Noxafil.
- To ensure delivery of the correct dose, ONLY the provided notched tip syringes should be used for preparation and administration.
- Make sure to follow the instructions of your doctor. The doctor will tell you if and when to stop giving Noxafil to your child.

How much to take

The recommended dose for children aged 2 to less than 18 years, weighing 10 to 40 kg, is shown in the below table.

Weight (kg)	Dose (volume)
10-<12 kg	90 mg (3 mL)
12-<17 kg	120 mg (4 mL)
17-<21 kg	150 mg (5 mL)
21-<26 kg	180 mg (6 mL)
26-<36 kg	210 mg (7 mL)
36-40 kg	240 mg (8 mL)

On Day 1 the recommended dose is administered twice.

After Day 1, the recommended dose is administered once daily.

For children weighing > 40 kg, it is recommended to use Noxafil tablets if they can swallow whole tablets.

The length of treatment may depend on the type of infection or the length of time the immune system is not working properly and may be individually changed by the doctor. Do not change the dose or the treatment regimen before consulting the doctor that prescribed the medicine.

If you or your child takes more Noxafil than you should

If you think that you or your child may have taken too much Noxafil, talk to a doctor or go to the hospital straight away.

If you forget to take Noxafil

- If you forget a dose, take it or give it to your child as soon as you remember it.
- However, if it is almost time for the next dose, skip the missed dose and go back to the regular schedule.
- Do not take a double dose to make up for a forgotten dose.

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

4. Possible side effects

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

Serious side effects

Tell your doctor, pharmacist or nurse straight away if you notice any of the following serious side effects – you or your child may need urgent medical treatment:

- nausea or vomit (feeling or being sick), diarrhoea
- signs of liver problems - these include yellowing of your skin or whites of the eyes, unusually dark urine or pale faeces, feeling sick for no reason, stomach problems, loss of appetite or unusual tiredness or weakness, an increase in liver enzymes shown up in blood tests
- allergic reaction

Other side effects

Tell your doctor, pharmacist or nurse if you notice any of the following side effects:

Common: the following may affect up to 1 in 10 people

- a change in the salt level in your blood shown in blood tests - signs include feeling confused or weak
- abnormal skin sensations, such as numbness, tingling, itching, creeping, pricking or burning
- headache
- low potassium levels – shown up in blood tests
- low magnesium levels – shown up in blood tests

- high blood pressure
- loss of appetite, stomach pain or upset stomach, passing wind, dry mouth, changes in your taste
- heartburn (a burning sensation in the chest rising up to the throat)
- low levels of “neutrophils” a type of white blood cell (neutropenia) – this can make you more likely to get infections and be shown up in blood tests
- fever
- feeling weak, dizzy, tired or sleepy
- rash
- itching
- constipation
- rectal discomfort

Uncommon: the following may affect up to 1 in 100 people

- anaemia - signs include headaches, feeling tired or dizzy, being short of breath or looking pale and a low level of haemoglobin shown up in blood tests
- low level of platelets (thrombocytopenia) shown in blood tests – this may lead to bleeding
- low level of “leukocytes” a type of white blood cell (leukopenia) shown in blood tests – this can make you more likely to get infections
- high level of “eosinophils” a type of white blood cell (eosinophilia) – this can happen if you have inflammation
- inflammation of the blood vessels
- heart rhythm problems
- fits (convulsions)
- nerve damage (neuropathy)
- abnormal heart rhythm – shown up on a heart trace (ECG), palpitations, slow or fast heartbeat, high or low blood pressure
- low blood pressure
- inflammation of the pancreas (pancreatitis) – this may cause severe stomach pain
- oxygen supply to the spleen is interrupted (splenic infarction) - this may cause severe stomach pain
- severe kidney problems – signs include passing more or less urine, that is a different colour than usual
- high blood levels of creatinine – shown in blood tests
- cough, hiccups
- nose bleeds
- severe sharp chest pain when breathing in (pleuritic pain)
- swelling of lymph glands (lymphadenopathy)
- reduced feeling of sensitivity especially on the skin
- tremor
- high or low blood sugar levels
- blurred vision, sensitivity to light
- hair loss (alopecia)
- mouth ulcers
- shivering, feeling generally unwell
- pain, back or neck pain, pain in arms or legs
- water retention (oedema)
- menstrual problems (abnormal vaginal bleeding)
- inability to sleep (insomnia)
- being completely or partially unable to talk
- swelling of the mouth
- abnormal dreams, or difficulty sleeping
- problems with co-ordination or balance
- mucosal inflammation
- stuffy nose

