Summary of Product Characteristics

BISODAC-HF 2.5 mg, 5 mg & 10 mg

(Bisoprolol Fumarate 2.5 mg, 5 mg & 10 mg Tablets)

R_x Only

NAME OF THE DRUG PRODUCT

Bisoprolol Fumarate Tablets 2.5 mg
Bisoprolol Fumarate Tablets 5 mg
Bisoprolol Fumarate Tablets 10 mg

(TRADE) NAME OF THE PRODUCT **BISODAC-HF 2.5**
BISODAC-HF 5
BISODAC-HF 10

STRENGTH: 2.5 mg, 5 mg and 10 mg.

PHARMACEUTICAL DOSAGE FORM: Film-coated tablet

QUALITATIVE AND QUANTITATIVE COMPOSITIONS

Bisoprolol Fumarate Tablets 2.5 mg
Each film-coated tablet contains Bisoprolol Fumarate Ph.Eur. 2.5 mg

Bisoprolol Fumarate Tablets 5 mg
Each film-coated tablet contains Bisoprolol Fumarate Ph.Eur. 5 mg

Bisoprolol Fumarate Tablets 10 mg
Each film-coated tablet contains Bisoprolol Fumarate Ph.Eur. 10 mg

PHARMACEUTICAL FORM

BISODAC-HF 2.5 mg: White, circular, biconvex, film-coated tablets debossed with 'P and break line' on one side and '2' on the other side.
BISODAC-HF 5 mg: White, circular, biconvex, film-coated tablets debossed with 'P and break line' on one side and '5' on the other side.
BISODAC-HF 10 mg: White, circular, biconvex, film-coated tablets debossed with 'P and break line' on one side and '10' on the other side.

Therapeutic indications

For 2.5 mg

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

For 5mg & 10 mg

- Treatment of high blood pressure (hypertension)
- Treatment of coronary heart disease (angina pectoris)
- Treatment of stable chronic heart failure with reduced systolic left ventricular function in addition to ACE inhibitors, and diuretics, and optionally cardiac glycosides.

Posology and method of administration

Recommended Dose for 5 mg & 10 mg

Treatment of hypertension or angina pectoris

In all cases the dose regimen is adjusted individually by your doctor, in particular according to the pulse rate and therapeutic success.
The usual initial dose is 5mg bisoprolol fumarate once daily. If necessary, the dose may be increased to 10mg bisoprolol fumarate once daily.
The maximum recommended dose is 20mg bisoprolol fumarate once daily.
BISODAC-HF must be used with caution in patients with hypertension or angina pectoris and accompanying heart failure.

For 2.5 mg, 5 mg & 10 mg

Treatment of stable chronic heart failure

Standard treatment of CHF consists of an ACE inhibitor (or an angiotensin receptor blocker in case of intolerance to ACE inhibitors), a betablocker, diuretics, and when appropriate cardiac glycosides. The initiation of treatment of stable chronic heart failure with BISODAC-HF necessitates a special titration phase.
Precondition for treatment with bisoprolol is stable chronic heart failure without acute failure.
It is recommended that the treating physician be experienced in the management of chronic heart failure.
The treatment of stable chronic heart failure with bisoprolol is initiated according to the following titration scheme, individual adaptation may be necessary depending on how well the patient tolerates each dose, i.e. the dose is to be increased only, if the previous dose is well tolerated.

1st week	1.25 mg	bisoprolol fumarate once daily*
2nd week	2.5 mg	bisoprolol fumarate once daily*
3rd week	3.75 mg	bisoprolol fumarate once daily*
4th–7th week	5 mg	bisoprolol fumarate once daily@
8th–11th week	7.5 mg	bisoprolol fumarate once daily@
12th week and beyond	10mg	bisoprolol fumarate once daily as maintenance treatment*@

* BISODAC-HF 10 is not suitable for initial treatment of stable chronic heart failure. Lower strengths are available for this purpose.
@ BISODAC-HF 2.5 is suitable for initial treatment of stable chronic heart failure. Higher strengths are available for maintenance treatment.
The maximum recommended dose is 10mg bisoprolol fumarate once daily.
Close monitoring of vital signs (blood pressure, heart rate) and symptoms of worsening heart failure is recommended during the titration phase. Symptoms may already occur within the first day after initiating therapy.

