**PACKAGE LEAFLET**

**TYREZ 5 mg film-coated tablets**
**TYREZ 10 mg film-coated tablets**
**bisoprolol fumarate**

**Read all of this leaflet carefully before you start using this medicine, as 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

**In this leaflet:**


## 1. WHAT TYREZ IS AND WHAT IT IS USED FOR

TYREZ belongs to a group of medicines known as beta adrenergic receptor antagonists (beta-blockers). These medicines protect the heart from being burdened excessively.

Bisoprolol fumarate is used to treat the following:
- high blood pressure;
- angina pectoris (a sensation of tightness in the chest);
- heart failure that causes breathlessness brought on by exercise, or liquid retention. In this case, TYREZ can be used as an additional treatment in combination with other medicines for the treatment of heart failure.

## 2. BEFORE YOU TAKE TYREZ

**Do not take TYREZ**
- if you are allergic (hypersensitive) to bisoprolol fumarate or any of the other ingredients of TYREZ;

- if you have a cardiogenic shock (a severe cardiac dysfunction, the symptoms of which are a rapid and weak pulse, low blood pressure, cold and clammy skin, weakness and fainting);
- if you have ever suffered from severe wheezing or severe asthma as they may affect your breathing;
- if you have slow heart rate (less than 60 beats per minute). Contact your doctor if you are not sure.
- if you have very low blood pressure;
- if you have severe blood circulation problems (which may cause a tingling sensation in your fingers and toes, they may also turn pale or blue),
- if you have certain serious heart rhythm problems;
- if you have acute heart failure which has occured recently or has not yet been stabilised and requires hospital treatment;
- if you have a metabolic disorder in which there is excessive accumulation of acids in the body known as metabolic acidosis. Consult your doctor if you are not sure;
- if you have an untreated tumour of the adrenal gland (phaeochromocytoma).
- if you take floctafenin (medicine to treat pain) or sultopride (used in mental disorders).

Contact your doctor if you are not sure about any of the above.

**Take special care with TYREZ**
- if you suffer from wheezing or other breathing problems (asthma) simultaneous treatment with bronchodilators is required and a higher dose of beta-2 adrenergic agonists may be necessary.
- if you have diabetes. The tablets may mask the symptoms of low blood sugar (e.g. a faster heart beat, unpleasant sensations of fast or strong beating of the heart, sweating);
- if you are on a diet with no solid food intake (strict fasting);
- if you are being treated for hypersensitivity (allergic) reactions. Bisoprolol may increase your sensitivity to substances you are allergic to and the severity of allergic reactions. Adrenaline treatment may not then have the desired effect, and the dose of adrenaline (epinephrine) may have to be increased;
- if you have a first degree AV block (conduction disorder of the heart);
- if you suffer from Prinzmetal's angina. This is a type of chest pain caused by a spasm of the coronary arteries that supply the heart muscle;
- if you have any problems with blood circulation in your limbs, e.g. in your palms and soles;
- if you are about to see your doctor or dentist or are to be admitted to a hospital in order to undergo surgery that requires anaesthesia, please inform your doctor about the medicines you are taking;
- if you suffer from or have suffered from psoriasis (a chronic skin condition characterised by dry and scaly patches on the skin);
- if you have phaeochromocytoma (a tumour of the adrenal gland). Prior to bisoprolol treatment, you will be prescribed a suitable anti-tumour treatment;
- if you have a thyroid disorder. TYREZ tablets may mask the symptoms of hyperthyroidism (an overactive thyroid).

Currently there is no information available on heart failure treatment using bisoprolol in patients with the following diseases and conditions:

- diabetes treated with insulin (type I),
- severe impairment of kidney function,
- severe impairment of liver function,
- certain heart diseases,
- a heart attack within the last three months.

Treatment of heart failure with bisoprolol should be carried out under regular medical supervision. This is indispensable particularly at the beginning of treatment.

The bisoprolol treatment should not be stopped suddenly unless there are clear indications for doing so.

