

VI.2.1 Overview of disease epidemiology

Not applicable. This is a generic application. Our SmPC comply with the innovator product regarding indications and adverse events.

VI.2.2 Summary of treatment benefits

Not applicable. This is a generic application. Our SmPC comply with the innovator product regarding indications and adverse events.

VI.2.3 Unknowns relating to treatment benefits

Not applicable. This is a generic application. Our SmPC comply with the innovator product regarding indications and adverse events.

VI.2.4 Summary of safety concerns

Important identified risks		
Risk	What is known	Preventability
Heart problems (cardiac disorders)	<p>Bisoprolol work by affecting the body's response to some nerve impulses, especially in the heart. As a result, bisoprolol slows down the heart rate and makes the heart more efficient at pumping blood around the body. The patients with problems of the heart may already have reduced contractility therefore the additional reduction may result in increased risk of additional heart problems.</p> <p>However, the heart problems are already expectable consequence of the long-term elevation of blood pressure and angina pectoris.</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Do not take <Invented name> if you have one of the following heart problems:</p> <ul style="list-style-type: none">- acute heart failure.- worsening heart failure requiring an injection of medicines into a vein, that increase the force of contraction of the heart.- low blood pressure.- certain heart conditions causing a very slow heart rate or irregular heartbeat and you have not been fitted with a pacemaker.- cardiogenic shock, which is an acute serious heart condition causing low blood pressure and circulatory failure. <p>Talk to your doctor or pharmacist before taking</p>

Important identified risks		
Risk	What is known	Preventability
		<p><Invented name>. If you have any of the following conditions tell your doctor before taking <Invented name> tablets; he or she may want to take special care (for example give additional treatment or perform more frequent checks):</p> <ul style="list-style-type: none"> - certain heart diseases such as disturbances in heart rhythm, or severe chest pain at rest (Prinzmetal's angina). - first degree heart block (a condition in which nerve signals to the heart are disturbed, possibly causing it occasionally to skip a beat, or beat irregularly). <p>Like all medicines, this medicine can cause side effects, although not everybody gets them.</p> <p>To prevent serious reactions, speak to a doctor immediately if a side effect is severe, occurred suddenly or gets worse rapidly. The most serious side effects are related to the heart function:</p> <ul style="list-style-type: none"> - slowing of heart rate (may affect up to 1 in 10 people) - worsening of heart failure (may affect up to 1 in 10 people) - slow or irregular heartbeat (may affect up to 1 in 100 people) <p>If you feel dizzy or weak, or have breathing difficulties please contact your doctor as soon as possible.</p>
Hypersensitivity	These medications may cause	Routine pharmacovigilance by

Important identified risks		
Risk	What is known	Preventability
reactions	<p>allergic reactions as all medicines can.</p> <p>Additionally, bisoprolol may increase the sensitivity in patients undergoing desensitization therapy and therefore it is more likely they experience an allergic reaction, or such reaction may be more severe.</p>	<p>monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Yes, by monitoring for early symptoms and avoiding the drugs you are already known to be allergic of.</p> <ul style="list-style-type: none"> - Please tell your doctor if you are undergoing or are planning to undergo desensitization therapy (for example for the prevention of hay fever), because <Invented name> tablets may make it more likely that you experience an allergic reaction, or such reaction may be more severe. <p>Be careful and tell your doctor if you have experienced symptoms such as sudden wheeziness, chest pain, shortness of breath or difficulty in breathing, swelling of eyelids, face or lips, severe skin reactions or other allergic reactions.</p>
Sudden narrowing of airway by spasm of bronchi (Bronchospasm)	<p>Beta blockers act by affecting body's response to some nerve impulses. Some of the beta blockers have a lot of effect on the lungs. Bisoprolol acts mostly in the heart and vessels however minor effect on the lungs can not be excluded, especially in patients with bronchial asthma or other chronic obstructive lung diseases.</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Do not take <Invented name> if you have one of the following conditions:</p> <ul style="list-style-type: none"> - severe asthma or severe chronic lung disease. <p>Talk to your doctor or pharmacist before taking <Invented name>. If you have</p>

Important identified risks		
Risk	What is known	Preventability
		<p>any of the following conditions tell your doctor before taking <Invented name> tablets; he or she may want to take special care (for example give additional treatment or perform more frequent checks):</p> <ul style="list-style-type: none"> - less severe asthma or chronic lung disease. <p>Like all medicines, this medicine can cause side effects, although not everybody gets them.</p> <p>To prevent serious reactions, speak to a doctor immediately if a side effect is severe, occurred suddenly or gets worse rapidly.</p> <p>Further side effects are listed about that:</p> <ul style="list-style-type: none"> - breathing problems in patients with asthma or chronic lung disease
<p>A rare, usually noncancerous (benign) tumor that develops in the core of an adrenal gland (Pheochromocytoma)</p>	<p>Pheochromocytomas are a type of tumor of the adrenal glands that can release high levels of epinephrine and norepinephrine.</p> <p>In patients with pheochromocytoma bisoprolol must not be administered until after alpha-receptor blockade.</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Do not take <Invented name> if you have one of the following conditions:</p> <ul style="list-style-type: none"> - untreated phaeochromocytoma, which is a rare tumour of the adrenal gland. <p>Talk to your doctor or pharmacist before taking <Invented name>.If you have any of the following conditions tell your doctor before taking <Invented name> tablets; he or she may want to take special care (for example give additional treatment or perform</p>