- difficulty breathing
- chest discomfort
- feeling bloated
- mild to severe nausea, vomiting, cramps and diarrhoea, usually caused by a virus, stomach pain
- belching
- feeling jittery

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

- pneumonia – signs include feeling short of breath and producing discoloured phlegm
- high blood pressure in the blood vessels in the lungs (pulmonary hypertension) this can cause serious damage to your lungs and heart
- blood problems such as unusual blood clotting or prolonged bleeding
- severe allergic reactions, including widespread blistering rash and skin peeling
- mental problems such as hearing voices or seeing things that are not there
- fainting
- having problems thinking or talking, having jerking movements, especially in your hands that you cannot control
- stroke – signs include pain, weakness, numbness, or tingling in the limbs
- having a blind or dark spot in your field of vision
- heart failure or heart attack which could lead to the heart stopping beating and death, heart rhythm problems, with sudden death
- blood clots in your legs (deep vein thrombosis) – signs include intense pain or swelling of the legs
- blood clots in your lungs (pulmonary embolism) – signs include feeling short of breath or pain while breathing
- bleeding into your stomach or gut – signs include vomiting blood or passing blood in your stool
- a blockage in your gut (intestinal obstruction) especially in the “ileum”. The blockage will prevent the contents of your intestine from passing through to the lower bowel – signs include feeling bloated, vomiting, severe constipation, loss of appetite, and cramps
- “haemolytic uraemic syndrome” when red blood cells breakup (haemolysis) which may happen with or without kidney failure
- “pancytopenia” low level of all blood cells (red and white blood cells and platelets) shown in blood tests
- large purple discolourations on the skin (thrombotic thrombocytopenic purpura)
- swelling of the face or tongue
- depression
- double vision
- breast pain
- adrenal glands not working properly – this may cause weakness, tiredness, loss of appetite, skin discolouration
- pituitary gland not working properly – this may cause low blood levels of some hormones that affect the function of the male or female sex organs
- hearing problems
- pseudoaldosteronism, which results in high blood pressure with a low potassium level (shown in blood test)

Not known: frequency cannot be estimated from the available data

- some patients have also reported feeling confused after taking Noxafil.
- redness of the skin

Tell your doctor, pharmacist or nurse if you notice any of the side effects listed above.

Reporting of side effects

If you or your child gets 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 or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Noxafil

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 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 or solvent via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

See the instructions for use booklet for the right way to dispose of your leftover medicine.

6. Contents of the pack and other information

What Noxafil contains

The active substance is posaconazole. Each single-use sachet of gastro-resistant powder for oral suspension is an off-white to yellow powder containing 300 mg of posaconazole.

The other ingredient is: hypromellose acetate succinate.

The solvent contains the following ingredients: purified water, glycerol (E 422), methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate, sodium dihydrogen phosphate monohydrate, citric acid anhydrous (E330), xanthan gum (E415), sodium citrate (E331), saccharin sodium (E954), microcrystalline cellulose and carmellose sodium, carrageenan calcium sulfate trisodium phosphate (E407), sorbitol solution (E420), potassium sorbate (E202), flavour berry citrus sweet (containing propylene glycol (E1520), water, natural and artificial flavour), antifoam Af emulsion (containing polyethylene glycol (E1521), octamethyl cyclotetrasiloxane, decamethylcyclopentasiloxane and poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy).

What Noxafil looks like and contents of the pack

Noxafil gastro-resistant powder and solvent for oral suspension is supplied as a pack containing:

Package 1: The kit contains 8 child-resistant single-use sachets (PET/aluminium/LLDPE), two 3 mL (green) notched tip syringes, two 10 mL (blue) notched tip syringes, two mixing cups, one 473 mL solvent bottle (HDPE) with polypropylene (PP) closure with a foil induction seal liner, and one bottle adapter for the solvent bottle.

Package 2: A box of six 3 mL (green) and six 10 mL (blue) notched tip syringes.

Each single-use sachet contains 300 mg of posaconazole which is suspended in 9 mL of solvent to obtain 10 mL total of suspension with a final concentration of approximately 30 mg per mL.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Merck Sharp & Dohme (UK) Limited, 120 Moorgate, London, EC2M 6UR, United Kingdom.

Manufacturer: Merck Sharp & Dohme B. V. Waarderweg 39, 2031 BN, Haarlem, The Netherlands.

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