安成國際藥業股份有限公司
TWi Pharmaceuticals, Inc.

Safety Data Sheet

Labetalol Hydrochloride Tablets, 100 mg, 200 mg, 300 mg

SECTION 1 IDENTIFICATION

Product identifier	Labetalol Hydrochloride Tablets, 100 mg, 200 mg and 300 mg
Recommended use	Indicated in the management of hypertension. May be used alone or in combination with other antihypertensive agents, especially thiazide and loop diuretics
Supplier	
Company name	TWi Pharmaceuticals USA, Inc.
Address	115 West Century Road, Suite 180, Paramus, NJ 07652
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E-mail address	QA.Service@twipharma.com
Emergency phone number	1-844-518-2989

SECTION 2 HAZARD IDENTIFICATION

Dose and Administration

DOSAGE MUST BE INDIVIDUALIZED. The recommended initial dosage is 100 mg twice daily whether used alone or added to a diuretic regimen. After 2 or 3 days, using standing blood pressure as an indicator, dosage may be titrated in increments of 100 mg b.i.d. every 2 or 3 days.

The usual maintenance dosage of labetalol hydrochloride tablets is between 200 mg and 400 mg twice daily.

Since the full antihypertensive effect of labetalol hydrochloride tablets is usually seen within the first 1 to 3 hours of the initial dose or dose increment, the assurance of a lack of an exaggerated hypotensive response can be clinically established in the office setting.

The antihypertensive effects of continued dosing can be measured at subsequent visits, approximately 12 hours after a dose, to determine whether further titration is necessary.

Patients with severe hypertension may require from 1200 mg to

2400 mg per day, with or without thiazide diuretics. Should side effects (principally nausea or dizziness) occur with these doses administered b.i.d. (twice daily), the same total daily dose administered t.i.d. (three times daily) may improve tolerability and facilitate further titration. Titration increments should not exceed 200 mg b.i.d. (twice daily).

When a diuretic is added, an additive antihypertensive effect can be expected. In some cases this may necessitate a labetalol hydrochloride tablet dosage adjustment. As with most antihypertensive drugs, optimal dosages of labetalol hydrochloride tablets are usually lower in patients also receiving a diuretic. When transferring patients from other antihypertensive drugs, labetalol hydrochloride tablets should be introduced as recommended and the dosage of the existing therapy progressively decreased.

Adverse Effects

Most adverse effects are mild and transient and occur early in the course of treatment. In controlled clinical trials of 3 to 4 months duration, discontinuation of labetalol hydrochloride tablets due to one or more adverse effects was required in 7% of all patients. In these same trials, other agents with solely beta-

	blocking activity used in the control groups led to discontinuation in 8% to 10% of patients and acentrally acting alpha-agonist led to discontinuation in 30% of patients.
Over Dose Effect	Overdosage with labetalol hydrochloride causes excessive hypotension that is posture sensitive and sometimes excessive bradycardia. Patients should be placed supine and their legs raised, if necessary, to improve the blood supply to the brain. If over dosage with labetalol hydrochloride follows oral ingestion, gastric lavage or pharmacologically induced emesis (using syrup of ipecac) may be useful for removal of the drug shortly after ingestion. The following additional measures should be employed if necessary: Excessive bradycardia - administer atropine or epinephrine. Cardiac failure - administer a digitalis glycoside and a diuretic. Dopamine or dobutamine may also be useful. Hypotension - administer vasopressors, e.g., norepinephrine. There is pharmacologic evidence that norepinephrine may be the drug of choice. Bronchospasm - administer epinephrine and/or an aerosolized beta2-agonist. Seizures – administer diazepam. In severe beta-blocker overdose resulting in hypotension and/or bradycardia, glucagon has been shown to be effective when administered in large doses (5 mg to 10 mg rapidly over 30 seconds, followed by continuous infusion of 5 mg per hour that can be reduced as the patient improves). Neither hemodialysis nor peritoneal dialysis removes a significant amount of labetalol hydrochloride from the general circulation (<1%). The oral LD50 value of labetalol hydrochloride in the mouse is approximately 600 mg/kg and in the rat is > 2 g/kg. The intravenous LD50 in these species is 50 mg/kg to 60 mg/kg.
Contraindications	Labetalol hydrochloride is contraindicated in bronchial asthma, overt cardiac failure, greater-than-first-degree heart block, cardiogenic shock, severe bradycardia, other conditions associated with severe and prolonged hypotension and in patients with a history of hypersensitivity to any component of the product. Beta-blockers, even those with apparent cardio selectivity, should not be used in patients with a history of obstructive airway disease, including asthma.
Pregnancy Comments	Teratogenic studies were performed with labetalol in rats and rabbits at oral doses up to approximately six and four times the maximum recommended human dose (MRHD), respectively. No reproducible evidence of fetal malformations was observed. Increased fetal resorptions were seen in both species at doses approximating the MRHD. A teratology study performed with labetalol in rabbits at intravenous doses up to 1.7 times the MRHD revealed no evidence of drug-related harm to the fetus. There are no adequate and well controlled studies in pregnant women. Labetalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

SECTION 3 COMPOSITION/INFORMATION ON INGREDIENTS

Component	Exposure Limit	CAS No.
Principle Component:		