In patients with hypertension, angina pectoris and concomitant heart failure the treatment should not be stopped suddenly. The dosage should be decreased gradually, by halving the dose each week.

If you think that any of the above may apply to you or have applied to you in the past, please inform your doctor.

**Taking other medicines**
**Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.**
Certain medicines must not be taken simultaneously with bisoprolol, while others may require certain modifications (e.g. a dosage adjustment).

Inform your doctor if you are using or taking any of the following medicines simultaneously with TYREZ:

- medicines for controlling the blood pressure or for the treatment of heart problems (e.g. amiodarone, amlodipine, clonidine, digitalis glycosides, diltiazem, disopyramide, felodipine, flecainide, lidocaine, methyldopa, moxonidine, phenytoin, propafenone, quinidine, rilmenidine, verapamil);
- sedatives and medicines for the treatment of psychoses (mental disorders), e.g. sultopride, barbiturates (also used for the treatment of epilepsy), phenothiazines (also used in the prevention and treatment of nausea and vomiting);
- antidepressants such as tricyclic antidepressants and MAO-A inhibitors;
- medicines used during surgery as anaesthetics (see also "Take special care with TYREZ");
- some medicines for pain relief (e.g. floctafenin, acetylsalicylic acid, diclofenac, indomethacin, ibuprofen, naproxen);
- medicines for the treatment of asthma, a blocked nose or certain eye disorders, such as glaucoma (increased pressure in the eye) or dilated pupils;
- some medicines for the treatment of shock (e.g. adrenaline, dobutamine, noradrenaline);
- mefloquine, a medicine used for the treatment of malaria.

All of these medicines, including bisoprolol, may have an effect on your blood pressure and/or heart function.
- insulin or other anti-diabetic medicines. The ability to lower blood glucose may be enhanced. The warning signs of a decreased level of blood glucose may be masked.

**Taking TYREZ with food and drink**
TYREZ tablets may be taken with or without food. The recommended dose - whole tablet/s and/or half a tablet - should be swallowed whole, with some liquid, and should not be chewed or crushed.

The medicine may cause dizziness and light-headedness, which are more pronounced if alcohol is taken at the same time. If you experience such effects, you should avoid drinking alcohol.

**Pregnancy and breast-feeding**
TYREZ may have harmful effects on pregnancy and/or the unborn child. There is an increased risk of premature birth, miscarriage, low blood glucose levels, and a slow heartbeat in the child. It may also influence the child's growth. Therefore, pregnant women must not take bisoprolol.

It is not known whether bisoprolol passes into breast milk. Therefore, this medicine is not recommended while breastfeeding.

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

**Driving and using machines**
TYREZ has no or negligible influence on the ability to drive and use machines.

## 3. HOW TO TAKE TYREZ

Always use TYREZ exactly as your doctor has told you. Consult your doctor or pharmacist if you are not sure.

Your doctor will tell you how many tablets to take. Take TYREZ tablets in the morning: before, during or after breakfast. The recommended dose (whole tablet/s and/or half a tablet) - should be swallowed whole, with some liquid, and should not be chewed or crushed.

**The usual dose is:**

***High blood pressure/angina pectoris:***
*Adults*
Dose is determined individually.
The recommended starting dose is 5 mg once daily.
The normal dose for adults is 10 mg once daily. The doctor may increase or decrease the dose as needed.
The maximum dose is 20 mg once daily.

*Severe impairment of liver or kidney function*
In severe impairment of liver or kidney function the daily dose should not exceed 10 mg.

*Elderly patients*
A dose adjustment is generally not required. The treatment will be started with the lowest possible dose.

*Use in children*
The safety and effectiveness of the use of TYREZ in children have not yet been established.

