FRONT

3026130

Besicor

BISOPROLOL TABLETS BP

PACKAGE INSERT

COMPOSITION

Besicor 2,5(Bisoprolol Tablets BP 2.5mg)
Each film coated tablet contains:

Bisoprolol Fumarate Ph.Eur.	2.5mg
Excipients	q.s
Colour: Titanium dioxide	

Besicor 5(Bisoprolol Tablets BP 5mg)
Each film coated tablet contains:

Bisoprolol Fumarate Ph.Eu	5mg
Excipients	q.s
Colour: Titanium dioxide	

Besicor 10(Bisoprolol Tablets BP 10mg)
Each film coated tablet contains:

Bisoprolol Fumarate Ph.Eur	10mg
Excipients	q.s

Colour: Lake of sunset yellow, lake of quinoline yellow and titanium dioxide

DOSAGE FORM

Tablets

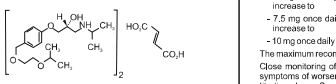
Distribution Category: Prescription Only Medicine or POM

DESCRIPTION

Bisoprolol fumarate is a synthetic (2RS)-1-[4-[[2-(1-Methylethoxy)ethoxy]methyl]Phenoxy]-3-[(1-methylethyl) amino]propan-2-ol fumarate

2-Propanol,1-[4-[[2-(1-methylethoxy)ethoxy]methyl]Phenoxy]-3-[(1methylethyl)amino]-,(±)-,(E)-2-butenedioate (2:1) (salt)

(±)-1-[α-(2-Isopropoxyethoxy)-p-tolyl]oxy]-3-(isopropylamino)-2-propanol fumarate (2:1) (salt) with molecular formula (C18 H31NO4)2 . C4H4O4. Bisoprolol fumarate having molecular weight of 766.96 The chemical structure is



EXCIPIENT LIST

Besicor 2,5(Bisoprolol Tablets BP 2.5mg)

Bisoprolol fumarate Ph.Eur., Silicified microcrystalline cellulose USPNF, Crospovidone BP, Magnesium Stearate BP, Instacoat universal A05R03281 white IH, Purified water.

Besicor 5(Bisoprolol Tablets BP 5mg)

Bisoprolol fumarate Ph.Eur., Silicified microcrystalline cellulose USPNF, Crospovidone BP, Magnesium Stearate BP, Instacoat universal A05R03281 white IH, Purified water.

Besicor 10(Bisoprolol Tablets BP 10mg)

Bisoprol Fumarate Ph.Eur, Silicified microcrystalline cellulose USPNF, Crospovidone BP, Magnesium Stearate BP, Instacoat universal A05R04676 yellow IH, Purified water.

CLINICAL PARTICULARS

Therapeutic Indications

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, and diuretics, and optionally cardiac glycosides.

Dosage and Method of Administration

Bisoprolol fumarate tablet should be taken in morning and can be taken with food in morning. They should be swallowed in liquid and should not be chewed.

Posology

Treatment of hypertension and chronic stable angina pectoris

Adults

The dosage 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.

Patients with renal impairment

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

Patients with severe liver impairment

No dosage adjustment is required; however careful monitoring is advised.

Discontinuation of treatment

Treatment should not be stopped abruptly. The dosage should be diminished slowly by a weekly halving of the dose.

Treatment of stable chronic heart failure

Adults

Standard treatment of CHF consists of an ACE inhibitor (or an angiotensin receptor blocker in case of intolerance to ACE inhibitors), a beta-blocker, diuretics, and when appropriate cardiac glycosides. Patients should be stable (without acute failure) when bisoprolol treatment is initiated.

It is recommended that the treating physician should be experienced in the management of chronic heart failure.

Transient worsening of heart failure, hypotension, or bradycardia may occur during the titration period and thereafter.

Titration phase

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.

Close monitoring of vital signs (heart rate, blood pressure) and symptoms of worsening heart failure is recommended during the titration phase. Symptoms may already occur within the first day after initiating the therapy.

Treatment modification

If the maximum recommended dose is not well tolerated, gradual dose reduction may be considered.

In case of transient worsening of heart failure, hypotension, or bradycardia reconsideration of the dosage of the concomitant medication is recommended. It may also be necessary to temporarily lower the dose of bisoprolol or to consider discontinuation.

