Probis®

Bisoprolol Fumarate USP

Composition

Probis® 1.25 tablet: Each coated tablet contains Bisoprolol Fumarate USP 1.25 mg.
Probis® 2.5 tablet: Each coated tablet contains Bisoprolol Fumarate USP 2.5 mg.
Probis® 5 tablet: Each coated tablet contains Bisoprolol Fumarate USP 5 mg.

Pharmacology

Probis® is a preparation of Bisoprolol Fumarate. Bisoprolol is a potent highly β_1-selective adrenoceptor blocking agent. As with other β_1-blocking agents, the method of acting in hypertension is unclear. However, it is known that Bisoprolol reduces plasma renin activity markedly. Bisoprolol by inhibiting the cardiac beta-receptors inhibits the response given to sympathetic activation. That results in the decrease of heart rate and contractility this way decreasing the oxygen demand of the cardiac muscle.

Indication

Probis® is indicated for-

- Treatment of hypertension
- Treatment of stable chronic angina
- Treatment of stable chronic heart failure with reduced systolic left ventricular function in addition to ACE inhibitors, diuretics and optionally cardiac glycosides

Dose and administration

Route of administration: **Probis®** tablet is taken in oral route. **Probis®** tablet should be taken in morning and can be taken with food.

Hypertension and chronic stable angina pectoris
Adults
The dose should be individually adjusted. It is recommended to start with 5 mg per day. The usual dose is 10 mg once daily with a maximum recommended dose of 20 mg per day. Treatment should not be stopped abruptly. The dose should be diminished slowly by a weekly halving of the dose.

Renal impairment
In patients with severe renal impairment (creatinine clearance < 20 ml/min) the dose should not exceed 10 mg once daily. This dose may eventually be divided into halves.

Stable chronic heart failure
Patients should be stable (without acute failure) when bisoprolol treatment is initiated. The treatment of stable chronic heart failure with bisoprolol requires a titration phase. The treatment with bisoprolol is to be started with a gradual uptitration according to the following steps:

- 1.25 mg once daily for 1 week, if well tolerated increase to
- 2.5 mg once daily for a further week, if well tolerated increase to
- 3.75 mg once daily for a further week, if well tolerated increase to
- 5 mg once daily for the 4 following weeks, if well tolerated increase to
- 7.5 mg once daily for the 4 following weeks, if well tolerated increase to
- 10 mg once daily for the maintenance therapy.

The maximum recommended dose is 10 mg once daily. If the maximum recommended dose is not well tolerated, gradual dose reduction may be considered. If discontinuation is considered, gradual dose decrease is recommended, since abrupt withdrawal may lead to acute deterioration of the patient's condition.

Renal or hepatic impairment
There is no information regarding pharmacokinetics of bisoprolol in patients with chronic heart failure and with impaired hepatic or renal function. Uptitration of the dose in these populations should therefore be made with additional caution.

Contraindication

Bisoprolol is contraindicated in patients with known hypersensitivity to bisoprolol or any other components of this product. Bisoprolol is also contraindicated in Chronic heart failure patients with:

- Acute heart failure or during episodes of heart failure decompensation requiring IV inotropic therapy
- Cardiogenic shock
- Second or third degree AV block (without a pacemaker)
- Sick sinus syndrome
- Sinoatrial block
- Symptomatic bradycardia
- Symptomatic hypotension
- Severe bronchial asthma or severe chronic obstructive pulmonary disease
- Late stages of peripheral arterial occlusive disease and Raynaud's syndrome
- Untreated phaeochromocytoma
- Metabolic acidosis.

Warning and precaution

In patients with ischemic heart disease the cessation of therapy with bisoprolol must not be done abruptly unless clearly indicated, because this may lead to transition worsening of heart condition. Bisoprolol must be used with caution in-

- Bronchospasm (bronchial asthma, obstructive airways diseases)
- Diabetes mellitus with large fluctuations in blood glucose values
- Strict fasting
- Ongoing desensitisation therapy
- First degree AV block
- Prinzmetal's angina
- Peripheral arterial occlusive disease
- General anaesthesia.

Patients with psoriasis or with a history of psoriasis should only be given beta-blockers after carefully balancing the benefits against the risks. In patients with phaeochromocytoma, bisoprolol must not be administered until after alpha-receptor blockade.

Side effects

The most common side effects are dizziness, headache, bradycardia (in patients with chronic heart failure), worsening of pre-existing heart failure (in patients with chronic heart failure), feeling of coldness or numbness in the extremities, hypotension especially in patient with heart failure, nausea, vomiting, diarrhea, constipation, asthenia (in patients with chronic heart failure) and fatigue.

Use in pregnancy and lactation

Pregnancy: Bisoprolol is not recommended during pregnancy unless clearly necessary.

Lactation: There are no data on the excretion of bisoprolol in human milk. Therefore, breastfeeding is not recommended during administration of bisoprolol.

Use in children and adolescents

Safety and effectiveness in pediatric patients have not been established.

Drug interaction

Drug interaction with medication: Bisoprolol should not be combined with other beta-blocking agents. Coadministration of catecholamine depleting drugs, such as reserpine or guanethidine and bisoprolol may produce excessive reduction of sympathetic activity. In patients receiving concurrent therapy with clonidine, if therapy is to be discontinued, it is suggested that bisoprolol be discontinued for several days before the withdrawal of clonidine. Bisoprolol should be used with care when myocardial depressants or inhibitors of AV conduction, such as certain calcium antagonists (particularly of the phenylalkylamine [verapamil] and benzothiazepine [diltiazem] classes) or antiarrhythmic agents, such as disopyramide, are used concurrently. Both digitalis glycosides and beta-blockers slow atrioventricular conduction and decrease heart rate. Concomitant use can increase the risk of bradycardia. Concurrent use of rifampin increases the metabolic clearance of bisoprolol, resulting in a shortened elimination half-life of bisoprolol. While taking beta-blockers, patients with a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge, either accidental, diagnostic or therapeutic.

Drug interaction with food and others: Not applicable.

Overdose

The most common signs expected with overdose of a beta-blocker are bradycardia, hypotension, bronchospasm, acute cardiac insufficiency and hypoglycemia. If overdose occurs, discontinuation of bisoprolol treatment and supportive and symptomatic treatment is recommended.

Storage

Store in a cool (below 30ºC) and dry place protected from light. Keep away from the reach of children.

Packing

Probis® 1.25 tablet: Carton of 30 tablets in blister pack.
Probis® 2.5 tablet: Carton of 50 tablets in blister pack.
Probis® 5 tablet: Carton of 50 tablets in blister pack.

® Registered Trade Mark

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