SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE MEDICINAL PRODUCT

Revelol XL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated extended-release tablet
contains Metoprolol Succinate USP 47.5mg
equivalent to
Metoprolol Tartrate..... 50 mg

Excipient with known effect: Isopropyl Alcohol

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic

Indications Hypertension

Metoprolol succinate extended-release tablets are indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents.

Angina Pectoris

Metoprolol succinate extended-release tablets are indicated in the long-term treatment of angina pectoris.

Heart Failure

Metoprolol succinate extended-release tablets are indicated for the treatment of stable, symptomatic (NYHA Class II or III) heart failure of ischemic, hypertensive, or cardiomyopathic origin. It was studied in patients already receiving ACE inhibitors, diuretics, and, in the majority of cases, digitalis. In this population, metoprolol succinate extended-release tablets decreased the rate of mortality plus hospitalization, largely through a reduction in cardiovascular mortality and hospitalizations for heart failure.

4.2. Posology and Method of Administration

Metoprolol succinate extended-release tablets is an extended-release tablet intended for once daily administration.

The tablet should be swallowed as whole with liquid and should not be chewed or crushed.

When switching from immediate release metoprolol tablet to metoprolol succinate extended-release tablets, the same total daily dose of metoprolol succinate extended-release tablets should be used. As with immediate release metoprolol, dosages of metoprolol succinate extended-release tablets should be individualized and titration may be needed in

some patients.

Hypertension

The usual initial dosage is 25 to 100 mg daily in a single dose, whether used alone or added to a diuretic. The dosage may be increased at weekly (or longer) intervals until optimum blood pressure reduction is achieved. In general, the maximum effect of any given dosage level will be apparent after 1 week of therapy. Dosages above 400 mg per day have not been studied.

Angina Pectoris

The dosage of metoprolol succinate extended-release tablets should be individualized. The usual initial dosage is 100 mg daily, given in a single dose. The dosage may be gradually increased at weekly intervals until optimum clinical response has been obtained or there is a pronounced slowing of the heart rate. Dosages above 400 mg per day have not been studied. If treatment is to be discontinued, the dosage should be reduced gradually over a period of 1–2 weeks. **Heart Failure**

Dosage must be individualized and closely monitored during up-titration. Prior to initiation of metoprolol succinate extended-release tablets, the dosing of diuretics, ACE inhibitors, and digitalis (if used) should be stabilized. The recommended starting dose of metoprolol succinate extended-release tablets is 25 mg once daily for two weeks in patients with NYHA class II heart failure and 12.5 mg once daily in patients with more severe heart failure. The dose should then be doubled every two weeks to the highest dosage level tolerated by the patient or up to 200 mg of metoprolol succinate extended-release tablets. If transient worsening of heart failure occurs, it may be treated with increased doses of diuretics, and it may also be necessary to lower the dose of metoprolol succinate extended-release tablets or temporarily discontinue it. The dose of metoprolol succinate extended-release tablets should not be increased until symptoms of worsening heart failure have been stabilized. Initial difficulty with titration should not preclude later attempts to introduce metoprolol succinate extended-release tablets. If heart failure patients experience symptomatic bradycardia, the dose of metoprolol succinate extended-release tablets should be reduced.

Elderly patients and patients with renal or hepatic impairment

Dosage adjustment is not routinely required in the elderly or in patients with renal failure, but dosage may need to be reduced in patients with significant hepatic dysfunction when metoprolol elimination may be impaired.

4.3. Contra-indications

Metoprolol succinate extended-release tablets are contraindicated in:

- patients who are hypersensitive to any component of this product or any beta blocker
- severe bradycardia
- heart block greater than first degree
- cardiogenic shock

- decompensated cardiac failure
- sick sinus syndrome (unless a permanent pacemaker is in place)
- severe peripheral arterial disease

The drug is also contraindicated when myocardial infarction is complicated by significant bradycardia, first degree heart block, systolic hypotension (less than 100mm Hg) and/or severe heart failure.
hypotension (less than 100mm Hg) and/or severe heart failure.