The reintroduction and/or uptitration of bisoprolol should always be considered when the patient becomes stable again.

If discontinuation is considered, gradual dose decrease is recommended, since abrupt withdrawal may lead to acute deterioration of the patient's condition.

Treatment of stable chronic heart failure with bisoprolol is generally a long-term treatment.

Special population

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.

Elderly

No dosage adjustment is normally required.

Paediatric population

There is no paediatric experience with bisoprolol, therefore its use cannot be recommended for children.

Method of administration

Oral

Contraindications

Bisoprolol is contraindicated in chronic heart failure patients with:

Acute heart failure or during episodes of heart failure decompensation requiring i.v. 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
- Hypersensitivity to the active substance or to any of the excipients

Special warnings and precaution for use

Applies only to chronic heart failure:

The treatment of stable chronic heart failure with bisoprolol has to be initiated with special titration phase.

Applies to all indications:

Especially 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.

Precautions:

Applies only to hypertension or angina pectoris:

Bisoprolol must be used with caution in patients with hypertension or angina pectoris and accompanying heart failure.

Applies only to chronic heart failure:

The initiation of treatment with bisoprolol necessitates regular monitoring. For posology and method of administration please.

There is no therapeutic experience of bisoprolol treatment of heart failure in patients with the following diseases and conditions:

- Insulin dependent diabetes mellitus (type I)
- Severely impaired renal function
- Severely impaired hepatic function
- Restrictive cardiomyopathy
- Congenital heart disease
- Haemodynamically significant organic valvular disease
- Myocardial infarction within 3 months

Applies to all indications:

Bisoprolol must be used with caution in:

- Bronchospasm (bronchial asthma, obstructive airways diseases).

In bronchial asthma or other chronic obstructive lung diseases, which may cause symptoms, bronchodilating therapy is recommended to be given concomitantly. Occasionally an increase of the airway resistance may occur in patients with asthma, therefore the dose of beta2-stimulants may have to be increased.

- Diabetes mellitus with large fluctuations in blood glucose values; symptoms of hypoglycaemia (e.g. tachycardia, palpitations or sweating) can be masked.
- Strict fasting
- Ongoing desensitisation therapy

As with other beta-blockers, bisoprolol may increase both the sensitivity towards allergens and the severity of anaphylactic reactions. Adrenaline treatment does not always give the expected therapeutic effect.

- First degree AV block
- Prinzmetal's angina
- Peripheral arterial occlusive disease (intensification of complaints might happen especially during the start of therapy)
- General anaesthesia

In patients undergoing general anaesthesia beta-blockade reduces the incidence of arrhythmias and myocardial ischemia during induction and intubation, and the post-operative period. It is currently recommended that maintenance beta-blockade be continued peri-operatively. The anaesthesist must be aware of beta-blockade because of the potential for interactions with other drugs, resulting in bradyarrhythmias, attenuation of the reflex tachycardia and the decreased reflex ability to compensate for blood loss. If it is thought necessary to withdraw beta-blocker therapy before surgery, this should be done gradually and completed about 48 hours before anaesthesia.

Patients with psoriasis or with a history of psoriasis should only be given beta-blockers (e.g. bisoprolol) after carefully balancing the benefits against the risks.

In patients with phaeochromocytomabisoprolol must not be administered until after alpha-receptor blockade.

Under treatment with bisoprolol the symptoms of a thyreotoxicosis may be masked.

Interaction with other medicinal products

Combinations not recommended

Applies only to chronic heart failure:

➢Class I antiarrhythmic drugs (e.g. quinidine, disopyramide; lidocaine, phenytoin; flecainide, propafenone): Effect on atrio-ventricular conduction time may be potentiated and negative inotropic effect increased.

Applies to all indications:

➢Calcium antagonists of the verapamil type and to a lesser extent of the diltiazem type: Negative influence on contractility and atrio-ventricular conduction. Intravenous administration of verapamil in patients on β-blocker treatment may lead to profound hypotension and atrioventricular block.