***Heart failure (decreased pumping strength of the heart):***
*Adults*
Before starting to take TYREZ you will already be taking an ACE inhibitor (a medicine that dilates blood vessels and thus lowers blood pressure), a diuretic (a medicine that increases the excretion of urine and thus lowers blood pressure) or a cardiac glycoside (a heart/blood pressure medicine).
Your doctor will gradually increase the dose until a therapeutic effect is achieved:
1.25 mg once daily for one week: if well tolerated, the dose is increased to
2.5 mg once daily for another week: if well tolerated, the dose is increased to
3.75 mg once daily for another week: if well tolerated, the dose is increased to
5 mg once daily for another 4 weeks: if well tolerated, the dose is increased to
7.5 mg once daily for another 4 weeks: if well tolerated, the dose is increased to
10 mg once daily for maintenance treatment.

The maximum dose is 10 mg once daily.

For initial titration phase (1.25 to3.75 mg/day) dividable TYREZ 2.5 mg tablets are available.

Your doctor will determine the most suitable dose for you, taking in account, among other things, any possible adverse effects.

After the first 1.25 mg dose, your doctor will check your blood pressure, heart rate and the presence of any heart function disorder.

*Impaired liver or kidney function*
In patients with impaired liver or kidney function: your doctor will be especially cautious when increasing the dose.

*Elderly patients*
A dose adjustment is generally not required.

*Use in children*
The safety and effectiveness of TYREZ in children have not yet been established.

**If you find the effect of TYREZ to be too strong or too weak, talk to your doctor or pharmacist.**

**Dividing the tablet**

Place the tablet on a solid, flat surface with the scored side facing up. Press on the centre of the tablet with your thumb and the tablet will break in half.

**Duration of treatment**
Treatment with TYREZ is usually long-term.

**If you take more TYREZ than you should**
**Notify your doctor or a pharmacist immediately** if you have accidently taken more tablets than you should. Take any remaining tablets or this leaflet with you so that the medical staff will know exactly which medicine you have taken. Overdose symptoms may include dizziness, light-headedness, fatigue, shortness of breath and/or wheezing**.** Other symptoms such as a slow heartbeat, low blood pressure, acute heart failure and low blood glucose (signs of which are a feeling of hunger, sweating and palpitations) may also occur.

**If you forget to take TYREZ**
Do not take a double dose to make up for a missed dose. Take your usual dose as soon as you remember it and then continue with your usual dosing schedule the next day.

**If you stop taking TYREZ**
TYREZ treatment should not be stopped abruptly. A sudden discontinuation may aggravate your condition. Upon completion of the treatment, doses should be gradually decreased over a period of several weeks in accordance with your doctor's instructions.

**Should you have any further questions on how to use this medicine, , consult your doctor or pharmacist.**

## 4. POSSIBLE SIDE EFFECTS

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

Adverse side effects are classified according to the following frequencies:

| | |
|---|---|
| Very common: | affects more than 1 user in10 |
| Common: | affects 1 to 10 users in 100 |
| Uncommon: | affects 1 to 10 users in 1,000 |
| Rare: | affects 1 to 10 users in 10,000 |
| Very rare: | affects less than 1 user in 10,000 |
| Frequency not known: | cannot be estimated from the available data |

The following side effects may occur:

**Very common side effects** (affect more than 1 user in 10):

- slow heartbeat. In the treatment of hypertension or angina pectoris this side effect is uncommon.

**Common side effects** (affect 1 to 10 users in 100):
- exhaustion; In the treatment of hypertension or angina pectoris this side effect is uncommon.
- dizziness, tiredness and headache (especially at the beginning of treatment in patients with hypertension and angina pectoris; these side effects are generally mild and often disappear within 1-2 months);
- feeling of coldness or numbness in the extremities (fingers,toes, ears and nose); a more frequent occurrence of a cramp-like pain in the legs when walking;
- aggravation of existing heart failure. In the treatment of hypertension or angina pectoris this side effect is uncommon.
- significant decrease in blood pressure (hypotension), particularly in patients with heart failure;
- feeling sick (nausea), vomiting;
- diarrhoea;
- constipation.

