β-Cor® 2.5

Bisoprolol fumarate 2.5 mg

Composition: One film-coated tablet contains 2.5 mg bisoprolol fumarate (2:1).

Substance group: Cardioselective beta-receptor blocker

Indications: Treatment of stable chronic, moderate to severe heart failure (myocardial insufficiency) with impaired systolic ventricular function (ejection fraction < 35%, determined by echocardiography) in addition to ACE inhibitors and diuretics, and optionally cardiac glycosides.

Contraindications: Bisoprolol fumarate 2.5 mg must not be taken in:

-acute myocardial insufficiency (heart failure) or during deterioration (decompensation) of heart failure requiring intravenous therapy with substances increasing the contractility of the heart.

-shock induced by disorders of cardiac function (cardiogenic shock)

-severe disturbances of atrioventricular impulse conduction (second or third degree AV block) without a pacemaker

-sick sinus syndrome

-disturbed impulse conduction between sinus node and atrium (sinoatrial block)

-markedly slowed heart beat (pulse rate less than 60 beats/min) before the start of treatment

-markedly decreased blood pressure (systolic blood pressure below 100 mm Hg)

-severe bronchial asthma or severe chronic obstructive lung disease

-late stages of peripheral arterial occlusive disease or vascular spasms in toes and fingers (Raynaud's syndrome)

-untreated tumours of the adrenal medulla (phaeochromocytoma)

-metabolic acidosis

-known hypersensitivity to bisoprolol.

In the following cases you may take bisoprolol fumarate 2.5 mg only under certain conditions and with particular caution: Please ask your doctor about this. This also applies if you have been affected by any of the following in the past

- Bronchospasm (bronchial asthma, obstructive airways diseases)
- Treatment with inhalation anaesthetics
- Diabetes mellitus with extremely fluctuating blood glucose levels; symptoms of markedly reduced blood glucose (hypoglycaemia) can be masked
- Strict fasting
- Ongoing desensitisation therapy
- Mild disturbances of atrioventricular impulse conduction (first degree AV block)
- Disturbed cardiac blood flow due to vasospasms of the coronary vessels (Prinzmetal's angina)
- Peripheral arterial occlusive disease (intensification of complaints may occur especially when starting therapy)

In patients with a personal or family history of psoriasis, beta- receptor blockers (Bisoprolol fumarate 2.5 mg) should only be used if the benefit-to- risk ratio has been carefully weighed.In patients with a tumour of the adrenal medulla (phaeochromocytoma) bisoprolol fumarate 2.5 mg may only be administered after previous alpha-receptor blockade.

Pregnancy & Nursing: During pregnancy bisoprolol fumarate 2.5 mg should only by used after the doctor has carefully weighed the benefit-to-risk ratio. In general beta-blockers reduce placental blood flow and can affect the development of the unborn child. Placental and uterine blood flow as well as the growth of the unborn child must be monitored and, if required, alternative therapeutic measures considered. The newborn child must be monitored closely after delivery. Symptoms of reduced blood glucose and slowed pulse rate generally occur within the first 3 days of life. It is not known whether bisoprolol passes into breast milk. Therefore, breastfeeding is not recommended during bisoprolol fumarate 2.5 mg therapy.

Special age Group: Bisoprolol fumarate 2.5 mg should not be used in children as no adequate therapeutic experience in this context is available. No dose adjustment is required in elderly patients. No adequate therapeutic experience is available to date with regard to heart failure patients over 80 years of age.

Precautions for use and warnings: The treatment of myocardial insufficiency with bisoprolol fumarate 2.5 mg requires regular monitoring. This is absolutely necessary especially at the start of therapy. In bronchial asthma or other chronic obstructive pulmonary diseases that may be associated with symptoms concomitant bronchodilator therapy is indicated. An increase in airways resistance may occasionally occur in asthma patients, requiring a higher B2-sympathomimetic dose. Like other beta-blockers, bisoprolol can increase the sensitivity to allergens and the severity of anaphylactic reactions, i.e. acute general allergic reactions. Adrenaline does not always produce the desired therapeutic effect in these cases. The symptoms of thyroid hyperfunction (thyrotoxicosis) can be masked by bisoprolol. So far no adequate therapeutic experience is available for bisoprolol fumarate 2.5 mg in heart failure patients with concomitant insulin- dependent type-I diabetes mellitus, impaired kidney function (serum creatinine > 34 mg/dl), impaired liver function, restrictive cardiomyopathy, congenital heart diseases or haemodynamically relevant cardiac valve diseases. No adequate therapeutic experience is available either in patients with mild heart failure (NYHA II) as well as heart failure and myocardial infarction within the last 3 months. Therapy with bisoprolol should not be discontinued abruptly without compelling indication.

What must you pay attention to if you are driving a vehicle, operating machinery, or working without a firm hold?