➢Centrally acting antihypertensive drugs such as clonidine and others (e.g. methyldopa, moxonodine, rilmenidine): Concomitant use of centrally acting antihypertensive drugs may worsen heart failure by a decrease in the central sympathetic tonus (reduction of heart rate and cardiac output, vasodilation). Abrupt withdrawal, particularly if prior to beta-blocker discontinuation, may increase risk of "rebound hypertension".

Combinations to be used with caution

Applies only to hypertension or angina pectoris:

Class-I antiarrhythmic drugs (e.g. quinidine, disopyramide; lidocaine, phenytoin; flecainide propafenone): Effect on atrio-ventricular conduction time may be potentiated and negative inotropic effect increased.

Applies to all indications

➢Calcium antagonists of the dihydropyridine type such as felodipine and amlodipine: Concomitant use may increase the risk of hypotension, and an increase in the risk of a further deterioration of the ventricular pump function in patients with heart failure cannot be excluded.

➢Class-III antiarrhythmic drugs (e.g. amiodarone): Effect on atrio-ventricular conduction time may be potentiated.

➢Topical beta-blockers (e.g. eye drops for glaucoma treatment) may add to the systemic effects of bisoprolol.

➢Parasympathomimetic drugs: Concomitant use may increase atrio-ventricular conduction time and the risk of bradycardia.

➢Insulin and oral antidiabetic drugs: Increase of blood sugar lowering effect. Blockade of beta-adrenoreceptors may mask symptoms of hypoglycaemia.

➢Anaesthetic agents: Attenuation of the reflex tachycardia and increase of the risk of hypotension.

➢Digitalis glycosides: Reduction of heart rate, increase of atrio-ventricular conduction time.

➢Non-steroidal anti-inflammatory drugs (NSAIDs): NSAIDs may reduce the hypotensive effect of bisoprolol.

➢β-Sympathomimetic agents (e.g. isoprenaline, dobutamine): Combination with bisoprolol may reduce the effect of both agents.

➢Sympathomimetics that activate both β- and α-adrenoceptors (e.g. noradrenaline,adrenaline): Combination with bisoprolol may unmask the α-adrenoceptor-mediatedvasoconstrictor effects of these agents leading to blood pressure increase and exacerbated intermittent claudication. Such interactions are considered to be more likely with nonselective β-blockers.

➢Concomitant use with antihypertensive agents as well as with other drugs with blood pressure lowering potential (e.g. tricyclic antidepressants, barbiturates, phenothiazines) may increase the risk of hypotension.

Combinations to be considered

➢Mefloquine: increased risk of bradycardia

➢Monoamine oxidase inhibitors (except MAO-B inhibitors): Enhanced hypotensive effect of the beta-blockers but also risk for hypertensive crisis.

➢Rifampicin: Slight reduction of the half-life of bisoprolol due to the induction of hepatic drug metabolising enzymes. Normally no dosage adjustment is necessary.

➢Mefloquine: increased risk of bradycardia

➢Monoamine oxidase inhibitors (except MAO-B inhibitors): Enhanced hypotensive effect of the beta-blockers but also risk for hypertensive crisis.

➢Rifampicin: Slight reduction of the half-life of bisoprolol due to the induction of hepatic drug metabolising enzymes. Normally no dosage adjustment is necessary.

➢Ergotamine derivatives: Exacerbation of peripheral circulatory disturbances.

Pregnancy&Lactation

Pregnancy

Bisoprolol has pharmacological effects that may cause harmful effects on pregnancy and/or the fetus/newborn. In general, beta-adrenoceptor blockers reduce placental perfusion, which has been associated with growth retardation, intrauterine death, abortion or early labour. Adverse effects (e.g. hypoglycaemia and bradycardia) may occur in the fetus and newborn infant. If treatment with beta-adrenoceptor blockers is necessary, beta1-selective adrenoceptor blockers are preferable.

Bisoprolol is not recommended during pregnancy unless clearly necessary. If treatment with bisoprolol is considered necessary, the uteroplacental blood flow and the fetal growth should be monitored. In case of harmful effects on pregnancy or the fetus alternative treatment should be reccomended. The newborn infant must be closely monitored. Symptoms of hypoglycaemia and bradycardia are generally to be expected within the first 3 days.

