Product Monograph

Including Patient Medication Information

[Pr]Labetalol Hydrochloride Injection in 5% Dextrose

Labetalol hydrochloride

Solution

For intravenous (IV) use

1 mg / mL (Ready to use, 200 mL bag)

[Pr]Labetalol Hydrochloride Injection in 0.72% Sodium Chloride

Labetalol hydrochloride

Solution

For intravenous (IV) use

1 mg / mL (Ready to use, 100 mL bag, 200 mL bag and 300 mL bag)

Antihypertensive Agent

Hikma Canada Ltd.,

5995 Avebury Road, Suite 804

Mississauga, ON

Canada L5R 3P9

Date of Revision:
APR 24, 2025

Control Number: 276831

Recent Major Label Changes

Not applicable	Not applicable

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Health Professional Information

1. Indications

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride is indicated for the emergency treatment of severe hypertension when prompt and urgent reduction of blood pressure is essential.

1.1. Pediatrics (< 18 years of age)

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2. Geriatrics

Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness. Lower doses of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride are likely to be required in elderly patients, see 7.1.4 Geriatrics and 4.2 Recommended Dose and Dosage Adjustment, Geriatric patients

2. Contraindications

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride is contraindicated in patients:

- who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient or component of the container. For a complete listing, See 6 Dosage Forms, Strengths, Composition and Packaging
- exhibiting sinus bradycardia or sick sinus syndrome.
- with uncontrolled congestive heart failure.
- with cardiogenic shock and states of hypoperfusion.
- with asthma or a history of obstructive lung disease.
- with greater than first degree atrioventricular (AV) block.
- with severe peripheral arterial circulatory disorders

3. Serious Warnings and Precautions Box

Severe hepatocellular injury

- Injury has occurred after both short term and long-term treatment with labetalol hydrochloride and may be slowly progressive despite minimal symptomatology. The hepatic injury is usually reversible but rare cases of hepatic necrosis and death have been reported. (see 7 Warnings and Precautions, Hepatic/Biliary/Pancreatic and Monitoring and Laboratory Tests).

4. Dosage and Administration

4.1. Dosing Considerations

Labetalol HCl in Sodium Chloride Injection and Labetalol HCl in Dextrose Injection are ready-to-use solutions and do not require further dilution.

The administration of intravenous Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol

Hydrochloride Injection in 0.72% Sodium Chloride should be restricted to hospitalized patients. Dosage must be individualized according to the patient's weight, the severity of their hypertension and to their response during dosing.

Patients should be kept supine during the period of intravenous drug administration because a substantial fall in blood pressure on standing may be anticipated in these patients. The patient's ability to tolerate the upright position (e.g. use of toilet facilities) should be established prior to them getting up, especially within the three hours post-infusion.

The blood pressure should be monitored prior, during and after completion of the infusion. Rapid or excessive falls in either systolic or diastolic blood pressure during intravenous treatment should be avoided. In patients with excessive systolic hypertension, the decrease in systolic pressure should be used as an indicator of effectiveness in addition to the response of the diastolic pressure.

4.2. Recommended Dose and Dosage Adjustment

Slow Continuous Infusion

- To gradually reduce blood pressure, slowly drip solution into the vein
- The amount of solution required will be determined by the response during dosing and may be adjusted until the optimal blood pressure is achieved.

1. To reduce high blood pressure in pregnancy

   - Administer 20 mg of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride over 60 minutes
   - The dose may then be doubled every 30 minutes until blood pressure has been reduced or the dose has reached 160 mg per hour
   - A higher dose may be used occasionally if the potential benefits justifies the potential risk to the fetus.

2. To reduce high blood pressure after a heart attack

   - Administer 15 mg of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride, injection over 60 minutes
   - The dose may then be gradually increased up to a maximum of 120 mg per hour if needed.

3. To reduce high blood pressure for other reasons such as severe hypertension

   - Administer 2 mg/min of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride, injection until blood pressure has reached 95 mmHg.
   - The total dose given is usually between 50 mg and 200 mg. Higher doses up to 300 mg may be used when lower doses are not effective.

In case when high blood pressure needs to be reduced in cases other than after a heart attack or during a pregnancy, the rate of infusion may be adjusted downward according to the patient's age, weight, health, the severity of hypertension, prior therapy, and their response during treatment. To facilitate a desired rate

of infusion, the diluted solution can be infused using a controlled administration mechanism, e.g. graduated burette or mechanically driven infusion pump.

Since the half-life of labetalol hydrochloride is 5 to 8 hours, steady-state blood levels (in the face of a constant rate of infusion) would not be reached during the usual infusion time period. The infusion should be continued until a satisfactory response is obtained and should then be stopped and oral medication started when it has been established that the supine diastolic blood pressure has begun to rise. The effective intravenous dose is usually in the range of 50 to 200 mg. A total dose of up to 300 mg may be required in some patients.

Geriatric Patients: Lower doses of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride are likely to be required in elderly patients (see 7 Warnings and Precautions, Special Populations). Close monitoring and strict observation of adverse reactions are recommended during and after the administration of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride.

Pediatrics: Health Canada has not authorized an indication for pediatric use.

Hepatic Impairment: Patients with liver function impairment may require lower doses since metabolism of the drug may decrease in these patients (see 7 Warnings and Precautions, Special Populations).

4.4. Administration

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should be administered by a slow continuous infusion.

Dosing of labetalol hydrochloride should be limited to a maximum of 300 mg.

Labetalol HCl in Sodium Chloride Injection and Labetalol HCl in Dextrose Injection are ready-to-use solutions and do not require further dilution. Check for leaks by squeezing the bag firmly. If leaks are found, discard the solution, as sterility may be impaired. Do not add any additional medications to the bag.