Treatment modification

If during the titration' phase or thereafter, transient worsening of heart failure, hypotension or bradycardia occurs, reconsideration of the dosage of concomitant medication is recommended. It may also be necessary to temporarily lower the dose of bisoprolol or to consider discontinuation.
The reintroduction and/or up titration of bisoprolol should always be considered when the patient becomes stable again.

Duration of treatment

Treatment with BISODAC-HF is generally a long-term therapy.
Do not stop treatment abruptly or change the recommended dose without talking to your doctor first since this might lead to a transitory worsening of heart condition.
Especially in patients with ischaernic heart disease, treatment must not be discontinued suddenly. If discontinuation is necessary, the daily dose is gradually decreased.

Special populations

Renal or hepatic impairment:

- *Treatment of hypertension or angina pectoris*: In patients with liver or kidney function disorders of mild to moderate severity no dosage adjustment is normally required. In patients with severe renal impairment (creatinine clearance < 20 ml/min) and in patients with severe hepatic impairment a daily dose of 10mg bisoprolol fumarate must not be exceeded.
- *Treatment of stable chronic heart failure:* There is no information regarding pharmacokinetics of bisoprolol in patients with chronic heart failure and concomitant hepatic or renal impairment. Titration of the dose in these populations must therefore be made with particular caution.

Elderly: No dosage adjustment is required.
Children: There is no paediatric experience with bisoprolol, therefore its use cannot be recommended for children.

Administration

BISODAC-HF tablets are taken in the morning with or without food. They are swallowed with some liquid and not to be chewed.

Route of administration : ORAL

Contraindications

BISODAC-HF must not be used in patients with:

- acute heart failure or during episodes of heart failure decompensation requiring intravenous therapy with substances increasing the contractility of the heart,
- shock induced by disorders of cardiac function (cardiogenic shock),
- severe disturbances of atrioventricular conduction (second or third degree AV block) without a pacemaker,
- sick sinus syndrome,
- sinoatrial block,
- slowed heart rate, causing symptoms (symptomatic bradycardia),
- decreased blood pressure, causing symptoms (symptomatic hypotension),
- severe bronchial asthma or severe chronic obstructive pulmonary disease,
- severe forms of peripheral arterial occlusive disease or Raynaud's syndrome,
- untreated tumours of the adrenal gland (phaeochromocytoma),
- metabolic acidosis,
- hypersensitivity to bisoprolol or to any of the excipients

Warnings and precautions

The following section describes when BISODAC-HF must be used with special caution:

- diabetes mellitus with extremely fluctuating blood glucose levels: symptoms of markedly reduced blood glucose (hypoglycaemia) such astachycardia, palpitations or sweating can be masked,
- strict fasting,
- ongoing desensitization therapy,
- mild disturbances of atrioventricular conduction (first degree AV block),
- disturbed blood flow in the coronary vessels due to vasospasms (Prinzmetal's angina),
- peripheral arterial occlusive disease (aggravation of symptoms may occur especially when starting therapy),
- Patients with psoriasis or with a personal history of psoriasis.

Respiratory system

In bronchial asthma or other symptomatic chronic obstructive pulmonary diseases concomitant bronchodilator therapy is indicated. An increase in airway resistance may occasionally occur in patients with asthma, requiring a higher dose of beta2-sympathomimetics.

Allergic reactions

Beta-blockers, including BISODAC-HF, may increase the sensitivity to allergens and the severity of anaphylactic reactions because the adrenergic counter regulation under beta- blockade may be alleviated. Treatment with adrenaline may not always yield the expected therapeutic effect.

General anaesthesia

In patients undergoing general anaesthesia the anesthetist must be aware of beta-blockade. If it is thought necessary to withdraw BISODAC-HF before surgery, this should be done gradually and completed about 48 hours prior to anaesthesia.

