Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Summary of safety concerns	
Important identified risks	- Cardiac disorders - Bronchospasm - Pheochromocytoma
Important potential risks	No important potential risks have been identified.
Important missing information	No important missing information has been identified.

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Not applicable.

VI.1.3 Summary of Post authorisation efficacy development plan

Not applicable.

VI.1.4 Summary table of risk minimisation measures

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Cardiac disorders	(Proposed) content in SmPC: **Contraindications in section 4.3** **Special warnings and precautions for use in section 4.4** **Interaction with other medicinal products and other forms of interaction in section 4.5** **Undesirable effects - listed in section 4.8**	None proposed
Bronchospasm	(Proposed) content in SmPC: **Posology and method of administration in section 4.2** **Contraindications in section 4.3** **Special warnings and precautions for use in section 4.4** **Undesirable effects - listed in section 4.8**	None proposed
Pheochromocytoma	(Proposed) content in SmPC: **Contraindications in section 4.3** **Special warnings and precautions for use in section 4.4**	None proposed

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Metoprolol succinate belongs to a group of medicines called beta-blockers that affects the heart and circulation (blood flow through arteries and veins). Metoprolol reduces the effect of stress hormones on the heart during physical and mental effort. It leads to the heart to beat more slowly (heart rate decreases) in these situations. Metoprolol is used to treat angina (chest pain) and hypertension (high blood pressure). It is also used to treat or prevent heart attack.

VI.2.2 Summary of treatment benefits

<Invented name> is used to treat:

- high blood pressure (hypertension),
- a tight pain in the chest caused by insufficient oxygen to the heart (angina pectoris),
- irregular heart rhythm (arrhythmia),
- palpitations (feeling your heart beat) due to non-organic (functional) heart disorders,
- stable heart failure with symptoms (such as shortness of breath or swollen ankles), when taken together with other medicines for heart failure.

<Invented name> is used to prevent:

- further heart attacks or damage to the heart after a heart attack,
- migraine.

<Invented name> is used to treat high blood pressure in children and adolescents aged 6 to 18 years.

Randomized clinical trials with β-blockers have reported improved survival and reduced need for hospitalizations for worsening heart failure in patients with chronic symptomatic systolic heart failure.

Analysis showed that the benefit of treatment with metoprolol succinate controled release preparation in heart failure extends to patients with diabetes, including those with diabetes and severe heart failure. Metoprolol controled release preparation is very well tolerated with no evidence of the risks traditionally attributed to β-blockade such as hypo- and hyperglycemia and improves the quality of life by decreasing hospitalizations for heart failure, and also increase survival.

VI.2.3 Unknowns relating to treatment benefits

<Invented name> is a generic medicine and is bioequivalent to the reference medicine, its benefits and risks are taken as being the same as the reference medicine’s.

VI.2.4 Summary of safety concerns

Important identified risks		
Risk	**What is known**	**Preventability**
Heart problems (Cardiac disorders)	Metoprolol is a beta-blocker that affects the heart and circulation (blood flow through arteries and veins). It is used to treat angina (chest pain) and hypertension (high blood pressure). It is also used to treat or prevent heart attack. Therapy with metoprolol is one of several preferred initial therapies in hypertensive patients with ischemic heart disease, heart failure, or diabetes mellitus. 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. However, the heart problems are already expectable consequence of the long-term elevation of blood pressure and angina pectoris.	Routine pharmacovigilance by monitoring for early symptoms is sufficient. Metoprolol should not be taken in cases of untreated heart failure, treatment to increase heart contractions, heart failure, a slow heart rate, shock caused by heart problems, heart conduction problems or heart rhythm problems (sick sinus syndrome), severe blood circulation problems (severe peripheral arterial disease), low blood pressure (hypotension). The doctor or pharmacist should be informed if the patient suffers from blood circulation problems which may cause fingers and toes to tingle or turn pale or blue, has tight chest pain usually occurring during the night (Prinzmetal's angina), suffers from a heart conduction disorder (heart block), has a heart failure. The doctor or pharmacist should be informed if the patient are taking, have recently taken or might take any other medicines. The following medicines can increase the effect on lowering blood pressure: medicines for cardiovascular diseases. Like all medicines, this medicine can cause side effects, although not everybody gets them.
Sudden narrowing of airway by spasm of bronchi (Bronchospasm)	In general, beta-blockers should not be used in patients with bronchospastic diseases. Beta blockade may adversely affect pulmonary function by counteracting the bronchodilation produced by catecholamine stimulation of beta-2 receptors. If beta-blocker therapy is necessary in these patients, an agent with beta-1 selectivity (e.g., metoprolol) is considered safer, but should be used with caution	Routine pharmacovigilance by monitoring for early symptoms is sufficient. Metoprolol should not be taken in cases of severe asthma or COPD (chronic obstructive pulmonary disease). The doctor or pharmacist should be informed if the patient has asthma. The doctor or pharmacist should be

Important identified risks		
Risk	**What is known**	**Preventability**
	nonetheless. Cardioselectivity is not absolute and can be lost with larger doses.	informed if the patient are taking, have recently taken or might take any other medicines. Like all medicines, this medicine can cause side effects, although not everybody gets them.
A rare, usually noncancerous (benign) tumor that develops in the core of an adrenal gland (Pheochromocytoma)	Pheochromocytomas are a type of tumor of the adrenal glands that can release high levels of epinephrine and norepinephrine. If metoprolol succinate extended-release is used in the setting of pheochromocytoma, it should be given in combination with an alpha blocker, and only after the alpha blocker has been initiated. Administration of beta-blockers alone in the setting of pheochromocytoma has been associated with a paradoxical increase in blood pressure due to the attenuation of beta-mediated vasodilatation in skeletal muscle.	Routine pharmacovigilance by monitoring for early symptoms is sufficient. Metoprolol should not be taken in cases of untreated phaeochromocytoma (high blood pressure due to a rare tumour in one of the adrenal glands). The doctor or pharmacist should be informed if the patient has high blood pressure due to a rare tumour in one of the adrenal glands (phaeochromocytoma).

Important potential risks	
Risk	**What is known**
No important potential risks have been identified.	/

Important missing information	
Risk	**What is known**
No important missing information has been identified.	/

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not 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.