Dutoprol® Tablets

SAFETY DATA SHEET

According to Federal Register/ Vol. 77, No.58/ Mon Mar 26, 2012/Rules & Regulations

Date of Issue: January 5, 2016, Supersedes: Jun 17, 2013, Version 1.0

SECTION 1: Identification

1.1. Product identifier

Product form	:	Tablets
Product identifier	:	Dutoprol® Tablets
Other means of identification	:	Dutoprol® 100/12.5 mg Tablet; Dutoprol® 50/12.5 mg Tablet; Dutoprol® 25/12.5 mg Tablet; NDC Code 59212-087-30; NDC Code 59212-095-30; NDC Code 59212-097-30

1.2. Recommended use of the chemical and restriction\ns on use

Pharmaceutical Agent. Use only as per Product Monograph for the treatment of hypertension, to lower blood pressure. (See Product Monograph for further information).

1.3. Name, address and telephone number of the chemical manufacturer, importer, or other responsible party

Concordia Pharmaceuticals Inc.
5 Canewood Industrial Park
St. Michael, Barbados BB11005

1.4. Emergency phone number

Emergency number	:	1-877-370-1142 (8:30 am – 4:30 pm EST)

SECTION 2: Hazards identification

This product is a pharmaceutical as defined under the Federal Food, Drug and Cosmetic Act, in solid, final form for direct administration to the patient and as such it is exempt from coverage under US GHS Hazard Communication Standard (2012)

This SDS and classification are provided in case of the unlikely event of crushing of the capsules and release of dust from capsules only.

2.1. Classification of the substance or mixture

Classification (GHS-US)

Not required; however, the classification (if applicable, would be) (Cat = Category):

Skin Irritant Cat 2

Eye Irritant Cat 2A

Mutagen Cat 2

Carcinogen Cat 2

Reproductive Toxicity Cat 2

STOT-SE 3 – Resp. Irritant, CNS Effects

2.2. Label elements

GHS-US labeling

Not required; however, the labelling (if applicable would be):

WARNING

Causes skin irritation.

Causes serious eye irritation.

Suspected of causing genetic defects.

Suspected of causing cancer.

Suspected of damaging the unborn child.

May cause harm to breast-fed children

May cause drowsiness or dizziness.

May cause respiratory irritation.

PREVENTION:

Obtain special instructions before use.

Do not handle until all safety precautions have been read and understood.

Avoid contact during pregnancy/while nursing.

Do not breathe dusts.

Wear protective gloves, protective clothing, eye protection, face protection, respiratory protection.

Do not eat, drink or smoke when using this product.

Take off contaminated clothing and wash it before reuse.

Wash hands thoroughly after handling.

RESPONSE:

Call a poison center or doctor if you feel unwell.

If exposed or concerned: Get medical advice or attention.

If in eyes: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

If eye irritation persists: Get medical advice/attention.

If on skin: Wash with plenty of soap and water.

If skin irritation occurs: Get medical advice/attention.

If inhaled: Remove person to fresh air and keep comfortable for breathing.

STORAGE:

Store locked up.

DISPOSAL:

Dispose of contents/container in accordance with local, regional, national, international regulations.

2.3. Other hazards

No additional information available

2.4. Unknown acute toxicity (GHS-US)

100/12.5 mg Tablet

16% of the mixture consists of ingredients of unknown acute oral toxicity.

89% of the mixture consists of ingredients of unknown acute dermal toxicity.

61% of the mixture consists of ingredients of unknown acute inhalation toxicity.

50/12.5 mg Tablet

19% of the mixture consists of ingredients of unknown acute oral toxicity.

88% of the mixture consists of ingredients of unknown acute dermal toxicity.

54% of the mixture consists of ingredients of unknown acute inhalation toxicity.

25/12.5 mg Tablet

17% of the mixture consists of ingredients of unknown acute oral toxicity.

86% of the mixture consists of ingredients of unknown acute dermal toxicity.

54% of the mixture consists of ingredients of unknown acute inhalation toxicity.