Once infusion has finished discard any remaining solution at 24 hours.

5. Overdose

Symptoms
The signs and symptoms associated with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride overdosage are excessive hypotension which is posture-sensitive, and sometimes, excessive bradycardia.

Treatment
Patients should be laid supine and their legs raised, if necessary. Hemodialysis removes less than 1% of circulating labetalol, and is therefore not recommended as a method to manage overdoses.

If overdose occurs, provide general supportive and specific symptomatic treatment. Based on expected pharmacologic actions and recommendations for other beta-blockers, the following additional measures should be employed if necessary, including stopping Labetalol Hydrochloride Injection in 5% Dextrose and

Labetalol Hydrochloride Injection in 0.72% Sodium Chloride when clinically warranted;

- **Excessive Bradycardia**: Administer atropine intravenously to induce vagal blockage. If bradycardia persists, isoproterenol may be administered cautiously. In refractory cases, the use of a cardiac pacemaker may be considered.
- **Congestive Heart Failure**: Conventional therapy with cardiac glycosides and diuretics.
- **Hypotension**: Administer vasopressors, e.g. norepinephrine.
- **Bronchospasm**: Administer a $beta_2$-stimulating agent and/or a theophylline preparation.
- **Heart block (second or third degree):** Monitor and treat with isoproterenol infusion. Under some circumstances, transthoracic or transvenous pacemaker placement may be necessary.
- **Hypoglycemia:** Administer intravenous glucose. Repeated dose of intravenous glucose or possibly glucagon may be required.

Oliguric renal failure has been reported after massive overdosage of labetalol hydrochloride orally. In one case, the use of dopamine to increase blood pressure may have aggravated the renal failure.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

Table 1– Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form / Strength /Composition	Non-medicinal Ingredients
Intravenous Infusion	Solution,1 mg / mL, Labetalol Hydrochloride in 5% dextrose	Dextrose anhydrous, disodium edetate, citric acid and/or sodium hydroxide to adjust pH, and water for injection.
Intravenous Infusion	Solution,1 mg / mL, Labetalol Hydrochloride in 0.72% Sodium Chloride	Sodium chloride, anhydrous dextrose, disodium edetate, citric acid and/or sodium hydroxide to adjust pH, and water for injection.

Labetalol Hydrochloride Injection in 5% Dextrose: Each mL contains: labetalol hydrochloride 1 mg, dextrose anhydrous 45 mg, disodium edetate 0.02 mg, monohydrate citric acid and/or sodium hydroxide to adjust pH, and water for injection.

Labetalol Hydrochloride Injection in 5% Dextrose, 1 mg/mL, is available in 200 mL bags boxes of 10.

Labetalol Hydrochloride Injection in 0.72% Sodium Chloride: Each mL contains 1 mg of labetalol Hydrochloride, 7.2 mg sodium chloride, 9 mg of anhydrous dextrose, 0.02 mg of edetate disodium; and citric acid monohydrate and sodium hydroxide, to adjust pH, and water for injection.

Labetalol Hydrochloride Injection in 0.72% Sodium Chloride is available as 1 mg/mL in 100, 200, or 300 mL bags. Box of 10 bags.

7. Warnings and Precautions

General
Symptomatic postural hypotension is likely to occur if patients are tilted or allowed to assume the upright position within 3 hours of receiving Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride. Patients should be kept in a supine position during the period of intravenous drug administration because a substantial fall in blood pressure on standing may be anticipated in these patients. The patient's ability to tolerate the upright position should be established before permitting any ambulation (see 4.1 Dosing Considerations).

Cardiovascular

Cardiac Failure
Cardiac failure should be controlled with digitalis and diuretics before labetalol hydrochloride treatment is initiated. Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should not be given to patients with digitalis-resistant heart failure. Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure and inhibition with beta-blockade always carries the potential hazard of further depressing myocardial contractibility and precipitating cardiac failure. A few patients developed heart failure while on labetalol hydrochloride. Therefore, administration of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride to patients with controlled failure or those likely to develop such failure, must be carried out under careful supervision. The drug does not abolish the inotropic action of digitalis on heart muscle.

Sinus Bradycardia
Severe sinus bradycardia may occur with the use of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride from unopposed vagal activity remaining after blockade of $beta_1$-adrenergic receptors; in such cases, dosage should be reduced.

Severe Peripheral Artery Disorders
Beta-blockers may aggravate the symptoms of severe peripheral arterial circulatory disorders, mainly due to their blood pressure lowering effect. Caution should be exercised in individuals with such disorders.

Non-dihydropyridine Calcium Channel Blockers

The combination of non-dihydropyridine calcium channel blockers of the verapamil and diltiazem type and beta-blockers warrants caution since additive effects on myocardial contractility, heart rate and AV conduction have been observed. Close medical supervision is recommended (see 9 Drug Interactions).

Endocrine and Metabolism

Diabetes and Hypoglycemia
Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should be used with caution in patients subject to hypoglycemic episodes since beta-receptor blocking drugs may mask some of the manifestations of hypoglycemia, particularly tachycardia and may

enhance hypoglycemia in patients prone to this condition.

Also, diabetics on insulin or oral hypoglycemic medication may have an increased tendency towards hypoglycemia when treated with these drugs. Patients subject to spontaneous hypoglycemia and diabetic patients receiving insulin or oral hypoglycemic agents should be advised about these possibilities.