Phaeachramocytoma

In patients with a tumour of the adrenal gland (phaeochromocytoma) BISODAC-HF may only be administered after previous alpha-receptor blockade.

Thyrotoxicosis

Under treatment with BISODAC-HF the symptoms of a thyroid hyperfunction (thyrotoxicosis) may be masked.

Special populations

So far no sufficient therapeutic experience is available for BISODAC-HF in patients with heart failure and concomitant insulin dependent type I diabetes mellitus, severely impaired kidney function, severely impaired hepatic function, restrictive cardiomyopathy, congenital heart diseases or hemodynamically relevant organic valvular heart disease.
No sufficient therapeutic experience is available either in patients with heart failure and myocardial infarction within the last 3 months.
There is insufficient experience with bisoprolol in children, therefore the use of BISODAC- HF cannot be recommended for children.

Interaction with other medicinal products and other forms of interaction

Combinations not recommended

- 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 beta-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 further decrease 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

- Calcium antagonists of the dihydropyridine type such as nifedipine: 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-I antiarrhythmic drugs (e.g. disopyramide, quinidine): Effect on atrio-ventricular conduction time may be potentiated and negative inotropic effect increased
- 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: Intensification 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 (for further information on general anaesthesia see also section 4.4).
- 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.
- Beta-sympathomimetic agents (e.g. isoprenaline, dobutamine): Combination with bisoprolol may reduce the effect of both agents.
- Sympathomimetics that activate both beta- and alpha-adrenoceptors (e.g. noradrenaline, adrenaline): Combination with bisoprolol may unmask the alpha-adrenoceptor-mediated vasoconstrictor effects of these agents leading to blood pressure increase and exacerbated intermittent claudication. Such interactions are considered to be more likely with nonselective beta-blockers. Higher doses of adrenaline may be necessary for treatment of allergic reactions.
- 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.
- Moxisylyte: Possibly causes severe postural 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.

Pregnancy and lactation

During pregnancy BISODAC-HF is only recommended following careful assessment of benefit to-risk ratio by the doctor. In general, beta-blockers reduce placental blood flow and may 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, in case of harmful effects on pregnancy or the foetus, alternative therapeutic measures considered.
The newborn infant must be monitored closely after delivery. Symptoms of reduced blood glucose and slowed pulse rate generally may occur within the first 3days of life.
There are no data on the excretion of bisoprolol in human breast milk or the safety of bisoprolol exposure in infants. Therefore administration of BISODAC-HF is not recommended during breastfeeding.

Effects on ability to drive and use machines

In a study with patients suffering from coronary heart disease bisoprolol did not affect the driving performance of the patients. However, depending on the individual patients response to treatment an effect on the ability to drive a vehicle or to use machines may be impaired. This needs to be considered particularly at the start of treatment, upon change of medication, or in conjunction with alcohol.

Undesirable effects

The adverse effects described below are sorted according to system organ classes. Frequencies are classified as follows:
Very common (affects more than 1 person in 10)
Common (affects less than 1person in 10)
Uncommon (affects less than 1 person in 100) Rare (affects less than 1 person in 1,000)
Very rare (affects less than 1 person in 10,000)

- *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; bradycardia (in patients with hypertension or angina pectoris): worsening of pre-existing heart failure (in patients with hypertension or angina pectoris)
- *Investigations*
  Rare: increased triglycerides, increased liver enzymes (ALAT, ASAT)
- *Nervous system disorders*
  Common: dizziness*, headache*
- *Eye disorders*
  Rare: reduced tear flow (to be considered if the patient uses contact lenses) Very rare: conjunctivitis
- *Ear and labyrinth disorders*
  Rare: hearing disorders
- *Respiratory, thoracic and mediostinal 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
- *Skin and subcutaneous tissue disorders*
  Rare: hypersensitivity reactions such as itching, flush, rash
  Very rare: alopecia. Beta-blockers may provoke or worsen psoriasis or induce psoriasis like rash.
- *Musculoskeletal and connective tissue disorders*
  Uncommon: muscle weakness, muscle cramps
- *Vascular disorders*
  Common: feeling of coldness or numbness in the extremities, hypotension especially in patients with heart failure
- *General disorders*
  Common: asthenia (in patients with chronic heart failure), fatigue* Uncommon: asthenia (in patients with hypertension or angina pectoris)
- *Hepatobilary disorders*
  Rare: hepatitis
- *Reproductive system and breast disorders*
  Rare: potency disorders
- *Psychiatric disorders*
  Uncommon: depression, sleep disorders Rare: nightmares, hallucinations