SECTION 3: Composition/information on ingredients

3.1. Substance

Not applicable

3.2. Mixture

Name	Product identifier	%	Classification (GHS-US)
Metoprolol succinate	(CAS No) 98418-47-4	26% (100/12.5 mg tablet) 14% (50/12.5 mg tablet) 12% (25/12.5 mg tablet)	Acute Tox. 4(Oral), Eye Irritant 2A Skin Irritant 2 Repro Cat 2 STOT-SE-3 – RI/Narc
Hydrochlorothiazide	(CAS No) 58-93-5	3% (100/12.5 mg tablet) 4% (50/12.5 mg tablet) 6% (25/12.5 mg tablet)	Acute Tox, 4 (Oral) Muta Cat 2
Titanium dioxide	(CAS No) 13463-67-7	0.6% (100/12.5 mg tablet) 0.4% (50/12.5 mg tablet) 0.7% (25/12.5 mg tablet)	Carc Cat 2
Starch	(CAS No) 9005-25-8	2% (100/12.5 mg tablet) 2% (50/12.5 mg tablet) 5% (25/12.5 mg tablet)	STOT-SE 3 - RI

SECTION 4: First-aid measures

4.1. Description of first aid measures

First-aid measures after inhalation : No specific first-aid measures for routine handling. In case of breathing difficulties, seek medical advice. If tablets are crushed and loose powder is inhaled, remove person to fresh air and keep comfortable for breathing. Seek medical advice.

First-aid measures after skin contact : Normal handling is not anticipated to result in occupational exposure. In the event of occupational skin contact with crushed tablets or powder, wash contaminated area thoroughly with soap and water.

First-aid measures after eye contact : Flush eyes continuously with water for at least 15 minutes. Do not use a chemical neutralizer. Obtain medical assistance if symptoms occur.

First-aid measures after ingestion : In the event of occupational ingestion, seek medical advice. Induction of vomiting is not a recommended first-aid procedure. If victim is conscious rinse out mouth with water and give 200-300 mL of water to drink.

4.2. Most important symptoms and effects, both acute and delayed

Symptoms/injuries after inhalation : No symptoms expected during normal handling. Inhalation of crushed capsules may cause respiratory irritation lowering of blood pressure (resulting in dizziness, fatigue and headache), change in heart rhythm and gastrointestinal disorders.

Symptoms/injuries after skin contact : No symptoms are expected during normal handling. Skin contact with the content of the crushed capsules may cause skin irritation including swelling and redness.

Symptoms/injuries after eye contact : No symptoms are expected during normal handling. Eye contact with crushed capsules may cause eye irritation.

Symptoms/injuries after ingestion : In the event that the substance ingested symptoms may include: lowering of blood pressure (resulting in dizziness, fatigue and headache); change in heart rhythm; gastrointestinal disorders. May cause harm to the unborn child or to breast-feeding children

4.3. Indication of any immediate medical attention and special treatment needed

No specific antidotes known. Treat symptomatically. Refer to current prescribing information or to local poison control information centers.

SECTION 5: Fire-fighting measures

5.1. Extinguishing media

Suitable extinguishing media : Water, dry powder or foam extinguishers are recommended.

Unsuitable extinguishing media : None known.

5.2. Special hazards arising from the chemical

Fire hazard : The product is not expected to support combustion; however, the packaging is combustible. The product may decompose at high temperatures releasing hazardous decomposition products (See Section 10 for more information).

5.3. Advice for fire-fighters

Protection during firefighting : For single units (Packages): No special requirements needed. For larger amounts (multiple packages/pallets) of product: Since hazardous substances might be evolved from fires involving this material and associate packaging, self-contained breathing apparatus and full protective equipment are recommended for firefighters. Move containers from the fire area if possible without increased personal risk. If possible, contain and collect firefighting water for later disposal.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

General measures (Spills) : No special requirements for spills from single containers. For large spills, take precautions to prevent entry into waterways, sewers or surface drainage systems. Use protective clothing during clean-up prior to disposal of spilled material.

If the tablets are crushed or broken dust containing drug substance may be released. Minimize dust generation and accumulation. Do not breathe dust or touch dust without wearing appropriate PPE (See Section 8).

6.1.1. For non-emergency personnel

Emergency procedures : See Section 8 for appropriate PPE. Avoid unnecessary contact, especially with dust.

6.1.2. For emergency responders

Protective equipment : See Section 8 for appropriate PPE. Avoid unnecessary contact, especially with dust.

6.2. Environmental precautions

Prevent entry into waterways, sewers or surface drainage systems. Notify authorities if the product or solutions of the product enter sewers or public waters.

6.3. Methods and material for containment and cleaning up

For containment : Minimize dust generation and accumulation. Product may form flammable dust clouds in air if tablets are crushed and powder is released.

Methods for cleaning up : Wet-down all dusts and soak up contents of broken tablets with an inert absorbent material. Carefully collect material and place in a properly labeled waste container for disposal. Wash area of spill to remove from surfaces. Wash skin thoroughly after handling. Detergents can be used for clean-up and decontamination operations. No specific decontamination or detoxification procedures have been identified for this substance.

6.4. Reference to other sections

See Section 8. Exposure controls and personal protection.