Thyrotoxicosis
In patients with thyrotoxicosis, possible deleterious effects from long-term use of labetalol hydrochloride have not been adequately appraised. Beta-blockade may mask the clinical signs of continuing hyperthyroidism or complications, and give a false impression of improvement.
Therefore, these patients should be carefully monitored for thyroid function. Abrupt withdrawal of labetalol hydrochloride may be followed by an exacerbation of the symptoms of hyperthyroidism, or may precipitate a thyroid storm.

Pheochromocytoma
While labetalol hydrochloride has been shown to be effective in lowering the blood pressure and relieving symptoms in patients with pheochromocytoma, paradoxical hypertensive responses have been reported in a few patients with this tumour. Use caution when administering Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride to patients with known or suspected pheochromocytoma.

Hepatic/Biliary/Pancreatic

There have been rare reports of severe hepatocellular injury with labetalol hydrochloride therapy. Injury has occurred after both short term and long term treatment and may be slowly progressive despite minimal symptomatology. The hepatic injury is usually reversible but rare cases of hepatic necrosis and death have been reported. Appropriate laboratory testing should be performed at regular intervals during labetalol hydrochloride therapy. Tests should also be done at the first sign or symptom of liver dysfunction (eg., pruritus, dark urine, persistent anorexia, jaundice, right upper quadrant tenderness or unexplained flu-like symptoms). If there is laboratory evidence of liver injury or the patient is jaundiced, Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should be stopped and not restarted.

Hepatic impairment: Patients with liver function impairment will likely require lower doses since metabolism of the drug will be diminished (see 4 Dosage and Administration).

Immune

Risk of Anaphylactic Reactions
While taking beta-blockers, patients with a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge. There may be increased difficulty in treating an allergic-type reaction in patients on beta- blockers. In these patients, the reaction may be more severe due to pharmacological effects of beta-blockers and problems with fluid changes. Epinephrine should be administered with caution since it may not have its usual effects in the treatment of anaphylaxis. On the one hand, larger doses of epinephrine may be needed to overcome the bronchospasm, while on the other, these doses can be associated with excessive alpha adrenergic stimulation with consequent hypertension, reflex bradycardia and heart block and possible potentiation of bronchospasm. Alternatives to the use of large doses of epinephrine include vigorous supportive care such as fluids and the use of beta agonists, including parenteral salbutamol or isoproterenol to overcome bronchospasm and norepinephrine to overcome hypotension.

Monitoring and Laboratory Tests
Appropriate liver function laboratory testing should be performed at regular intervals during Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride therapy (see 7 warnings and Precautions, Hepatic/Biliary/Pancreatic section).

Bronchospastic Diseases
Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should not be used in patients with asthma or a history of obstructive airway disease unless there is no suitable alternative treatment available. In such cases, the risk of inducing bronchospasm should be appreciated, therefore, careful monitoring of patients is mandatory and bronchodilators should be used concomitantly. In patients already on therapy, the dose of bronchodilators may have to be increased. In spite of these precautions the patient's respiratory status may worsen, and in such cases Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should be discontinued. If bronchospasm should occur after the use of labetalol hydrochloride, it can be treated with a $beta_2$- adrenergic receptor stimulant by inhalation, e.g. salbutamol (the dose of which may need to be greater than the usual dose in asthma), and, if necessary, intravenous atropine 1 mg.

Cerebral Hypoperfusion
During treatment with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride, signs of cerebral hypoperfusion may occur if blood pressure is reduced too rapidly. Signs include: confusion, somnolence, lightheadedness, dizziness, nausea, vomiting, pallor, sweating, blurred vision, headache, hallucinations and loss of consciousness. Symptoms and signs of myocardial hypoperfusion include chest pain and ischemic changes in the electrocardiogram. Although they have not been seen with the use of intravenous labetalol hydrochloride, a number of other adverse reactions including cerebral infarction and optic nerve infarction have been reported with other agents when severely elevated blood pressure was reduced over time-courses of several hours to as long as 1 or 2 days. The desired blood pressure lowering should therefore be achieved over as long a period of time as is compatible with the patient's status.

Ophthalmologic
Animal studies have shown that labetalol binds to the melanin of the uveal tract. The significance of this in humans is not known but periodic ophthalmic examinations are advisable while the patient is taking labetalol hydrochloride.

Peri-Operative Considerations

In patients undergoing surgery: The management of patients being treated with beta-blockers and undergoing surgery is controversial. Although beta-adrenergic-receptor blockade impairs the ability of the heart to respond to beta-adrenergically mediated reflex stimuli, abrupt discontinuation of therapy with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride may be followed by severe complications (see 7 Warnings and Precautions). Some patients receiving beta- adrenergic-blocking agents have been subject to protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients with angina undergoing elective surgery, Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should be withdrawn gradually following the recommendation given under "Abrupt Cessation of Therapy" (see 7 Warnings and Precautions).

In emergency surgery, since labetalol hydrochloride is a competitive inhibitor of beta-adrenergic- receptor

agonists, its effects may be reversed, if necessary, by sufficient doses of such agonists as isoproterenol.

Skin

Oculomucocutaneous Syndrome
Various skin rashes and conjunctival xerosis have been reported with beta-blockers. A severe syndrome (oculomucocutaneous syndrome) whose signs include conjunctivitis sicca and psoriasiform rashes, otitis, and sclerosing serositis has occurred with the chronic use of one beta- adrenergic blocking agent (practolol). This syndrome has not been observed in association with labetalol hydrochloride or any other such agent. However, physicians should be alert to the possibility of such reactions and should discontinue treatment in the event that they occur.

7.1. Special Populations

7.1.1. Pregnant Women

Although no teratogenic effects were seen in animal testing, the safety of the use of labetalol hydrochloride during pregnancy has not been established. Labetalol crosses the placental barrier in women and has been found to bind to the eyes of fetal animals. Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride should be used in pregnant women only if the expected benefit to the mother justifies the potential risk to the fetus.