Important identified risks		
Risk	What is known	Preventability
		<p>more frequent checks):</p> <ul style="list-style-type: none"> - tumour of the adrenal gland (phaeochromocytoma).
<p>Interaction with certain medicines used to treat irregular or abnormal heartbeat (Interaction with with class IV antiarrhythmic and class I antiarrhythmic drugs)</p>	<p>Bisoprolol acts on electricity of the heart resulting in slowing down the heart rate and making the heart more efficient at pumping blood around the body. Class IV and class I antiarrhythmic drugs also act on electricity of the heart therefore the use with bisoprolol may result in an amplified slowing of the rate of the heart.</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Tell your doctor or pharmacist if you are taking any other medication.</p> <p><u>Do not take the following medicines with <Invented name> tablets without special advice from your doctor:</u></p> <ul style="list-style-type: none"> - certain medicines used to treat irregular or abnormal heartbeat (Class I antiarrhythmic medicines such as quinidine, disopyramide, lidocaine, phenytoin; flecainide, propafenone). - certain medicines used to treat high blood pressure, angina pectoris or irregular heartbeat (calcium antagonists such as verapamil and diltiazem). <p><u>Check with your doctor before taking the following medicines with <Invented name> tablets; your doctor may need to check your condition more frequently:</u></p> <ul style="list-style-type: none"> - certain medicines used to treat high blood pressure or angina pectoris or abnormal heart beat (dihydropyridine-type calcium antagonists, such as nifedipine, felodipine and amlodipine).

Important identified risks		
Risk	What is known	Preventability
		- certain medicines used to treat irregular or abnormal heartbeat (Class III antiarrhythmic medicines such as amiodarone).

Important potential risks		
	What is known	Preventability
Patients with high blood sugar (Diabetic patients)	<p>Diabetes mellitus, or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the pancreas does not produce enough insulin, or because cells do not respond to the insulin that is produced.</p> <p>Bisoprolol may mask some of the warning symptoms of low blood sugar, such as increased heart rate, tremor and nausea. People with diabetes should carefully monitor their blood sugar while taking this medicine.</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Talk to your doctor or pharmacist before taking <Invented name>.If you have any of the following conditions tell your doctor before taking <Invented name> tablets; he or she may want to take special care (for example give additional treatment or perform more frequent checks):</p> <ul style="list-style-type: none"> - diabetes. <p>Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.</p> <p><u>Check with your doctor before taking the following medicines with <Invented name> tablets; your doctor may need to check your condition more frequently:</u></p> <ul style="list-style-type: none"> - antidiabetic medicines including insulin.
Patients with a scaly skin rash (Patients with psoriasis)	<p>Psoriasis is an immune-mediated disease that affects the skin. It is typically a lifelong condition. There is currently no cure, but various treatments can help to control the symptoms.</p> <p>Bisoprolol can worsen the symptoms</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Talk to your doctor or pharmacist before taking <Invented name>.If</p>

	<p>of psoriasis. Patients with psoriasis or with a history of psoriasis should only be given βblockers (e.g. bisoprolol) after carefully balancing the benefits against the risks.</p>	<p>you have any of the following conditions tell your doctor before taking <Invented name> tablets; he or she may want to take special care (for example give additional treatment or perform more frequent checks):</p> <ul style="list-style-type: none"> - history of a scaly skin rash (psoriasis). <p>Like all medicines, this medicine can cause side effects, although not everybody gets them. To prevent serious reactions, speak to a doctor immediately if a side effect is severe, occurred suddenly or gets worse rapidly. Further side effects are listed about that:</p> <ul style="list-style-type: none"> - appearance or worsening of scaly skin rash (psoriasis); psoriasis-like rash.
<p>Patients with risk of thyroid disorder (Patients with risk of thyrotoxicosis)</p>	<p>Thyrotoxicosis is the name given to the clinical effects experienced due to an excess of thyroid hormones in the bloodstream. Hormones produced by the thyroid gland control how fast or slow the body works (basal metabolic rate). Too much thyroid hormone (thyroxine and triiodothyronine) can therefore cause an increase in how fast the body functions. This results in the signs and symptoms of thyrotoxicosis.</p> <p>Under treatment with bisoprolol the symptoms of a thyrotoxicosis may be masked.</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>Talk to your doctor or pharmacist before taking <Invented name>.If you have any of the following conditions tell your doctor before taking <Invented name> tablets; he or she may want to take special care (for example give additional treatment or perform more frequent checks):</p> <ul style="list-style-type: none"> - thyroid disorder.
<p>Patients undergoing surgery with narcosis</p>	<p>In patients undergoing general anesthesia 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 of beta-blockade be continued peri-operatively.</p>	<p>Routine pharmacovigilance by monitoring for early symptoms is sufficient.</p> <p>The proposed PIL advises about:</p> <p>In addition, tell your doctor if you are going to have:</p> <ul style="list-style-type: none"> - anaesthesia (for example for surgery), because <Invented name> tablets may influence

		<p>how your body reacts to this situation.</p> <p>Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.</p> <p><u>Check with your doctor before taking the following medicines with <Invented name> tablets; your doctor may need to check your condition more frequently:</u></p> <ul style="list-style-type: none"> - anaesthetic agents (for example during surgery).
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<u>Important missing information</u>		
	What is known	Preventability
Use in children	Bisoprolol should not be used in children as no adequate therapeutic experience in this context is available.	<p>No missing information, the proposed PIL contains the following information about use in children:</p> <p>Children and adolescents</p> <p><Invented name> is not recommended for use in children or adolescents.</p> <p>This is a generic application. The proposed PIL complies with the innovator's product. When new information that may impact the current safety specification will be received, additional safety actions in regards to the Pharmacovigilance plan or additional Risk minimization measures will be taken.</p>

VI.2.5 Summary of additional risk minimization measures by safety concern

No additional risk minimization measures are considered necessary.

VI.2.6 Planned post authorization development plan (if applicable)

No postauthorisation studies are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable, this is the first Risk management plan.