Breastfeeding

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

Effects on ability to drive and use machines

In a study with coronary heart disease patients bisoprolol did not impair driving performance. However, due to individual variations in reactions to the drug, the ability to drive a vehicle or to operate machinery may be impaired. This should be considered particularly at start of treatment and upon change of medication as well as in conjunction with alcohol.

Undesirable effects

The following definitions apply to the frequency terminology used hereafter:

Very common (≥ 1/10)
Common (≥ 1/100, < 1/10)
Uncommon (≥ 1/1,000, < 1/100)
Rare (≥ 1/10,000, < 1/1,000)
Very rare (< 1/10,000)

Psychiatric disorders:

Uncommon: sleep disorders, depression.
Rare: nightmares, hallucinations.

Nervous system disorders:

Common: dizziness*, headache*
Rare: syncope

Eye disorders:

Rare: reduced tear flow (to be considered if the patient uses lenses).
Very rare: conjunctivitis.

Ear and labyrinth disorders:

Rare: hearing disorders.

Cardiac disorders:

Very common: bradycardia (in patients with chronic heart failure).
Common: worsening of pre-existing heart failure (in patients with chronic heart failure).
Uncommon: AV-conduction disturbances, worsening of pre-existing heart failure (in patients with hypertension or angina pectoris); bradycardia (in patients with hypertension or angina pectoris).

Vascular disorders:

Common: feeling of coldness or numbness in the extremities, hypotension especially in patient with heart failure.

Respiratory, thoracic and mediastinal disorders:

Uncommon: bronchospasm in patients with bronchial asthma or a history of obstructive airways disease.
Rare: allergic rhinitis.

Gastrointestinal disorders:

Common: gastrointestinal complaints such as nausea, vomiting, diarrhoea, constipation.

Hepatobiliary disorders:

Rare: hepatitis.

Skin and subcutaneous tissue disorders:

Rare: hypersensitivity reactions (such as itching, flush, rash).
Very rare: beta-blockers may provoke or worsen psoriasis or induce psoriasis-like rash, alopecia.

Musculoskeletal and connective tissue disorders:

Uncommon: muscular weakness and cramps.

Reproductive system and breast disorders:

Rare: potency disorders

General disorders:

Common: asthenia (in patients with chronic heart failure), fatigue*.
Uncommon: asthenia (in patients with hypertension or angina pectoris)

Investigations:

Rare: increased triglycerides, increased liver enzymes (ALAT, ASAT).

Applies only to hypertension or angina pectoris:

*These symptoms especially occur at the beginning of the therapy. They are generally mild and usually disappear within 1 - 2 weeks.

Overdose

The most common signs expected with overdose of a beta-blocker are bradycardia, hypotension, bronchospasm, acute cardiac insufficiency and hypoglycaemia. There is limited experience with overdose of bisoprolol, only a few cases of overdose with bisoprolol have been reported. Bradycardia and/or hypotension were noted. All patients recovered. There is a wide inter-individual variation in sensitivity to one single high dose of bisoprolol and patients with heart failure are probably very sensitive.

In general, if overdose occurs, discontinuation of bisoprolol treatment and supportive and symptomatic treatment is recommended.

Based on the expected pharmacologic actions and recommendations for other beta-blockers, the following general measures may be considered when clinically warranted.

Bradycardia: Administer intravenous atropine. If the response is inadequate, isoprenaline or another agent with positive chronotropic properties may be given cautiously. Under some circumstances, transvenous pacemaker insertion may be necessary.

Hypotension: Intravenous fluids and vasopressors should be administered. Intravenous glucagon may be useful.

AV block (second or third degree): Patients should be carefully monitored and treated with isoprenaline infusion or temporary pacing.

Acute worsening of heart failure: Administer i.v. diuretics, inotropic agents, vasodilating agents.

Bronchospasm: Administer bronchodilator therapy such as isoprenaline, beta2-sympathomimetic drugs and/or aminophylline.

Hypoglycemia: Administer i.v. glucose.Limited data suggest that bisoprolol is hardly dialyzable

PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta blocking agent
ATC Code: C07BB07

Pharmacodynamic properties

Mechanism of action

Bisoprolol is a potent highly beta1-selective-adrenoceptor blocking agent, lacking intrinsic stimulating and without relevant membrane stabilising activity. It only shows low affinity to the beta2-receptor of the smooth muscles of bronchi and vessels as well as to the beta2-receptors concerned with metabolic regulation. Therefore, bisoprolol is generally not to be expected to influence the airway resistance and beta2-mediated metabolic effects. Its beta1-selectivity extends beyond the therapeutic dose range.