7.1.2. Nursing Women

Labetalol has been found in the breast milk of lactating women. If the use of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride is considered essential, then mothers should stop nursing.

7.1.3. Pediatrics (< 18 years of age)

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4. Geriatric patients
The hypotensive response is greater in elderly following oral or intravenous administration. Therefore, lower doses of Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride are likely to be required in elderly patients (see 4 Dosage and Administration).

8. Adverse Reactions

8.1. Adverse Drug Reaction Overview

The most serious reported adverse effects of labetalol hydrochloride are severe postural hypotension, jaundice and bronchospasm.

8.2. Clinical Trial Adverse Drug Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions

observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

In well controlled clinical trials, the most common transient adverse reactions reported at routinely administered therapeutic doses, were postural hypotension and/or dizziness (16.9%), fatigue/malaise (13.1%), and headache (8.0%). Other transient effects include acute retention of urine and difficulty in micturition. The following summarizes the adverse effects reported.

Cardiovascular: Postural hypotension/dizziness (16.9%), angina pectoris (3.2%), Raynaud's phenomenon (3.2%), pedal edema (1.9%), palpitations (1.3%), bradycardia (<1%).

Gastrointestinal: Nausea/vomiting (6.1%), dyspepsia (1.9%) , constipation (1.6%), dry mouth/sore throat (1.6%).

Respiratory: Dyspnea (3.8%), nasal congestion (1.3%).

Dermatological: Drug rash (3.2%), paresthesia (especially "scalp tingling") (3.8%), pruritus (0.6%) and angioedema.

Urogenital: Impotence (2.2%), failure of ejaculation (0.6%), dysuria (0.6%).

Musculoskeletal: Aches/pains (3.5%), muscle cramps (1.3%).

Central Nervous System: Fatigue/malaise (13.1%), headache (8.0%), depression (2.6%), loss of libido (1.3%), dreaming (1.3%).

Miscellaneous: Visual blurring (4.2%), epistaxis (1.6%).

In addition, in the more extensive trials, bronchospasm and severe bradycardia were reported with an incidence of less than 1%. There are rare reports of raised liver function tests, jaundice (both hepatic and cholestatic), and hepatic necrosis (see 7 Warnings and Precautions, Hepatic/Biliary/Pancreatic).

8.4. Abnormal Hematologic and Clinical Chemistry Findings

Elevations of BUN and serum creatinine following bolus injections were reported in 6.8% of patients.

8.5. Post-Market Adverse Drug Reactions

Other published or unpublished reports describe other rare, isolated adverse events in patients who were taking labetalol hydrochloride (oral or injectable), as follows: bronchospasm and reduction in peak expiratory flow rate (PEFR), difficulty in micturition including acute urinary retention, ejaculatory failure, Peyronie's disease, toxic myopathy, tremor, taste distortion, hypersensitivity, hypoesthesia, rashes of various types such as generalized maculopapular, lichenoid, urticarial, bullous lichen planus, psoriasiform, facial erythema, reversible alopecia and very rarely drug fever. A skin lesion resembling disseminated lupus erythematosus occurred rarely in one patient receiving a high dose of labetalol hydrochloride. There are rare reports of patients who developed lupus-like syndromes while on labetalol hydrochloride which cleared upon discontinuation of treatment. Positive antinuclear factor and antimitochondrial antibodies have been reported in patients receiving the drug, but the significance of these findings is not clear.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always

possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

9. Drug Interactions

9.2. Drug Interactions Overview

Care should be taken if Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride is used concomitantly with either Class I antiarrhythmic agents or calcium antagonists of the verapamil class since these drugs may potentiate the cardiac depressant activities of labetalol hydrochloride (see 7 Warnings and Precautions, Cardiovascular).

When used with diuretics and/or other antihypertensive agents the dose of labetalol hydrochloride must be appropriately adjusted (see 4 Dosage and Administration).

9.4. Drug-Drug Interactions

Halothane: Labetalol hydrochloride and halothane have additive hypotensive effects. High doses of halothane (3%) with labetalol hydrochloride predispose the patient to the myocardial depressant effects of halothane and an undesirable reduction in myocardial performance. The anesthesiologist should be informed when a patient is receiving labetalol hydrochloride.

Nitroglycerin: Labetalol hydrochloride blunts the reflex tachycardia produced by nitroglycerin without preventing its hypotensive effect. When labetalol hydrochloride is used with nitroglycerin in patients with angina pectoris, additional antihypertensive effects may occur.

Tricyclic antidepressants: In one survey, 2.3% of patients taking labetalol hydrochloride in combination with tricyclic antidepressants experienced tremor as compared to 0.7% reported to occur with labetalol hydrochloride alone. The contribution of each of the treatments to this adverse reaction is unknown, but the possibility of a drug interaction cannot be excluded.

Fingolimod: Concomitant use of fingolimod with beta blockers may potentiate bradycardic effects and is not recommended. Where such co-administration is considered necessary, appropriate monitoring at treatment initiation, i.e. at least overnight monitoring, is recommended.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7. Drug-Laboratory Test Interactions

The presence of a metabolite of labetalol hydrochloride in the urine may result in falsely elevated levels of urinary catecholamines when measured by a nonspecific trihydroxyindole (THI) reaction. In screening patients suspected of having a pheochromocytoma and being treated with labetalol hydrochloride, specific radioenzymatic or high performance liquid chromatographic assay techniques should be used to determine levels of catecholamines or their metabolites.