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Precautions for safe handling : Avoid breaking or crushing tablets. If tablets are crushed or broken, dust may be released. Avoid breathing dust and avoid contact with skin, eyes and clothing. Use explosion-proof local exhaust ventilation or respiratory protection for operations which generate dust. Wash thoroughly after handling.

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions : Keep container tightly closed. Store at room temperature. No known incompatibilities.

7.3. Specific end use(s)

Pharmaceutical agent for the control of hypertension.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

The following components have applicable exposure limits. In the event of possible dust/powder generation from these tablets, we have provided the following information to enable users to safely handle the product in that form.

Metoprolol succinate (CAS# 94818-47-4)		
ACGIH	TLV-TWA	None established
OSHA	PEL-TWA	None established

Hydrochlorothiazide (CAS# 58-93-5)		
ACGIH	TLV-TWA	None established

Hydrochlorothiazide (CAS# 58-93-5)		
OSHA	PEL-TWA	None established

Titanium dioxide (CAS# 13463-67-7)		
ACGIH	TLV-TWA	10 mg/m^3
OSHA	PEL-TWA	15 mg/m^3 (total dust)

Starch (CAS# 9005-25-8)		
ACGIH	TLV-TWA	10 mg/m^3
OSHA	PEL-TWA	15 mg/m^3 (total dust) 5 mg/m^3 (respirable fraction)

8.2. Exposure controls

Appropriate engineering controls : None required for normal handling of this material. If tablets are crushed or broken, dust containing drug substance may be released. If dust is generated, local explosion-proof, exhaust ventilation may be required. Local circumstances may affect required exposure controls. Perform a site-specific risk assessment.

Hand protection : If tablets are crushed or broken, dust containing drug substance may be released and impervious gloves should be worn to prevent skin exposure. If the product is dissolved in a solvent, ensure glove material is also resistant to the solvent.

Eye protection : If tablets are crushed or broken, dust containing drug substance may be released. Wear safety glasses with side shields or goggles where risk of eye exposure exists.

Skin and body protection : If tablets are crushed or broken, dust containing drug substance may be released. Wear suitable working clothes to present skin exposure. Consider using a full-chemical-protective suit if conditions warrant.

Respiratory protection : If tablets are crushed or broken, dust containing drug substance may be released. Wear NIOSH-approved respirator if concentrations exceed exposure limits.

Other information : When using, do not eat, drink or smoke. All decisions regarding PPE and other exposure controls must be decided based upon a workplace risk assessment and should consider local regulatory requirements for selection and use.

The Information above should not be used in isolation and should be considered in the context of the workplace risk assessment and determined on a case-by-case basis.

Consult a qualified safety and health professional for additional guidance, as needed.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state : Solid in tablet form.

Appearance : Yellow film-coated tablet.

Odor : No data available

Odor threshold : No data available

pH : No data available

Relative evaporation rate (butyl acetate=1) : No data available

Melting point / freezing point : No data available

Boiling point : No data available

Flash point : Not applicable

Upper/lower flammability or explosive limits : No data available

Auto-ignition temperature : No data available

Decomposition temperature : No data available

Flammability (solid, gas) : No data available

Vapor pressure : No data available

Relative vapor density at 20 °C : No data available

Relative density : No data available

Solubility : ≥ 1 mg/L (Water)

Log Pow : No data available

Log Kow : No data available

Viscosity, kinematic : No data available

Viscosity, dynamic : No data available

Oxidizing properties	:	No data available

9.2. Other information

No additional information available

SECTION 10: Stability and reactivity

10.1. Reactivity

Not expected to present a significant hazard under anticipated conditions of normal use.

10.2. Chemical stability

Anticipated to be stable under anticipated conditions of normal use.

10.3. Possibility of hazardous reactions

Not expected to present a significant hazard under anticipated conditions of normal use.

10.4. Conditions to avoid

Avoid crushing tablets and creation of dusts as clouds of finely-divided organic materials may present a dust-explosion hazard.

10.5. Incompatible materials

Strong oxidizing agents.

10.6. Hazardous decomposition products

No hazardous decomposition products are anticipated during normal handling of this product. In case of fire carbon oxides, nitrogen oxides, sulfur oxides and hydrogen chloride gas may be released as decomposition products.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

INFORMATION ON LIKELY ROUTES OF EXPOSURE:

Routes of exposure may include oral, dermal, inhalation (in case of crushed tablets), or ingestion.