Hypertension or angina pectoris:

Bisoprolol is used for the treatment of hypertension and angina pectoris. As with other Beta- 1-blocking agents, the method of acting in hypertension is unclear. However, it is known that Bisoprolol reduces plasma renin activity markedly.

Antianginal mechanism: 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.

In acute administration in patients with coronary heart disease without chronic heart failure bisoprolol reduces the heart rate and stroke volume and thus the cardiac output and oxygen consumption. In chronic administration the initially elevated peripheral resistance decreases.

Pharmacokinetic properties

Bisoprolol is absorbed almost completely from the gastrointestinal tract. Together with the very small first pass effect in the liver, this results in a high bioavailability of approximately 90%. The plasma protein binding of bisoprolol is about 30 %.

The distribution volume is 3.5 l/kg. The total clearance is approximately 15l/h.

The plasma elimination half-life (10-12 hours) provides 24 hours efficacy following a once daily dosage.

Bisoprolol is excreted from the body by two routes, 50 % is metabolised by the liver to inactive metabolites which are then excreted by the kidneys. The remaining 50 % is excreted by the kidneys in an unmetabolised form. Since elimination takes place in the kidneys and the liver to the same extent a dosage adjustment is not required for patients with impaired liver function or renal insufficiency.

In patients with chronic heart failure (NYHA stage III) the plasma levels of bisoprolol are higher and the half-life is prolonged compared to healthy volunteers. Maximum plasma concentration at steady state is 64±21 ng/ml at a daily dose of 10 mg and the half-life is 17±5 hours.

PRECLINICAL SAFETY DATA

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or carcinogenicity.

Like other beta-blockers, bisoprolol caused maternal (decreased food intake and decreased body weight) and embryo/fetal toxicity (increased incidence of resorptions, reduced birth weight of the offspring, retarded physical development) at high doses but was not teratogenic.

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PHARMACEUTICAL PERTICULARS

Incompatibilities

Not applicable.

Shelf life

24 months

Storage Condition

Store below 30°C.

Name and Contents of Container

10 tablets in Alu-PVC/PVdC blister pack, 3 such blister in a printed carton along with Pack Insert.

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : +91-22-6606 1000 Fax : (0091) 22-66061200/ 300 Email : info@ajantapharma.com	Ajanta Pharma Limited Mirza-Palashbari Road, Village Kokjhar, Kamrup (R), Guwahati, Assam - 781128, India.

Version No.: 00

Last Revision Date: July 02, 2021

Besicor

BISOPROLOL TABLETS BP

PATIENT INFORMATION LEAFLET

Read all of this leaflet carefully before you start taking this medicine 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 or pharmacist.
- This medicine has been prescribed for you 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 or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Bisoprolol fumarate tablet is and what it is used for
2. What you need to know before you take Bisoprolol fumarate tablet
3. How to take Bisoprolol fumarate tablet
4. Possible side effects
5. How to store Bisoprolol fumarate tablet
6. Contents of the pack and other information

1. What Bisoprolol Fumarate tablets are and what they are used for

The active substance in this medicine is Bisoprolol fumarate. Bisoprolol fumarate belongs to group of medicines called beta-blockers. Beta-blocker protects heart from too much activity. This medicine works by affecting the body's response to some nerve impulses, especially in the heart. As a result, Bisoprolol fumarate slows down the heart rate and makes the heart more efficient at pumping blood around the body. Heart failure occurs when the heart muscle is weak and unable to pump enough blood to supply the body's need.

Bisoprolol 2.5 mg, 5 mg and 10 mg tablet are used in combination with other medicines to treat stable heart failure.