4.4. Special Warnings and Special Precautions for Use

4.5. WARNINGS

Ischemic heart disease: Following abrupt cessation of therapy with certain beta-blocking agents, exacerbations of angina pectoris and, in some cases, myocardial infarction have occurred. When discontinuing chronically administered metoprolol succinate extended-release tablets, particularly in patients with ischemic heart disease, the dosage should be gradually reduced over a period of 1–2 weeks and the patient should be carefully monitored. If angina markedly worsens or acute coronary insufficiency develops, the drug should be reinstated promptly, at least temporarily, and other measures appropriate for the management of unstable angina should be taken. Patients should be warned against interruption or discontinuation of therapy without the physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue metoprolol succinate extended-release tablets abruptly even in patients treated only for hypertension.

Bronchospastic diseases: Patients with bronchospastic diseases should, in general, not receive beta-blockers. Because of metoprolol's relative $beta_1$-selectivity, however, metoprolol succinate extended release tablets may be used with caution in patients with bronchospastic disease who do not respond to, or cannot tolerate, other antihypertensive treatment. Since $beta_1$-selectivity is not absolute, a $beta_2$-stimulating agent should be administered concomitantly, and the lowest possible dose should be used.

Major surgery: The necessity or desirability of withdrawing beta-blocking therapy prior to major surgery is controversial; the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

Metoprolol, like other beta-blockers, is a competitive inhibitor of beta-receptor agonists, and its effects can be reversed by administration of such agents, eg, dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in restarting and maintaining the heart beat has also been reported with beta-blockers.

Diabetes and hypoglycemia: Metoprolol succinate extended-release tablets should be used with caution in diabetic patients. Beta-blockers may mask tachycardia

occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected.

Thyrotoxicosis: Beta-adrenergic blockade may mask certain clinical signs (eg, tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta blockade, which might precipitate a thyroid storm.
Peripheral vascular disease: Beta-blockers can precipitate or aggravate symptoms of arterial insufficiency in patients with peripheral vascular disease. Caution should be exercised in such individuals.
Calcium channel blockers: Because of significant inotropic and chronotropic effects in patients treated with beta-blockers and calcium channel blockers of the verapamil and diltiazem type, caution should be exercised in patients treated with these agents concomitantly.
Others: While taking beta-blockers, patients with a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated challenge, either accidental, diagnostic, or therapeutic. Such patients may be unresponsive to the usual doses of epinephrine used to treat allergic reaction.

PRECAUTION
Metoprolol succinate extended release tablets should be used with caution in patients with impaired hepatic function.
In patients with pheochromocytoma, an alpha-blocking agent should be initiated prior to the use of any beta-blocking agent.
Worsening cardiac failure may occur during up-titration of metoprolol succinate extended release tablets. If such symptoms occur, diuretics should be increased and the dose of the drug should not be advanced until clinical stability is restored. It may be necessary to lower the dose of metoprolol succinate extended release tablets or temporarily discontinue it.
Metoprolol succinate extended-release tablets may be administered under careful clinical observation when heart failure has been controlled. Digitalisation and/or loop diuretic therapy should also be considered for patients with a history of heart failure or patients known to have a poor cardiac reserve.

Metoprolol may aggravate bradycardia, symptoms of peripheral arterial circulatory disorders and anaphylactic shock. If the patient develops increasing bradycardia, the metoprolol should be given in lower doses or gradually withdrawn.
Metoprolol succinate extended-release tablets should be given cautiously to patients with metabolic acidosis.
The drug should be given with caution, if at all, in patients with AV conduction defects.
The drug should be used with extreme caution in patients with substantial cardiomegaly.
As with all antihypertensive agents, a cautious dosage schedule is indicated in patients with severe coronary or cerebral arteriosclerosis.
Metoprolol succinate extended-release tablets therapy should be brought to the attention of the anaesthetist prior to general anaesthesia. In a

patient under beta blockade, the anaesthetic selected should be one exhibiting as little negative inotropic activity as possible (halothane/nitrous oxide).