**Uncommon side effects** (affects 1 to 10 users in 1,000):
- exhaustion. In the treatment of heart failure this side effect is common.
- dizziness (vertigo), especially when standing up suddenly (orthostatic hypotension);
- sleep disturbances;
- depression;
- slow heartbeat. In the treatment of heart failure this side effect is very common.
- irregular heartbeat;
- an aggravation of existing heart failure; In the treatment of heart failure this side effect is common.
- patients with asthma or a history of breathing problems may experience difficulty in breathing;
- muscle weakness and cramps.

**Rare side effects** (affects 1 to 10 users in 1,000):
- nightmares;
- hallucinations;
- fainting;
- hearing problems;
- inflammation of the nasal mucosa with runny nose and irritation;
- allergic reactions (itching, flush, rash);
- dry eyes as a result of reduced tear flow (caution is necessary if you use contact lenses);
- liver inflammation (hepatitis), which may cause abdominal pain, a loss of appetite and sometimes jaundice with yellowing of the whites of the eyes and the skin and dark urine;
- sexual dysfunction (potency disorders);
- an increased level of blood lipids (triglycerides) and liver enzymes.

**Very rare side effects** (affects less than 1 user in 10,000):
- aggravation of psoriasis or an onset of psoriasis-like dry, scaly rash;
- hair loss;
- itchy or red eyes (conjunctivitis).

**If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.**

## 5. HOW TO STORE TYREZ

Keep out of the reach and sight of children.

Do not use TYREZ after the expiry date which is stated on the carton, and the blister after 'EXP'. The first two digits indicate the month and the last four the year of the expiry date. The expiry date refers to the last day of that month.

Do not store above 25°C.
Store in the original package in order to protect from moisture.
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

**What TYREZ contains**
The active substance is bisoprolol fumarate.

TYREZ 5 mg film-coated tablets:
Each film-coated tablet contains 5 mg of bisoprolol fumarate equivalent to 4.24 mg of bisoprolol.
TYREZ 10 mg film-coated tablets:
Each film-coated tablet contains 10 mg of bisoprolol fumarate equivalent to 8.49 mg of bisoprolol.

The other ingredients are:
microcrystalline cellulose (E460), calcium hydrogen phosphate anhydrous (E341), sodium laurilsulfate, crospovidone (E1202), colloidal anhydrous silica (E551) and glycerol dibehenate in the tablet core, and hypromellose (E464), titanium dioxide (E171), macrogol 400 and yellow iron oxide (E172) in the film-coating.

**What TYREZ looks like and contents of the pack**
TYREZ 5 mg film-coated tablets are yellow, round, biconvex, film-coated tablets with a score line on one side. The score line can be used for dividing the tablet into two equal parts.

The tablets are available in perforated PVC/TE/PVDC/aluminium unit dose blister packs. Each blister pack contains 10 tablets. The printed cardboard box contains 30 tablets (3 blister packs) and a package leaflet.

TYREZ 10 mg film-coated tablets are ochre yellow, round, biconvex, film-coated tablets with a score line on one side.

The tablets are available in perforated PVC/TE/PVDC/aluminium unit dose blister packs. Each blister pack contains 10 tablets. The printed cardboard box contains 30 tablets (3 blister packs) and a package leaflet.

**Marketing Authorisation Holder and Manufacturer**
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**This medicinal product is authorised in the Member States of the EEA under the following names**

| | |
|---|---|
| Bulgaria | Tyrez 5 mg, 10 mg film-coated tablets/филмирани таблетки |
| Czech Republic | Tyrez 5 mg, 10 mg |
| Hungary | Dorez 5 mg, 10 mg filmtabletta |
| Poland | Borez |
| Slovak Republik | Tyrez 5 mg, 10 mg |
| Slovenia | Borez 5 mg, 10 mg filmsko obložene tablete |
| Romania | Borez 5 mg, 10 mg comprimate filmate |

**This leaflet was last approved in:**