Bisoprolol 5 mg and 10 mg tablet are also used to treat high blood pressure (=hypertension) and angina pectoris (Chest pain caused by blockages in the arteries that supply the heart muscle)

2. What you need to know before you take Bisoprolol Fumarate tablet

Do not take Bisoprolol fumarate tablet if:

- You are allergic to Bisoprolol fumarate or any of the other ingredients of this medicine
- You have severe asthma or sever chronic lung disease.
- You have severe blood circulation problem in limbs (such as Raynaud's syndrome), which may cause your fingers and toes to tingle or turn pale or blue.
- You have untreated phaeochromocytoma, which is a rare tumour of the adrenal gland (medulla).
- You have metabolic acidosis, which is a condition when there is too much acid in the blood.
- acute heart failure or heart failure that suddenly becomes worse and / or that may require hospital treatment
- slow heart rate
- Very low blood pressure
- Certain heart condition causing a very slow heart rate or irregular heartbeat.
- Cardiogenic shock, which is an acute serious heart condition causing low blood pressure and circulatory failure.

Warnings and Precautions

Talk to your doctor or pharmacist before taking this medicine, He or she may want to take special care (for example give additional treatment or perform more frequent checks) if you have any of the following conditions:

- diabetes
- strict fasting (fasting from solid food)
- certain heart disease such as disturbance in heart rhythm or severe chest pain at rest (Prinzmetal's angina)
- kidney or liver disease
- less severe blood circulation problem in your limbs
- less severe asthma or chronic lung disease
- history of a scaly skin rash (psoriasis)
- tumour of the adrenal gland (medulla) (phaeochromocytoma)
- thyroid disorder

In addition, tell your doctor if you are going to have:

- Desensitization therapy (for example for the prevention of hay fever), because Bisoprolol fumarate may make it more likely that you experience as allergic reaction or such reaction may be more severe.
- Anesthesia (for example for surgery) because this medicine may influence how your body react to this situation.

Other medicines and Bisoprolol Fumarate tablets

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

Do not take the following medicines with Bisoprolol fumarate tablets without special advice from your doctor:

- medicines for controlling the blood pressure or medicines for heart problems (such as amiodarone, amlodipine, clonidine, digitalis glycosides, diltiazem, disopyramide, felodipine, flecainide, lidocaine, methyldopa, moxonidine, phenytoin, propafenone, quinidine, rilmenidine, verapamil)
- medicines for depression e.g. imipramine, amitriptyline, moclobemide
- medicines to treat mental illness e.g. phenothiazines such as levomepromazine
- medicines used for anaesthesia during an operation
- medicines used to treat epilepsy e.g. barbiturates such as phenobarbital
- certain pain killers (for instance acetyl salicylic acid, diclofenac, indomethacin, ibuprofen, naproxen)
- medicines for asthma or medicines used for a blocked nose
- medicines used for certain eye disorders such as glaucoma (increased pressure in the eye) or used to widen the pupil of the eye
- certain medicines to treat clinical shock (e. g. adrenaline, dobutamine, noradrenaline)
- mefloquine, a medicine for malaria
- all these drugs as well as bisoprolol may influence the blood pressure and/or heart function.
- rifampicin for the treatment of infectionsmedicines to treat severe headaches or migraines (ergotamine derivatives).

Pregnancy and breast-feeding

Pregnancy

There is a risk that Bisoprolol fumarate tablet can harm the baby if it is used during pregnancy. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. He or she will determine whether you can take Bisoprolol fumarate Tablet during pregnancy.

Breast-feeding

It is not known whether Bisoprolol fumarate passes in to breast milk. Therefore, breastfeeding is not recommended during treatment with Bisoprolol fumarate tablet.

Driving and using machines

The ability to drive or operate machinery may be affected, depending on how well you tolerate the medicine. Be especially careful at the beginning of the treatment, when the dose is increased or when the medication is changed, and when combined with alcohol.

3. How to take Besicor tablets

Always take this medicine exactly as your doctor has told you. Check with your doctor or your pharmacist if you are not sure. Treatment with Bisoprolol fumarate tablet requires regular medical check-up. This is particularly important in the initiation of therapy and during dose increase.

Bisoprolol fumarate tablet should be taken in the morning, with or without food. Swallow the tablet/s whole with some water and do not chew or crush them. The tablet can be divided into equal doses.

Treatment with Bisoprolol fumarate tablet is usually prolonged.

The maximum recommended dose is 20 mg once per day.