Effect on ability to drive and use machines: In individual cases, as a result of a reduction in blood pressure, treatment with metoprolol succinate extended-release tablets may affect the ability to drive and operate machinery. This occurs especially at the start of treatment, when changing over from other preparations and during concomitant use of alcohol.
Patients should be advised to avoid operating automobiles and machinery or engaging in other tasks requiring alertness until the patient's response to therapy with metoprolol succinate extended-release tablets has been determined.
Patients should be warned of the potential hazards of driving or operating machinery if they experience side effects such as dizziness.

Usage in pregnancy and lactation
There are no adequate and well controlled studies in pregnant women. Metoprolol succinate extended-release tablets should be used during pregnancy only if clearly needed.
Metoprolol is excreted in breast milk in very small quantities. An infant consuming 1 liter of breast milk daily would receive a dose of less than 1 mg of the drug.

Caution should be exercised when metoprolol succinate extended-release tablets are administered to a nursing woman.

Usage in paediatrics
Studies are available on the use of metoprolol succinate extended-release tablets in paediatric hypertensive patients aged 6 to 16 years. Safety and effectiveness of the drug have not been established in patients < 6 years of age.

Usage in geriatrics
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy.

4.5. Interaction with other Medicinal Products and other forms of Interaction When metoprolol is administered with diuretic or other hypotensive drugs, the hypotensive effect of metoprolol may be increased. Catecholamine-depleting drugs (eg, reserpine, mono amine oxidase (MAO) inhibitors) may have an additive effect when given with beta-blocking agents. Patients treated with metoprolol succinate extended-release tablets plus a catecholamine depletor should therefore be closely observed for evidence of hypotension or marked bradycardia, which may produce vertigo, syncope, or postural hypotension.
Drugs that inhibit CYP2D6 such as quinidine, fluoxetine, paroxetine, and propafenone are likely to increase metoprolol concentration. These increases in plasma concentration would decrease the cardioselectivity of metoprolol.
Both digitalis glycosides and beta blockers slow atrioventricular conduction and decrease heart rate. Concomitant use can increase the risk of bradycardia.
Beta-blockers may exacerbate the rebound hypertension which can follow the withdrawal
of clonidine. If the two drugs are coadministered, metoprolol succinate extended-release tablets should be withdrawn several days before the gradual withdrawal of clonidine. If replacing clonidine by metoprolol therapy, the introduction of metoprolol should be delayed for several days after clonidine administration has stopped.

The administration of adrenaline to patients undergoing beta blockade can result in an increase in blood pressure and bradycardia although this is less likely to occur with beta1 selective drugs.
Metoprolol can reduce myocardial contractility and impair intracardiac conduction. Care should be exercised when drugs with similar activity e.g. antiarrhythmic agents (amiodarone), general anaesthetics are given concurrently.
Like all other beta blockers, metoprolol should not be given in combination with verapamil since this may cause bradycardia, hypotension and asystole.

Care should also be exercised when metoprolol succinate extended-release tablets are given in combination with sympathetic ganglion blocking agents, other beta blockers (also in the form of eye drops) or MAO inhibitors.
As beta blockers may affect the peripheral circulation, care should be exercised when drugs with similar activity e.g. ergotamine are given concurently.
Metoprolol will antagonise the beta1 effects of sympathomimetic agents but should have little influence on the bronchodilator effects of beta1-agonists at normal therapeutic doses.
Enzyme inducing agents (e.g. rifampicin) may reduce plasma concentration of metoprolol, whereas enzyme inhibitors (e.g. cimetidine) may increase plasma concentrations.
During concomitant ingestion of alcohol and metoprolol the concentration of blood alcohol may reach higher levels and may decrease more slowly.
Metoprolol may impair the elimination of lignocaine.
Indomethacin may reduce the antihypertensive effect of beta blockers.
Nitroglycerin may enhance the hypotensive effect of metoprolol succinate extended-release tablets.
The dosage of oral antidiabetic agents and also of insulin may have to be readjusted in patients receiving beta blockers.
The acute postural hypotension that can follow the first dose of prazosin may be increased in patients already taking a beta blocker.
Administration of a beta-adrenergic blocker with a vasodilator, such as hydralazine, in patients with uremia could cause pulmonary hypertension

secondary to beta adrenergic blockade of the pulmonary vasculature and to the increased cardiac output caused by the vasodilator.