10. Clinical Pharmacology

10.1. Mechanism of Action

Labetalol Hydrochloride is an adrenergic receptor blocking agent possessing both alpha$_1$ (post-synaptic) and beta-receptor blocking activity. Its action on beta-receptors is four times stronger than that on alpha-receptors. It antagonizes beta$_1$- and beta$_2$-receptors equally.

The mechanism of the antihypertensive action of labetalol has not been fully established. It is considered that labetalol lowers blood pressure by partially blocking the alpha-adrenoreceptors in the peripheral arterioles, thus causing vasodilation and a resulting reduction of peripheral resistance. At the same time, blockade of the beta-adrenoreceptors in the myocardium prevents reflex tachycardia and subsequent elevation of cardiac output. Peripheral vasodilation is achieved with incomplete blockade of alpha-adrenoreceptors in the arterioles and the barostatic reflexes remain sufficiently active to reduce the incidence of postural hypotension.

10.2. Pharmacodynamics

At rest, labetalol slightly reduces the heart rate, increases the stroke volume but does not significantly affect cardiac output. It reduces exercise-induced increases in systolic pressure and heart rate, again without significantly influencing cardiac output.

Following oral administration to hypertensive patients, labetalol decreases plasma renin activity and aldosterone levels, both at rest and during exercise, particularly when these were elevated prior to treatment. Labetalol is significantly more efficacious in hypertensive patients with high baseline plasma noradrenaline levels.

Following a bolus intravenous injection, the maximum antihypertensive effect occurs within 5 to 10 minutes in the majority of patients. However, in some patients the peak effect occurs considerably later.

10.3. Pharmacokinetics

Distribution: Rapid and extensive distribution within tissue compartments occurs after intravenous administration. The drug is approximately 50% bound to plasma proteins.

Metabolism: Labetalol is metabolized mostly by conjugation with glucuronic acid; the resulting metabolite is inactive.

Excretion: Labetalol and its metabolites are rapidly excreted in urine, and *via* bile into the feces. The plasma half-life of labetalol is approximately 5.5 hours after intravenous administration.

11. Storage, Stability and Disposal

Store between 15°C and 30°C in the original marketing pack to protect from light. Do not freeze.

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride: Do not remove from overwrap until ready to use.

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium

Chloride are preservative-free, clear, colorless to light yellow sterile solutions that are available in a single-dose single-port bag with an aluminum overwrap. The container closure is not made with natural rubber latex. It is available in the following presentations.

Product Name	Strength
Labetalol Hydrochloride Injection in 5% Dextrose	200 mg/200 mL (1 mg/mL) preservative-free
Labetalol Hydrochloride Injection in 0.72% Sodium Chloride	100 mg/100 mL (1 mg/mL) preservative-free
Labetalol Hydrochloride Injection in 0.72% Sodium Chloride	200 mg/200 mL (1 mg/mL) preservative-free
Labetalol Hydrochloride Injection in 0.72% Sodium Chloride	300 mg/300 mL (1 mg/mL) preservative-free

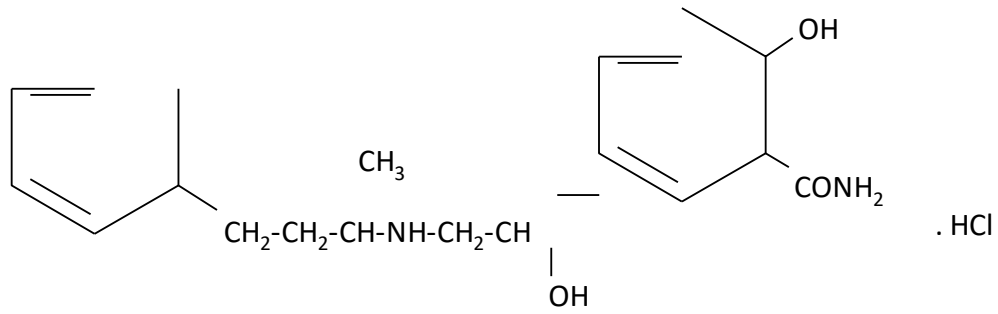
Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Non-proprietary name of the drug substance(s):	labetalol hydrochloride
Chemical Name:	2-hydroxy-5-[1-hydroxy-2-[(1-methyl-3-phenylpropyl)amino]ethyl] benzamide hydrochloride.
Molecular Formula:	$C_{19}H_{24}N_2O_3 \bullet HCl$
Molecular Weight:	364.9 g/mol

Structural Formula:



Physicochemical properties:	Labetalol hydrochloride is a white to off-white powder with a melting point around 180°Cwith decomposition.
Solubility:	Labetalol hydrochloride is soluble in water and in alcohol; itis insoluble in ether and methylene chloride.
pH:	The pH of a 1% w/v solution of labetalol hydrochloride is between 4.0- 5.0.

14. Clinical Trials

14.1. Clinical Trials by Indication

In a clinical pharmacologic study in severe hypertensives, an initial 0.25 mg/kg injection of labetalol administered to patients in the supine position decreased blood pressure by an average of 11/7 mmHg. Additional injections of 0.5 mg/kg at 15 minute intervals up to a total cumulative dose of 1.75 mg/kg of labetalol caused further dose-related decreases in blood pressure. Some patients required cumulative doses of up to 3.25 mg/kg. The maximal effect of each dose level occurred within 5 minutes. Following discontinuation of intravenous treatment with labetalol, the blood pressure rose gradually and progressively, approaching pretreatment baseline values within an average of 16 to 18 hours in the majority of patients.