Patient with kidney disease:

Patient with severe kidney disease should not exceed 10 mg of bisoprolol once daily. Please consult your doctor before starting to use this medicine.

Patient with liver disease:

Patient with severe liver disease should not exceed 10 mg of bisoprolol once daily. Please consult your doctor before starting to use this medicine.

Heart failure:

Before you start using bisoprolol fumarate tablet, you should already be taking other medicines for heart failure including any ACE inhibitor, a diuretic and (as an added option) a cardiac glycoside.

Treatment with Bisoprolol fumarate tablet must be started at a low dose and increased gradually. Your doctor will decide how to increase the dose, and this will normally be done in the following way:

- 1.25 mg bisoprolol fumarate once daily for a week
- 2.5 mg bisoprolol fumarate once daily for a week
- 3.75 mg bisoprolol fumarate once daily for a week
- 5 mg bisoprolol fumarate once daily for four weeks
- 7.5 mg bisoprolol fumarate once daily for four weeks
- 10 mg bisoprolol fumarate once daily for maintenance (on-going) therapy.

The maximum recommended daily dose of bisoprolol fumarate is 10 mg.

Depending on how well you tolerate the medicine, the doctor may also extend the time between dose increases. If your condition gets worse or if you no longer tolerate the drug, it may be necessary to lower the dose again or to stop treatment. For some patients a maintenance dose lower than 10 mg bisoprolol fumarate may be sufficient. Your doctor will tell you what to do. If you have to stop the treatment entirely, your doctor will usually advice you to reduce the dose gradually, as otherwise your condition may become worse.

Use in children

Bisoprolol fumarate tablet is not recommended for use in children.

Elderly patient

In general adjustment of the dose is not needed. It is recommended to start with lowest possible dose.

If you notice that the bisoprolol dose is too strong or does not work well enough, please consult your doctor or pharmacist.

If you take more Bisoprolol fumarate tablet than you should

If you take too much medicine, or if a child has swallowed the medicine by mistake ask your doctor or hospital for assessing risk and advice. Take this leaflet and any tablet you still have with you. You may feel slow heartbeat, severe breathing difficulties, dizziness or tremor (due to decreased blood sugar).

If you forget to take Bisoprolol fumarate tablet:

If you forget to take a dose, take it as soon as you remember it unless it is nearly time for your next dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking Bisoprolol fumarate tablet:

Do not stop treatment suddenly or change the recommended dose without talking to your doctor first.

If you need to stop treatment, it must be done gradually to avoid side effects.

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

Use in children

Bisoprolol fumarate tablet is not recommended for use in children.

Elderly patient

In general adjustment of the dose is not needed. It is recommended to start with lowest possible dose.

If you notice that the bisoprolol dose is too strong or does not work well enough, please consult your doctor or pharmacist.

If you take more Bisoprolol fumarate tablet than you should

If you take too much medicine, or if a child has swallowed the medicine by mistake ask your doctor or hospital for assessing risk and advice. Take this leaflet and any tablet you still have with you. You may feel slow heartbeat, severe breathing difficulties, dizziness or tremor (due to decreased blood sugar).

If you forget to take Bisoprolol fumarate tablet:

If you forget to take a dose, take it as soon as you remember it unless it is nearly time for your next dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking Bisoprolol fumarate tablet:

Do not stop treatment suddenly or change the recommended dose without talking to your doctor first.

If you need to stop treatment, it must be done gradually to avoid side effects.

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

4. Possible side effects

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

To prevent serious reaction, speak to a doctor immediately if a side effect is severe, occurs suddenly or gets worse rapidly. The most serious side effects are related to the heart function:

- Slowing of heart rate (may affect up to 1 in 10 people with chronic heart failure and may affect up to 1 in 100 people with hypertension or angina pectoris)
- Worsening of heart failure (may affect up to 1 in 10 people with chronic heart failure and may affect up to 1 in 100 people with hypertension or angina pectoris)
- Slow or irregular heartbeat (may affect more than 1 in 10 people with chronic heart failure)
- Worsening of symptom of blockage of the main blood vessel to the legs, especially at the start of treatment (Frequency not stated).

If you feel dizzy or weak or have breathing difficulties, please contact your doctor as soon as possible.