Labetalol Hydrochloride	Not Found	32780-64-6
Inactive ingredients:		
Lactose Monohydrate	Not Found	64044-51-5
Sodium starch glycolate	Not Found	9063-38-1
Corn Starch	Not Found	9005-25-8
Hydroxypropyl methyl Cellulose	Not Found	9004-65-3
Magnesium Stearate	Not Found	557-04-0
Opadry White (YS-1-7003)	Not Found	Not Applicable

SECTION 4 FIRST-AID MEASURES

Instructions by routes of exposure

Inhalation	Move to fresh air in case of accidental inhalation. Assure fresh air breathing.
Skin contact	Rinse skin with water/shower.
Eye contact	Rinse with water while holding the eyes wide open. Contact lenses should be removed.
Ingestion	Rinse mouth out with water.
Most important symptoms/ effects, both acute and delayed	No further relevant information available.
Immediate medical attention and special treatment	No further relevant information available.

SECTION 5 FIRE-FIGHTING MEASURES

Suitable extinguishing media	Use extinguishing media appropriate for surrounding fire. Extinguishing blanket. Carbon dioxide. Dry powder
Specific hazards arising from the chemical	No additional information available
Special protective equipment and precautions for firefighters	Small amounts: Use normal individual fire protective equipment. Large amounts: Not
Firefighting equipment/ instructions	Hand protection : Gloves Skin and body protection : Lab coat Respiratory protection : Quarter mask (DIN EN 140)
General fire hazards	No unusual fire or explosion hazards noted

SECTION 6 ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	Avoid raising dust. Wear suitable protective clothing, gloves and eye or face protection.
Methods and materials for	Sweep spilled substance into containers; if appropriate, moisten first to prevent

containment and cleanup	dusting. Ensure waste is collected and contained. Clean thoroughly. Poorly soluble in water. Clean with the help of detergents.
Environmental precautions	No additional information available.

SECTION 7 HANDLING AND STORAGE

Precautions for safe handling	Keep it dry & in a cool, well ventilated place away from heat. Store in original container.
Conditions for safe storage, including any incompatibilities	Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense in a tight, light-resistant container as defined in the USP with a child-resistant closure as required.

SECTION 8 EXPOSURE CONTROLS/PERSONAL PROTECTION

Biological limit values	No biological exposure limits noted for the ingredient(s).
Exposure guidelines	General ventilation normally adequate.
Engineering controls	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.
Individual protection measures, such as personal protective equipment	
Eye/face protection	If contact is likely, safety glasses with side shields are recommended.
Skin protection	For prolonged or repeated skin contact use suitable protective gloves.
Respiratory protection	Quarter mask (DIN EN 140)
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	Keep away from foodstuffs, beverages and feed. Wash hands before breaks and at the end of work. Routinely wash work clothing and protective equipment to remove contaminants. For advice on suitable monitoring methods, seek guidance from a qualified environment, health and safety professional.

SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

Appearance	
Physical state	Solid
Form	Round biconvex tablet
Color	White to off-white
Odor	Not available.
pH	Not available.
Melting point/freezing point	Not available.
Evaporation rate	Not available.
Flammability (solid, gas)	Not available.
Vapor pressure	Not available.
Vapor density	Not available.
Relative density	Not available.
Solubility(ies)	Not available
Reactivity in water	Not available

% Volatile by volume	Not available
Specific gravity	Not available.

SECTION 10 STABILITY AND REACTIVITY

Reactivity	The product is stable and non-reactive under normal conditions of use, storage and transport.
Chemical stability	Material is stable under normal conditions.
Possibility of hazardous reactions	No dangerous reaction known under conditions of normal use.
Conditions to avoid	Contact with incompatible materials.
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition	When heated to decomposition, emits dangerous fumes.
Hazardous reactions	No dangerous reaction known under conditions of normal use.

SECTION 11 TOXICOLOGICAL INFORMATION

General	Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.
Ingestion	Health injuries are not known or expected under normal use. Expected to be a low ingestion hazard. However, ingestion is not likely to be a primary route of occupational exposure.
Other	Not available

Symptoms related to the physical chemical and Toxicological characteristics	Not available
Information on toxicological effects Acute toxicity	Not available
Further information	Not available

SECTION 12 ECOLOGICAL INFORMATION

Poorly soluble in water. No data available on ecotoxicity.

SECTION 13 DISPOSAL CONSIDERATIONS

Dispose the waste in accordance with all applicable Federal, State and local laws.

SECTION 14 TRANSPORT INFORMATION

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG). In accordance with ADR / RID / IMDG / IATA / ADN

SECTION 15 REGULATORY INFORMATION

Generic Medicine. Under Approval by USFDA and the ANDA Number is 209603

SECTION 16 OTHER INFORMATION

Issue date	August 22, 2018
Version #	01
Disclaimer	TWi Pharmaceutical, Inc. cannot anticipate all conditions under which this information and its product, or the products of other manufacturers in combination with its product, may be used. It is the user's responsibility to ensure safe conditions for handling, storage and disposal of the product, and to assume liability for loss, injury, damage or expense due to improper use. The information in the sheet was written based on the best knowledge and experience currently available.