Applies only to *patients with 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.
Tell your doctor if you notice any of the side effects listed above or any other unwanted or unexpected effects. To prevent serious reactions, speak to a doctor immediately if aside effect is severe, occurred suddenly, or gets worse rapidly.

Overdose

The most frequent signs of BISODAC-HF over dose include slow heart rate (bradycardia), marked drop in blood pressure, acute heart failure, hypoglycemia and bronchospasm.
In the case of suspected BISODAC-HF overdose please inform your doctor immediately. The effect of overdose may vary from one person to the next and patients with heart failure are probably very sensitive.
Depending on the degree of overdose your doctor can then decide which measures to take.
In general, if overdose occurs, bisoprolol treatment is stopped and supportive and symptomatic treatment is provided. Limited data suggest that bisoprolol is hardly dialyzable.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Bisoprolol, the active ingredient of BISODAC-HF is a beta l- selective-adrenoceptor blocking agent, lacking intrinsic stimulating and relevant membrane stabilizing activity. It only shows very low affinity to the beta 2-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 beta l selectivity extends beyond the therapeutic dose range.

Pharmacokinetic properties

Absorption
Bisoprolol is almost completely absorbed from the gastrointestinal tract and undergoes only minimal first-pass metabolism resulting in an oral bioavailability of about 90%. Peak plasma concentrations occur 2 to 4 hours after oral doses.

Distribution
Bisoprolol is about 30% bound to plasma proteins. Bisoprolol is moderately lipid-soluble.

Metabolism
It is metabolised in the liver

Elimination
It has a plasma elimination half-life of 10 to 12 hours
It is excreted in urine, about 50% as unchanged drug and 50% as metabolites.

PHARMACEUTICAL PARTICULARS

List of excipients
Cellulose Microcrystalline, Calcium Hydrogen Phosphate Anhydrous, Silica Colloidal Anhydrous, Crospovidone, Magnesium Stearate, Hypromellose 6 cp, Titanium dioxide, Macrogol 400 and Purified Water.

Incompatibilities

Not applicable.

Shelf life

24 months.

Special precautions for storage

Store below 30 °C.

Nature and contents of container

BISODAC-HF 2.5 mg: 10's & 14's blister of Cold form (Alu-Alu) blister with peelable lidding foil or cold form (Alu-Alu) blister with push through lidding foil.
BISODAC-HF 5 mg: 10's & 14's blister of Cold form (Alu-Alu) blister with peelable lidding foil or cold form (Alu-Alu) blister with push through lidding foil.
BISODAC-HF 10 mg: 10's & 14's blister of Cold form (Alu-Alu) blister with peelable lidding foil or cold form (Alu-Alu) blister with push through lidding foil.

Manufactured by:

AUROBINDO

Aurobindo Pharma Limited
Unit III, Sy. Nos. 313 & 314, Bachupally (V), Bachupally Mandal, Medchal-Malkajgiri District, Telangana State, India.

Product Registration Holder:
Unimed Sdn Bhd
No. 53, Jalan Tembaga SD 5/2B,
Bandar Sri Damansara, 52200, Kuala Lumpur.

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AUROBINDO Packaging Development	Product Name: BISODAC-HF	Component: Leaflet	Item Code: P1520270	Date & Time: 13.12.2018 & 04:30 PM
				No. of Colours :1
	Customer / Country: APL_Malaysia	Version No.: 00	Reason of Issue: New	Black
Team Leader: Lova Raju	Dimensions: 160 x 430 mm	Font Type: Arial	Font Size: 8 pt	
Initiator: Kumar, Bharath				
Design Agency: vakils PREMEDIA	Pharmacode: 20270			

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Additional InformationNA

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