Similar results were obtained in the treatment of patients with severe hypertension requiring urgent blood pressure reduction with an initial dose of 20 mg (which corresponds to 0.25 mg/kg for an 80 kg patient) followed by additional doses of either 40 mg or 80 mg at 10-minute intervals to achieve the desired effect or up to a cumulative dose of 300 mg.

Labetalol hydrochloride administered as a continuous intravenous infusion with a mean dose of 136 mg (27 to 300 mg) over a period of 2 to 3 hours (mean of 2 hours and 39 minutes) lowered the blood pressure by an average of 60/35 mmHg.

Humans:
Intravenous labetalol hydrochloride, in doses of 10, 40 and 160 mg caused dose-related inhibition of phenylephrine-induced increase in mean blood pressure and of isoproterenol-induced tachycardia. After 40 mg of labetalol hydrochloride, a 2-fold increase in the dose of phenylephrine (ß -blockade) and an 8-fold increase in the dose of isoproterenol (ß-blockade) were required to elicit responses equivalent to pretreatment levels. The tachycardia induced by Valsalva manoeuvre was also abolished by the 40 mg IV dose.

Doses of 0.5 mg/kg of labetalol hydrochloride administered IV to 12 hypertensive patients resulted in the following statistically significant mean percentage changes: blood pressure was lowered by 18.5% ($p<0.001$) and total peripheral vascular resistance by 13.5 ± 22% ($p<0.02$). No significant changes in resting heart rate or cardiac output were observed.

Labetalol hydrochloride significantly reduced the pressor response to immersion of the hand in ice- cold water for 60 seconds (**cold pressor test**), signifying the postsynaptic ß -blocking action of the drug.

After oral treatment with labetalol hydrochloride (average dose 1200 mg), plasma renin and angiotensin II levels were reduced, especially if elevated prior to treatment. Intravenous labetalol hydrochloride, in doses of 1-2 mg/kg, reduced plasma levels of angiotensin II and aldosterone in hypertensive patients.

Effects on Pulmonary Function

A single 400 mg oral dose of labetalol hydrochloride administered to healthy male subjects caused a reduction in Peak Expiratory Flow Rate (PEFR) at rest and during exercise.

In 11 hypertensive asthmatic subjects, a 300 mg oral dose of labetalol hydrochloride caused a slight reduction in resting FEV_1, and significantly reduced the effect of inhaled salbutamol in FEV_1.

Other Effects
Labetalol hydrochloride administered to 17 hypertensive men in daily oral doses of 600 to 1200 mg caused a small increase in fasting blood glucose levels but no alteration in insulin activity or response to an oral glucose tolerance test.

16. Non-Clinical Toxicology

General toxicology

Table 2 - Acute Toxicity

Animal	Sex	Route of Administration	LD_{50} (in mg/kg)
Mouse	M	PO	655
Mouse	F	PO	577
Mouse	M	IV	53
Mouse	F	IV	49
Rat	M	PO	2 379
Rat	F	PO	2 055
Rat	M	IV	51
Rat	F	IV	50
Dog	M	IV	34
Dog	F	IV	38

Signs of Toxicity
Mice: hypoactivity, dyspnea, prostration, piloerection, ataxia, clonic convulsions.
Rats: hypoactivity, dyspnea, salivation, clonic convulsions.

Four beagle dogs were treated with single oral doses of labetalol hydrochloride 500, 750 and 1000 mg/kg. No deaths resulted. The following signs were observed in dogs treated with 750 mg/kg or higher: emesis, redness of the mucous membranes, dry nose, mild sedation, slight tachycardia, bradypnea and hypothermia.

In beagle dogs, death occurred within 15 minutes of an IV dose of 40 mg/kg and was preceded by prostration. Survivors (5/12) from doses up to 100 mg/kg experienced temporary lethargy, hypotension and bradycardia.

Subacute Toxicity
In rats, labetalol hydrochloride was administered by gavage in doses of 0, 50, 110 and 250 mg/kg/day (24 rats/dose) for 3 months. Polydipsia, dilute polyuria, proteinuria, elevated serum liver enzymes, polycythemia and nephrocalcinosis were noted. Cellular casts were found in the urine of animals in the high dose group.

Labetalol hydrochloride was administered IV to beagle dogs (10/sex) in doses of up to 20 mg/kg/day for 15 days. No drug-induced toxicity was noted.

Chronic Toxicity
Labetalol hydrochloride was administered by gavage to Wistar rats for 1 year in doses of 1, 100, 140, and 200 mg/kg/day (32 rats/dose). A slight, but statistically significant lengthening of the clotting time was found in all treated groups. Increased plasma levels of alkaline phosphatase, SGOT and SGPT were noted towards the end of the study period. Increases in heart weights were observed in all treated groups.

Labetalol hydrochloride was administered orally to beagle dogs in doses of 0, 25, 50 and 100 mg/kg once daily, 7 days per week for 52 weeks (6 dogs/dose).

Muscle tremors, abnormal gait, vomiting and loose stools of abnormal colour were observed at 50 and 100 mg/kg doses. Occult blood was occasionally seen in the fæces of animals in the high dose group.

One male and one female in the high dose group died during testing. Both showed gastrointestinal mucosal congestion and the female had increased blood urea and SGPT levels. Cause of death was not established.

Body weight gain was significantly lower in high dose males.

Four dogs developed minor corneal ulcers. Reflex tear secretion was normal in all animals. Heart rate

was reduced at all doses (ECG recordings).

No drug-related changes in gross weight of organs or histopathological findings were noted.

Genotoxicity
Studies with labetalol hydrochloride, using dominant lethal assays in mice and rats, and exposing microorganisms according to modified Ames tests, did not show any evidence of drug-related mutagenicity.