It was reported that bisoprolol did not affect the driving performance of the patients. However, due to individually different reactions to the drug, the ability to drive a vehicle, to operate machinery, or to work without a firm hold may be impaired. This is particularly the case at the start of treatment, when the dosage is increased or the medication changed, as well as in conjunction with alcohol.

Drug interactions: Simultaneous administration of the following drugs is not recommended:

Increased lowering of blood pressure, delayed atrioventricular impulse conduction as well as reduced contractility of the heart muscle have been observed after simultaneous use of calcium antagonists.

Concurrent use of bisoprolol and clonidine can lead to a stronger reduction of heart rate and to delayed impulse conduction in the heart.

Discontinuation of clonidine can also bring about an excessive increase in blood pressure. Simultaneous administration of monoamine oxidase inhibitors (except MAO-B inhibitors) can affect the blood pressure (lowering of blood pressure, but also excessive increase in blood pressure).

The following drugs may only be used at the same time under certain conditions and with particular caution:

The depressant effects of bisoprolol fumarate 2.5 mg and antiarrhythmics on impulse conduction and contractility of the heart can become additive. Parasympathomimetics (including tacrine) can prolong the atrioventricular conduction time. Other beta-blockers, even if contained in eye drops, potentiate the effect of bisoprolol fumarate 2.5 mg. Concomitant use of bisoprolol fumarate 2.5 mg and insulin or other drugs lowering the blood glucose level (oral antidiabetics) can potentiate the effect of the latter. Warning signs of reduced blood glucose (hypoglycemia) - especially accelerated pulse (tachycardia) - can be masked or suppressed. The concurrent administration of bisoprolol fumarate 2.5 mg and anaesthetics may lead to a pronounced drop in blood pressure. Counter-regulatory mechanisms, e.g. increase in heart rate (reflex tachycardia) can be impaired. Continuation of beta blockade reduces the risk of arrhythmia during initiation of anesthesia and intubation. The anaesthetist should be informed about treatment with bisoprolol fumarate 2.5. Concurrent therapy with bisoprolol fumarate 2.5 mg and digitalis can lead to marked slowing of the heart beat and of impulse conduction in the heart. Simultaneous administration of mefloquine also furthers a slowing of the heart beat. Prostaglandin synthesis inhibitors (e.g. acetylsalicylic acid) can reduce the antihypertensive effect of bisoprolol fumarate 2.5 mg. Concurrent administration of ergotamine derivatives (e.g. ergotamine containing drugs against migraine) and bisoprolol fumarate 2.5 mg can lead to an increase in peripheral circulatory disturbances. Concomitant administration of bisoprolol fumarate 2.5 mg and sympathomimetics can reduce the effect of the two substances. The treatment of allergic reactions may require an increased adrenaline dose. The antihypertensive effect of bisoprolol fumarate 2.5 mg can be potentiated by tricyclic antidepressants, barbiturates, phenothiazines and other antihypertensive drugs. Concomitant administration of rifampicin and bisoprolol fumarate 2.5 mg can slightly shorten the half-life of bisoprolol. Dose adjustment is in general not required.

Dosage instructions, mode and duration of administration: The following dosage instructions apply for bisoprolol fumarate 2.5 mg, unless your doctor has prescribed otherwise. Please follow these directions carefully, otherwise bisoprolol fumarate 2.5 mg cannot have the proper effect.

You should have stable chronic heart failure without any acute deterioration (decompensation) within the last 6 weeks. You should already be treated with an ACE inhibitor at optimal dosage (or, in the case of intolerance of ACE inhibitors, a different vasodilator), a diuretic and, if required, a digitalis preparation. This first-line medication should have remained largely unchanged for 2 weeks before starting therapy with bisoprolol fumarate 2.5 mg. Treatment with bisoprolol should be initiated with slow, gradual dose increases. The attending physician should have experience in the therapy of chronic heart failure. Bisoprolol fumarate 2.5 mg is intended for initial treatment. However, in some patients it may be sufficient for maintenance therapy. The following dose increases are recommended:

1.25 mg bisoprolol fumarate (equivalent to ½ tablet B-Cor 2.5 mg) once daily for 1 week. If this dose is well tolerated increase to 2.5 mg bisoprolol fumarate (equivalent to 1 tablet B-Cor 2.5 mg) once daily for 1 week. If this dose is well tolerated increase to 3.75 mg bisoprolol fumarate (equivalent to 1½ tablet B-Cor 2.5 mg) once daily for 1 week. If this dose is well tolerated increase to 5 mg bisoprolol fumarate once daily for 4 weeks. If this dose is well tolerated increase to 7.5 mg B-Cor once daily for 4 weeks. If this dose is well tolerated increase to 10 mg bisoprolol fumarate once daily as a maintenance dose. For dosages over 2.5 mg bisoprolol fumarate correspondingly higher-strength tablets of B-Cor are available. At the start of treatment with 1.25 mg bisoprolol fumarate (equivalent to ½ tablet B-Cor 2.5 mg) the patients should be monitored for 4 hours (blood pressure, heart rate, impulse conduction disorders as well as symptoms of heart failure). The recommended maximal dose of 10 mg bisoprolol fumarate per day is reached at the earliest after a dose increase over 12 weeks and should not be exceeded. A result of adverse reactions (e.g. slowing of heart beat with symptoms or drop in blood pressure or symptoms of deteriorating heart failure) may be that not all patients can be treated with the highest recommended dosage. If necessary, the beta-blocker dosage can be gradually reduced again, or the treatment (see below) can be discontinued and resumed again at a later time. If deterioration of heart failure or intolerance occur during the titration phase the attending physician is advised to reduce or, in the presence of compelling reasons, immediately discontinue bisoprolol. Treatment of stable chronic heart failure generally means long-term therapy.