4.7 Effects on Ability to Drive and Use Machines

Effect on ability to drive and use machines: In individual cases, as a result of a reduction in blood pressure, treatment with metoprolol succinate extended-release tablets may affect the ability to drive and operate machinery. This occurs especially at the start of treatment, when changing over from other preparations and during concomitant use of alcohol.

Patients should be advised to avoid operating automobiles and machinery or engaging in other tasks requiring alertness until the patient's response to therapy with metoprolol succinate extended-release tablets has been determined.

Patients should be warned of the potential hazards of driving or operating machinery if they experience side effects such as dizziness.

4.8 ADVERSE REACTIONS

Most adverse effects have been mild and transient**.** The following adverse reactions have been reported for immediate release metoprolol tartrate, metoprolol succinate and in post marketing experience:

Central Nervous System*:* Tiredness, dizziness, vertigo, reversible mental depression progressing to catatonia, mental confusion, short-term memory loss, anxiety/nervousness, hallucinations, paresthesia, headache, somnolence, nightmares, insomnia, an acute reversible syndrome characterized by disorientation for time and place, emotional lability, cerebrovascular disorder, slightly clouded sensorium, and decreased performance on neuropsychometrics

Cardiovascular*:* Shortness of breath and bradycardia, intensification of AV block, 2nd and 3rd degree heart block, cold extremities, arterial insufficiency, usually of the Raynaud type, palpitations, cardiogenic shock, congestive heart failure, peripheral edema, myocardial infarction, syncope, aggravated ventricular tachycardia/arrhythmia, chest pain, coronary artery disorder and hypotension ***Respiratory****:* Wheezing (bronchospasm), pneumonia and dyspnea ***Gastrointestinal****:* Diarrhea, nausea, dry mouth, gastric pain, constipation, flatulence, digestive tract disorders, hepatitis, abdominal pain, vomiting and heartburn

Hematologic*:* Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura and thrombocytopenia.

Hypersensitive reactions*:* Fever combined with aching and sore throat, laryngospasm, respiratory distress, pruritus or rash and worsening of psoriasis ***Musculoskeletal****:* arthralgia, musculoskeletal pain, fatigue

Reproductive*:* impotence, decreased libido

Skin*:* increased sweating, photosensitivity, urticaria

Special sense organs*:* taste disturbances, blurred vision, dry eyes and

tinnitus ***Miscellaneous****:* Peyronie's disease, reversible alopecia, diabetes mellitus or aggravated diabetes mellitus

Laboratory Tests

Clinical laboratory findings may include elevated levels of serum transaminase, alkaline phosphatase, and lactate dehydrogenase.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after Authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org/

4.9 Overdose

There have been a few reports but no specific information on overdosage with extended-release Metoprolol succinate.

Overdosage of extended-release Metoprolol succinate may lead to severe hypotension, sinus bradycardia, atrioventricular block, heart failure, cardiogenic shock, cardiac arrest, bronchospasm, impairment of consciousness/coma, nausea, vomiting, and cyanosis.

In general, patients with acute or recent myocardial infarction or congestive heart failure may be more hemodynamically unstable than other patients and should be treated accordingly. When possible, the patient should be treated under intensive care conditions.

On the basis of the pharmacologic actions of metoprolol, the following general measures should be employed:

***Elimination of the drug*:** Gastric lavage should be performed.

***Bradycardia*:** Atropine should be administered. If there is no response to vagal blockade, isoproterenol should be administered cautiously.