Carcinogenicity
Labetalol hydrochloride was admixed in the diet of CR/H Glaxo mice in doses of 0, 100, 140 and 200 mg/kg/day for 18 months (100 mice/dose). No drug-related carcinogenicity was apparent.

Sprague-Dawley CD rats were fed labetalol hydrochloride in doses of 0, 100, 140 and 225 mg/kg/day for 24 months (110 rats/dose). Increased incidences of ovarian cysts, corneal lesions, reactive lymphoid hyperplasia of the cervical lymph nodes, and enlargement of seminal vesicles were noted in the active treatment groups. No drug-related carcinogenicity was apparent.

Reproductive and developmental toxicology
Labetalol hydrochloride was administered by gavage to AHA rats in doses of 0, 50, 100 and 200 mg/kg/day (32 rats/dose) for 10 weeks prior to mating and throughout the mating period. A dose-related reduction in fertility was observed in the treated animals (F_0 generation). No reproductive impairment was noted in the subsequent F_1 and F_2 generations.

Primiparous Wistar rats were administered labetalol hydrochloride by gavage throughout pregnancy (19 days) in doses of 0, 125, 150, 175, 200, 250 and 300 mg/kg/day (8 rats/dose). No congenital malformations were observed. There was a retardation of fœtal growth in the 250 and 300 mg/kg dose groups.

Mated female New Zealand white rabbits were administered labetalol hydrochloride by gavage from day 7 through day 19 of gestation, in doses of 0, 50, 100 and 200 mg/kg/day (14 rabbits/dose). There were no apparent drug-related effects on the course of pregnancy or fœtaldevelopment.

17. Supporting Product Monographs

1. LABETALOL HYDROCHLORIDE INJECTION USP, Solution, 5mg / mL, control no. 262094, product monograph, Sandoz Canada Inc. 2022-09-20.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr] Labetalol Hydrochloride Injection in 5% Dextrose
[Pr]Labetalol Hydrochloride Injection in 0.72% Sodium Chloride

This patient medication information is written for the person who will be taking **Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This patient medication information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride**, talk to a healthcare professional.

Serious warnings and precautions box

Liver disorders: Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride may cause severe liver problems. This rare and serious side effect can develop progressively, and with very little symptoms. It is usually reversible, but there have been rare cases of hepatic necrosis (cell death in the liver), and even death.

What Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride are used for:

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride are used in adults for the emergency treatment of very high blood pressure. It is given when blood pressure needs to be lowered quickly.

How Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride work:

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride belong to a group of medicines called "beta-blockers". They lower blood pressure by:

- making your heart beat more slowly and less forcefully, and
- lowering your blood pressure by relaxing your blood vessels so that your blood flows more easily.

The ingredients in Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride are:

Medicinal ingredient: labetalol hydrochloride

Non-medicinal ingredients:

Labetalol Hydrochloride Injection in 5% Dextrose: dextrose anhydrous, disodium edetate, citric acid and/or sodium hydroxide to adjust pH, and water for injection.

Labetalol Hydrochloride Injection in 0.72% Sodium Chloride: sodium chloride, disodium edetate, citric acid and/or sodium hydroxide to adjust pH, and water for injection.

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride comes in the following dosage forms:

Solution: 1 mg/mL.

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride will not be used if you:

- Are allergic to labetalol hydrochloride or to any of the other ingredients in Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride.
- Have heart failure and you notice that your symptoms are getting worse. For example you feel more tired, are out of breath more often, or have swelling of the ankles.
- Have severe heart damage and your heart is not able to pump enough blood to meet your body's needs.
- Have a slow or irregular heartbeat.
- Have a problem with your heart's electrical conduction called atrioventricular block (also known as AV block).
- Have asthma or a history of other lung problems that cause airflow blockage and breathing problems (like bronchitis or emphysema).
- Have serious problems with blood flow in your feet and legs (severe peripheral artery disease).

To help avoid side effects and ensure proper use, you or your caregiver should talk to your healthcare professional before you are given Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride. Talk about any health conditions or problems you may have, including if you:

- Have heart failure. Your healthcare professional will ensure your condition is under control before giving you Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride.
- Have a history of fainting.
- Have, or are at risk for, diabetes. Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride may make you more prone to low blood sugar, especially if you also take insulin or oral diabetes medications.
- Have a condition called pheochromocytoma (a tumour of the adrenal gland).
- Have thyroid problems.
- Have liver problems.
- Have a history of severe allergic reactions.
- Are pregnant, think you might be pregnant, or are planning on becoming pregnant. Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride are not usually recommended for use during pregnancy. Your healthcare professional will consider the benefit of you being treated with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride against the risk to your unborn baby.
- Are breastfeeding or are planning to breastfeed. You should not breastfeed while receiving Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride.

- Are going to have an operation or surgery. Let the medical staff of the operation or surgery know, in particular the anesthetist, that you are taking Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride.
- Are taking any other medicines.
- Are 65 years of age or older.

Other warnings you should know about:

Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride can cause serious side effects, including:

- **Heart failure:** Patients taking Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride can develop heart failure. Your healthcare professional will check you for signs and symptoms of heart failure during your treatment with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride.

- **Bradycardia** (abnormally slow heartbeat): Your heart rate may lower while you are taking Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride. If it gets too low, your dose may be reduced or your healthcare professional may tell you how to safely stop your treatment with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride.

- **Allergic reactions:** While you are taking Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride:

    - a severe allergic reaction may be harder to treat.

    - you may be more likely to have a severe allergic reaction if you have a history of them.