Dosage in impaired liver and/or kidney function

Dose titration in heart failure patients with impaired liver or kidney function should be carried out with particular care since no pharmacokinetic investigations are available on this subject.

How and when should you take B-Cor 2.5 mg? You should take the tablet whole with some liquid in the morning before, during or after breakfast.

How long should you take B-Cor 2.5 mg? Treatment of stable chronic myocardial insufficiency is a long-term therapy. The dosage may only be changed by direction of your doctor. Also, treatment with B-Cor 2.5 mg should only be interrupted or discontinued prematurely by direction of your doctor. For termination of therapy with B-Cor 2.5 mg the dose should be gradually reduced (e.g. halving of the dose at weekly intervals). You should not discontinue treatment with B-Cor 2.5 mg abruptly as this may lead to temporary deterioration of the heart failure.

Incorrect intake and overdosage: In the case of suspected bisoprolol fumarate 2.5 mg overdosages please inform your doctor immediately. Depending on the extent of overdosage your doctor can then decide which measures to take. The most frequent signs of bisoprolol fumarate 2.5 mg overdosage include slowed heart beat (bradycardia), marked drop in blood pressure, bronchospasm, acute heart failure as well as hypoglycemia.In the case of overdosage therapy with bisoprolol fumarate 2.5 mg should be discontinued after consultation of the attending physician.

What must you pay attention to if you have taken too little bisoprolol fumarate 2.5 mg or have forgotten to take it?

Do not take the double dose the next time but continue your regimen as prescribed either under "Dosage instructions" or by your doctor.

Missing Dose: Please do not interrupt or stop treatment with bisoprolol fumarate 2.5 mg without having consulted your doctor. You should not discontinue treatment with bisoprolol fumarate 2.5 mg abruptly as this may lead to temporary deterioration of the heart failure. The dose should be gradually reduced (e.g. halving of the dose at weekly intervals).This should be observed especially in patients with disturbed coronary blood flow.

Adverse effects: Besides the desired main effects, drugs can also have undesirable effects, so-called adverse reactions, which by no means occur in every patient, however.

The following data are based on the therapeutic experience obtained after approval of bisoprolol for the therapy of hypertension as well as coronary heart disease.

- Central nervous system:

Occasionally: Tiredness*, exhaustion*, dizziness*, headache*

Rare: Sleep disorders, depression

Very rarely: Nightmares, hallucinations

- Eyes: Very rarely: Reduced tear flow (to be taken into consideration in patients wearing contact lenses) Single cases: conjunctivitis

- Ears: Very rarely: Hearing disorders

- Cardiovascular system: Occasionally: Sensation of cold and numb extremities Rare: Slowing of heart beat (bradycardia), disturbed atrioventricular impulse conduction (AV block), deterioration of heart failure, stronger drop in blood pressure (also when standing up from a supine position, orthostatic hypotension)

- Respiratory system: Rare: Bronchospasm in patients with a history of bronchial asthma or obstructive airways disease Very rarely:Allergic cold (rhinitis)

- Gastrointestinal tract: Occasionally: Nausea, vomiting, diarrhea, constipation

- Muscles and skeleton (locomotor system): Rare: Muscle weakness, muscle cramps

- Skin: Very rarely: Hypersensitivity reactions (itching, temporary flush, rash) Single cases: Beta- receptor blockers can trigger psoriasis, aggravate the condition or lead to psoriasiform rash. Loss of hair.

- Genito- urinary organs: Very rarely: Potency disorders

- Metabolism: Very rarely: Increased liver enzyme levels (GOT,GPT), hepatitis, increased triglyceride levels

*These symptoms occur especially at the start of treatment. They are mild and usually disappear within 1 to 2 weeks after the start of treatment.

If you should experience any adverse reactions not referred to in this package leaflet, you should report these also to your doctor or pharmacist.

What countermeasures are to be taken in the case of adverse reactions?

Your doctor will decide about any possibly required countermeasures.

Storage conditions: store below 30 °C

Presentation: 30 Film-coated tablet.

- A medicament is a product that affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who dispensed the medicament.
- The doctor and the pharmacist are experts in medicine.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep medicaments out of the reach of children.

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