***Hypotension*:** A vasopressor should be administered, eg, levarterenol or dopamine.

***Bronchospasm*:** A beta2-stimulating agent and/or a theophylline derivative should be administered.
***Cardiac failure*:** A digitalis glycoside and diuretics should be administered. In shock resulting from inadequate cardiac contractility, administration of dobutamine, isoproterenol, or glucagon may be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMICS

Metoprolol is β-1-selective (cardioselective) adrenergic receptor blocking agent. This preferential effect is not absolute, however, and at higher plasma concentrations, metoprolol also inhibits2-adrenoreceptors, chiefly located in the bronchial and vascular musculature. Metoprolol has no intrinsic sympathomimetic activity, and membrane-stabilizing activity is detectable only at plasma concentrations much greater than required for betablockade. It is moderately lipid soluble. Animal and human experiments indicate that metoprolol slows the sinus rate and decreases AV nodal conduction.
Clinical pharmacology studies have confirmed the beta-blocking activity of metoprolol in man, as shown by (1) reduction in heart rate and cardiac output at rest and upon exercise, (2) reduction of systolic blood pressure upon exercise, (3) inhibition of isoproterenol-induced tachycardia, and (4) reduction of reflex orthostatic tachycardia.

Hypertension

Metoprolol decreases blood pressure in both supine and standing positions. The mechanism of the antihypertensive effects of beta-blocking agents has not been elucidated. However, several possible mechanisms have been proposed: (1) competitive antagonism of catecholamines at peripheral (especially cardiac) adrenergic neuron sites, leading to decreased cardiac output; (2) a central effect leading to reduced sympathetic outflow to the periphery; and (3) suppression of renin activity.

Angina Pectoris

By blocking catecholamine-induced increases in heart rate, in velocity and extent of myocardial contraction, and in blood pressure, metoprolol reduces the oxygen
requirements of the heart at any given level of effort, thus making it useful in the long-term management of angina pectoris.

Heart Failure

The precise mechanism for the beneficial effects of beta-blockers in heart failure has not been elucidated.

5.2. PHARMACOKINETICS

In man, absorption of metoprolol is rapid and complete. Plasma levels following oral administration of conventional metoprolol tablets, however, approximate 50% of levels following intravenous administration, indicating about 50% first-pass metabolism. The bioavailability of metoprolol is not significantly affected by food following extended release

metoprolol succinate administration.
In comparison to conventional metoprolol, the plasma metoprolol levels following administration of extended release metoprolol succinate are characterized by lower peaks, longer time to peak and significantly lower peak to trough variation.
Metoprolol crosses the blood-brain barrier. Only a small fraction of the drug (about 12%) is bound to human serum albumin. Metoprolol is metabolized predominantly by CYP2D6. CYP2D6 can be inhibited by a number of drugs. Concomitant use of inhibiting drugs in poor metabolizers will increase blood levels of metoprolol several-fold, decreasing metoprolol's cardioselectivity.
Elimination is mainly by biotransformation in the liver, and the plasma half-life ranges from approximately 3 to 7 hours. Less than 5% of an oral dose of metoprolol is recovered unchanged in the urine; the rest is excreted by the kidneys as metabolites that appear to have no beta-blocking activity. The systemic availability and half-life of metoprolol in patients with renal failure do not differ to a clinically significant degree from those in normal subjects.

5.3. Preclinical Safety Data
Not applicable.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients

Microcrystalline Cellulose
Carbomer 941 (Carbopol 71 G)
Hypermellose (Methocel K 15 M premium)
Isopropyl Alcohol
Povidone (PVPK – 30)
Magnesium Stearate

6.1 Incompatibilities
None known

6.2 Shelf Life
24 months

6.3 Special Precautions for

Storage Store below 25^{o}C, in a dry place.

6.4 Nature and Contents of Container
Blister Strip of 10 Tablets
3 such Blister Strips are packed in a printed showbox.

7.0 Market authorisation holder
Ipca Laboratories Ltd
48, Kandivli Industrial Estate,
Kandivli (West) Mumbai 400 067, India.

8. Market authorisation number
H2008/19181/870/R1

9. Date of registration/renewal of registration
17/01/2026

10. Date of revision of the text.
22/08/2026