- **Hypotension (low blood pressure):** You should remain lying down on your back after receiving Labetalol Hydrochloride Injection in 5% Dextrose or Labetalol Hydrochloride Injection in 0.72% Sodium Chloride. Standing or sitting up too soon may cause low blood pressure and you may feel like fainting, dizzy or lightheaded. Your healthcare professional will tell you when you may stand or sit up.

See the **Serious side effects** and what to do about them table for more information on these and other serious side effects.

Check-ups and testing: Your healthcare professional will regularly monitor and assess your health before, during and after you are given Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride. They may do tests to monitor:

- The health of your heart, liver, eyes and thyroid.
- Your blood sugar levels.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride:

- medicines used to treat high blood pressure, chest pain and heart rhythm problems (such as verapamil, diltiazem, diuretics (also known as "water pills"), and nitroglycerin)
- anesthetic medicines used during surgery such as halothane
- medicines used to reduce the amount of acid in the stomach such as cimetidine
- medicines used to treat depression such as tricyclic antidepressants
- medicines used to treat Multiple Sclerosis such as fingolimod

How Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride is given:

- Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride will be given to you by a healthcare professional in a hospital.
- Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride will be given to you through a needle placed in a vein. This is called intravenous (IV) injection.
- You will be lying face up when receiving Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride. You should remain lying down on your back until your healthcare professional tells you that you may stand or sit up.

Usual dose:
Your healthcare professional will decide on the dose that is right for you. Your dose will depend on:

- your age
- your weight
- your health
- the severity of your high blood pressure
- previous treatment you received and
- how you respond during treatment.

Overdose:

Symptoms of overdose with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride may include:

- very low blood pressure (may occur when you go from lying or sitting to standing up)
- an abnormally slow or irregular heart beat
- heart failure (your heart doesn't pump enough blood for your body's needs)
- difficulty breathing, tightness in your chest
- low blood sugar.

If you think you, or a person you are caring for, have taken too much Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Possible side effects from using Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride:

These are not all the possible side effects you may have when taking Labetalol Hydrochloride

Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride. If you experience any side effects not listed here, tell your healthcare professional

Side effects with Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride may include:

- Dizziness
- Headache
- Nausea or Vomiting
- Lack of energy
- General feeling of discomfort
- Aches and pains
- Muscle cramps
- Shaking (tremor)
- Blurred vision
- Nosebleeds
- Indigestion
- Change in taste
- Constipation
- Dry mouth
- Sore throat
- Stuffy nose
- Feeling of "pins and needles" on the skin
- Itchy skin
- Inability to keep or maintain an erection
- Loss of sex drive

Serious side effects and what to do about them

Frequency / Side Effect / Symptom	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
Common			
Chest pain			√
Depression (sad mood that won't go away)**:** difficulty sleeping, sleeping too much, changes in appetite or weight, feelings of worthlessness, guilt, regret, helplessness or hopelessness, withdrawal from social situations, family, gatherings and activities with friends, reduced libido (sex drive), or thoughts of death or suicide		√	
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up)		√	

Palpitation (fast-beating, fluttering or pounding heart): skipping beats, beating too fast, pounding, fluttering rapidly		√	
Pedal edema (swelling in the feet and ankles): swollen or puffy feet and ankles, feeling heavy, achy or stiff		√	
Raynaud's phenomenon (episodes of reduced blood flow): cold feeling in fingers and toes (and sometimes nose, lips and ears), prickly or stinging feeling, change in skin colour to white then blue		√	
Uncommon			
Allergic Reaction: difficulty swallowing or breathing, wheezing, feeling sick to your stomach and throwing up, hives or rash, swelling of the face, lips, tongue or throat			√
Bradycardia (abnormally slow heartbeat): feeling dizzy or fainting		√	
Bronchospasm (when there is a sudden narrowing of the airway): difficulty breathing with wheezing or coughing		√	
Congestive Heart Failure (heart does not pump blood as well as it should)**:** shortness of breath, fatigue and weakness, swelling in ankles, legs and feet, cough, fluid retention, lack of appetite, nausea, rapid or irregular heartbeat, reduced ability to exercise		√	
Liver problems: yellowing of your skin and eyes (jaundice), right upper stomach area pain or swelling, nausea or vomiting, unusual dark urine, unusual tiredness, unexplained loss of appetite			√
Unknown			
Angioedema (swelling of tissue under the skin)**:** difficulty breathing, swollen face, hands and feet, genitals tongue, throat, swelling of the digestive tract causing diarrhea, nausea or vomiting			√
Hypoglycemia (low blood sugar): thirst, frequent urination, hunger, nausea and dizziness, fast heartbeat, tingling trembling, nervousness, sweating, low energy		√	
Lupus-like syndrome: joint pain, muscle pain, chest pain when you cough or breathe, breathing difficulties (shortness of breath or labored breathing)		√	
Peyronie's disease (a condition where scar tissue forms under the skin of the penis): penile pain, shortening of the penis, erection problems, or significant bend to the penis		√	

Skin reactions: rash, itchiness, flushing, red patches of skin covered with thick, silvery scales, dry cracked skin that may bleed, burning, or soreness		√	
Toxic myopathy (muscle damage caused by medications): muscle weakness (especially of your upper arms, shoulders and thighs), muscle cramps, stiffness and spasms, fatigue with exercise, lack of energy		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice

Storage:
Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride will be stored by your healthcare professional, hospital, or clinic.

If you want more information about Labetalol Hydrochloride Injection in 5% Dextrose and Labetalol Hydrochloride Injection in 0.72% Sodium Chloride:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by calling 1-800-656-0793.

This leaflet was prepared by Hikma Canada Limited.

Date of Revision: APR 24, 2025