

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS REGULATIONS**  
**(PREPARATIONS) 1986**

This medicine is marketed upon physician's prescription only

## **NOXAFIL® 100 mg gastro-resistant Tablets**

Each tablet contains:  
Posaconazole 100 mg

For a list of inactive ingredients see section 6 "FURTHER INFORMATION". See also section 2.6 "Important information about some of the ingredients of the medicine".

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

- This leaflet contains concise information about **NOXAFIL**. 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 medical condition seems similar to yours.
- **NOXAFIL** tablets is intended for use in adults (18 years of age and older).

### **1. WHAT NOXAFIL IS INTENDED FOR?**

**NOXAFIL** is used to prevent and treat different types of fungal infections.

**NOXAFIL** is used to treat the following types of fungal infections in adults when other antifungal medicines have not worked or you have had to stop taking them:

- infections caused by fungi of the *Aspergillus* family and are resistant to treatment with amphotericin B or itraconazole or when the patient cannot receive these medicines;
- infections caused by fungi of the *Fusarium* family and are resistant to treatment with amphotericin B or when the patient cannot receive this medicine;
- infections caused by fungi that cause the conditions known as "chromoblastomycosis" and "mycetoma" and are resistant to treatment with itraconazole or when the patient cannot receive this medicine;
- infections caused by a fungus called *Coccidioides* and are resistant to treatment with amphotericin B, itraconazole or fluconazole or when the patient cannot receive these medicines.
- fungal infection called Zygomycosis, in patients intolerant of or with disease that is refractory to alternative therapy.

This medicine can also be used to prevent fungal infections in adults 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).

**Therapeutic group:**

- Posaconazole belongs to a group of medicines called "antifungals".
- This medicine works by killing or stopping the growth of some types of fungi that can cause infections.

### **2. BEFORE YOU TAKE NOXAFIL**

**2.1 Do not take NOXAFIL if:**

- |   |
|---|
| <ul style="list-style-type: none"><li>• you are allergic (hypersensitive) to posaconazole or any of the other ingredients of this medicine (listed in section 6).</li></ul> |
|---|

- you are taking: terfenadine, astemizole, cisapride, pimozide, halofantrine, quinidine, any medicines that contain “ergot alkaloids” such as ergotamine or dihydroergotamine, or a medicine from the statin family such as simvastatin, atorvastatin or lovastatin.
- 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. If you are not sure, talk to your doctor or pharmacist before taking **NOXAFIL**.

See section **2.3 “Interactions with other medicines”** below for more information including information on other medicines which may interact with **NOXAFIL**.

## **2.2 Special warnings concerning use of NOXAFIL**

**Before starting treatment with NOXAFIL, tell your doctor if you:**

- have had an allergic reaction to another antifungal medicine such as ketoconazole, fluconazole, itraconazole or voriconazole.
- have or have ever had liver problems. You may need to have blood tests while you are taking this medicine.
- develop severe diarrhoea or vomiting, as these conditions may limit the effectiveness of this medicine.
- have an abnormal heart rhythm tracing (ECG) that shows a problem called long QTc interval
- have a weakness of the heart muscle or heart failure
- have a very slow heartbeat
- have heart rhythm disturbance
- have any problem with potassium, magnesium or calcium levels in your blood
- are 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 you are not sure), talk to your doctor or the pharmacist before taking **NOXAFIL**.

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

## **2.3 Interactions with other medicines**

**If you are taking or have recently taken or might take any other medicines, including non-prescription medicines and nutritional supplements, you should tell the attending doctor or pharmacist.**

**Do not take NOXAFIL if you are taking any of the following medicines:**

- 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 medicine of the statin family such as simvastatin, atorvastatin or lovastatin used to treat high levels of 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. If you are not sure, talk to your doctor or pharmacist before taking this medicine.

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 are taking (prescribed or non-prescribed).

Certain medicines may increase the risk of side effects caused by **NOXAFIL** due to 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 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 among others to prevent transplant rejection)
- tacrolimus and sirolimus (used to prevent transplant rejection)
- 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 you are not sure), talk to your doctor or pharmacist before taking **NOXAFIL**.