Further side effects are listed below according to how frequently they may occur:

Common (may affect up to 1 in 10 people):

- Tiredness*, feeling weak (In patient with chronic heart failure), dizziness*, headache*
- Feeling of coldness or numbness in hands or feet
- Low blood pressure, especially in patient with heart failure.
- Stomach or intestine problem such as nausea, vomiting, diarrhea or constipation.

Uncommon (may affect up to 1 in 100 people):

- Sleep disturbances
- Depression
- Breathing problems in patients with asthma or chronic lung disease
- Muscle weakness, muscle cramps.
- feeling weak (In patient with hypertension or angina pectoris)

Rare (may affect up to 1 in 1,000 people):

- Hearing problems
- Allergic runny nose (Blocked or runny nose
- Reduced tear flow (can be a problem if you wear contact lenses)
- Inflammation of liver which may cause yellowing of the skin or whites of the eyes
- Some blood test for liver function and fat content are different from normal value.
- Allergy-like reactions such as itching, flush, rash
- Impaired erection (Reduced sexual performance
- Nightmares, hallucinations
- Fainting

Very rare (may affect up to 1 in 10,000 people):

- Irritation and redness of eye (conjunctivitis)
- Hair loss
- Appearance or worsening of scaly skin rash (psoriasis): Psoriasis like rash.

* if treated for high blood pressure or angina then these symptoms occur especially at beginning of treatment, or if your dosage changes. They are generally mild or often disappear within 1 to 2 weeks.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effect not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Bisoprolol fumarate tablets

- 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 blister and carton after EXP. The expiry date refers to the last day of that month.
- Do not store above 30°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment

6. Contents of the pack and other information

WhatBisoprolol fumarate tablet contains:

The active ingredient is

Besicor 2.5(Bisoprolol Tablets BP 2.5mg)
Each film coated tablet contains:
Bisoprolol Fumarate Ph.Eur 2.5mg
Excipients q.s
Colour: Titanium dioxide

Besicor 5(Bisoprolol Tablets BP 5mg)
Each film coated tablet contains:
Bisoprolol Fumarate Ph.Eur 5mg
Excipients q.s
Colour: Titanium dioxide

Besicor 10(Bisoprolol Tablets BP 10mg)
Each film coated tablet contains:
Bisoprolol Fumarate Ph.Eur 10mg
Excipients q.s
Colour: Lake of sunset yellow, lake of quinoline yellow and titanium dioxide

List of Excipients:

Besicor 2.5(Bisoprolol Tablets BP 2.5mg)
Bisoprolol fumarate Ph.Eur., Silicified microcrystalline cellulose USPNF, Crospovidone BP, Magnesium Stearate BP, Instacoat universal A05R03281 white IH. Purified water.

Besicor 5(Bisoprolol Tablets BP 5mg)
Bisoprolol fumarate Ph.Eur., Silicified microcrystalline cellulose USPNF, Crospovidone BP, Magnesium Stearate BP, Instacoat universal A05R03281 white IH. Purified water.

Besicor 10(Bisoprolol Tablets BP 10mg)
Bisiprol Fumarate Ph.Eur, Silicified microcrystalline cellulose USPNF, Crospovidone BP, Magnesium Stearate BP, Instacoat universal A05R04676 yellow IH, Purified water.

What Bisoprolol fumarate tablet looks like and contents of the pack

Besicor 2.5(Besoprolol Tablets BP 2.5 mg)

White to off white, circular biconvex, film coated tablets with break line on one side.

Besicor 5(Besoprolol Tablets BP 5 mg)

White to off white, circular biconvex, film coated tablets with break line on one side.

Besicor 10(Besoprolol Tablets BP 10 mg)

Light orange to yellow coloured circular shaped biconvex film coated tablets with break line on one side and plain on other side.

110 tablets in Alu-PVC/PVdC blister pack, 3 such blister in a printed

carton along with Pack Insert.

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : +91-22-6606 1000 Fax : (0091) 22-66061200/ 300 Email : info@ajantapharma.com	Ajanta Pharma Limited Mirza-Palashbari Road, Village Kokjhar, Kamrup (R), Guwahati, Assam - 781128, India.

For any information about this medicinal product, please contact Manufacturing Authorization Holder.

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