## 2.4 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 of **NOXAFIL** may pass into breast milk.

## 2.5 Driving and using machines

You may feel dizzy, sleepy, or have blurred vision while taking **NOXAFIL**. These may affect your ability to drive or use tools or machines. If you suffer from these side effects, do not drive or use any tools or machines and contact your doctor.

## 2.6 Important information about some of the ingredients of the medicine

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

## 3. HOW SHOULD YOU USE NOXAFIL?

Do not switch between taking **NOXAFIL tablets** and **NOXAFIL oral suspension** without talking to your doctor or pharmacist because it may result in a lack of efficacy or an increased risk of adverse reactions.

Always take **NOXAFIL** as instructed by the doctor. You should check with your doctor or pharmacist if you are not sure.

The dosage and duration of treatment will be determined by the doctor only.

The usually recommended dose is:

300 mg (three 100 mg tablets) twice a day on the first day, then 300 mg (three 100 mg tablets) once a day, thereafter.

The length of treatment may depend on the type of infection that you have and may be individually adapted for you by your doctor. Do not adapt your dose yourself before consulting your doctor or change your treatment regimen, without consulting the attending doctor.

**Do not exceed the recommended dose.**

### Taking this medicine

- Swallow the tablet whole with some water.
- Do not crush, chew, break or dissolve the tablet (Clinical study data are lacking regarding the impact of these actions on the absorption of the tablet).
- Tablets may be taken with or without food.

### If you have accidentally taken a higher dose than you should

If you have taken an overdose of **NOXAFIL**, or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.

### If you forget to take NOXAFIL

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

Complete the full course of treatment as instructed by the doctor.

Even if there is an improvement in your health, do not discontinue use of this medicine before consulting your doctor.

Do not take medicines in the dark! Check the label and the dose each time you take your medicine. Wear glasses if you need them.

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

## 4. SIDE EFFECTS

Like all medicines, **NOXAFIL** can cause side effects, in some of the users.

Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

### **Serious side effects**

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

- nausea or vomit (feeling or being sick), diarrhoea
- signs of liver problems, which 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 or the pharmacist if you notice any of the following side effects:

#### Common side effects: 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) that can be shown up in blood tests. This can make you more likely to get infections
- fever
- feeling weak, dizzy, tired or sleepy
- rash
- itching
- constipation
- rectal discomfort

#### Uncommon side effects: 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
- 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 side effects: 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 the 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 (hemolysis) 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)

Side effects with unknown frequency: frequency cannot be estimated from the available data

- some patients have also reported feeling confused after taking **NOXAFIL**
- redness of the skin

If a side effect appears, if any of the side effects gets serious or if you notice a side effect not mentioned in this leaflet, consult your doctor.

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site ([www.health.gov.il](http://www.health.gov.il)) which refers to the online side effects reporting form, or by using the link: <https://sideeffects.health.gov.il/>

## 5. HOW TO STORE NOXAFIL?

- Avoid Poisoning! This medicine, as all other medicines, must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use **NOXAFIL** after the expiry date (exp. date) which is stated on the pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions:** Store below 30°C.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. FURTHER INFORMATION

**6.1** In addition to the active ingredient the medicine also contains the following inactive ingredients: hypromellose acetate succinate; hydroxypropylcellulose; cellulose, microcrystalline; croscarmellose sodium; silica dental type; magnesium stearate, polyvinyl alcohol, macrogol/PEG 3350, titanium dioxide, talc, iron oxide yellow.

### **6.2 What NOXAFIL tablets look like and contents of the pack**

**NOXAFIL 100 mg** gastro-resistant tablets are yellow-coated and capsule-shaped, of 17.5 mm length, debossed "100" on one side.

Pack sizes: packaged in a blister in cartons of 24 or 96 tablets.

Not all pack sizes may be marketed.

### **Marketing Authorization Holder and Importer:**

Merck Sharp & Dohme (Israel-1996) Company Ltd., 34 Ha'charash St., Hod-Hasharon.

**Drug registration no. listed in the official registry of the Ministry of Health:**

156-42-34550

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