SYMPTOMS RELATED TO THE PHYSICAL, CHEMICAL AND TOXICOLOGICAL CHARACTERISTICS:

Potential Adverse human health effects and symptoms	:	See below.
Symptoms/injuries after inhalation	:	No symptoms expected during normal handling. Inhalation of crushed capsules may cause respiratory irritation lowering of blood pressure (resulting in dizziness, fatigue and headache), change in heart rhythm and gastrointestinal disorders.
Symptoms/injuries after skin contact	:	No symptoms are expected during normal handling. Skin contact with the content of the crushed capsules may cause skin irritation including swelling and redness.
Symptoms/injuries after eye contact	:	No symptoms are expected during normal handling. Eye contact with crushed capsules may cause eye irritation.
Symptoms/injuries after ingestion	:	In the event that the substance ingested symptoms may include: lowering of blood pressure (resulting in dizziness, fatigue and headache); change in heart rhythm; gastrointestinal disorders. May cause harm to the unborn child or to breast-feeding children

DELAYED AND IMMEDIATE EFFECTS AND ALSO CHRONIC EFFECTS FROM SHORT- AND LONG-TERM EXPOSURE:

Acute toxicity	:	Not classified
Skin corrosion/irritation	:	If loose product comes into contact with skin this product may be irritating to skin based on the known hazards of the components.
Serious eye damage/irritation	:	If loose product comes into contact with eyes this product may be irritating to eyes based on the known hazards of the components.
Respiratory or skin sensitization	:	Based upon the known hazards of the components, this product is not anticipated to cause respiratory or skin sensitization.
Germ cell mutagenicity	:	A component of this product (hydrochlorothiazide) has been shown to cause mutagenicity in an *in vitro* Chinese Hamster Ovary Sister Chromatid Exchange (clastogenicity) test and an *in vitro* Mouse Lymphoma Cell assay. There is no known *in vivo* mutagenicity data available for this component and the mixture itself has not been tested for mutagenicity in *in vivo* or *in vitro* mutagenicity studies. Classification is normally reserved for substances showing at least some *in vivo* data indicating the need for classification, with the support of *in vitro* data. Given that *in vivo* data cannot be located, but there are a number of positive *in vitro* studies in different animals and animal tissues, to be cautious, if the classification criteria were applicable to this product, the product would be classified as a potential germ cell mutagen to be cautious.
Carcinogenicity	:	Titanium dioxide is possibly carcinogenic to humans (IARC 2B).

Reproductive toxicity : Studies in animals have shown that repeated doses of a component of this material causes embryo and fetotoxic effects. This is similar to other beta-blocking drugs which are known to cause harm to the unborn child. Fetal and neonatal toxicity in babies born to women receiving treatment during pregnancy has been reported. This component may also appear in breast milk. Although the effects were seen in situations where mothers were purposefully treated with the material, it is unclear if these effects would be likely due to anticipated workplace exposure. However, if the classification criteria were applicable to this product, then it would be cautious to classify the product as potentially harmful to the unborn child and to breastfed babies.

A combination of metoprolol tartrate (a similar component to the active material) and hydrochlorothiazide produced no adverse effects on the fertility and reproductive performance of male and female rats at doses of up to 200/50 mg/kg/day.

Specific target organ toxicity (single exposure) : No classifiable target organ effects after single exposure are anticipated based on the known hazards of the components. If loose product (not intended to be formed during occupational use) is inhaled, it may cause respiratory tract irritation or Central Nervous System (CNS) effects.

Specific target organ toxicity (repeated exposure) : No classifiable target organ effects after repeated exposure are anticipated based on the known hazards of the components.

Aspiration hazard : Not anticipated to be an aspiration hazard based on the nature of the material.

NUMERICAL MEASURES OF TOXICITY:

Product Data	
LD50 oral rat	Not available
LD50 dermal rabbit	Not available
LC50 Inhalation rat	Not available

Metoprolol succinate (94818-47-4)	
LD50 oral mouse	1500 mg/kg
LD50 dermal rabbit	Not available
LC50 inhalation mouse (ppm)	Not available

Hydrochlorothiazide (58-93-5)	
LD50 oral mouse	1175 mg/kg
LD50 dermal rabbit	Not available
LC50 inhalation rat	Not available

Titanium dioxide (13463-67-7)	
LD50 oral mouse	10,000 mg/kg
LD50 dermal rabbit	10,000 mg/kg
LC50 inhalation rat	6820 mg/m3/4H

Starch (9005-25-8)	
LD50 oral rat	Not available
LD50 dermal rabbit	Not available
LC50 inhalation rat	Not available

ATE Mixture:

Oral: >2000 mg/kg

Dermal: >5000 mg/kg

Inhalation: >5000 mg/m^3/4H

SECTION 12: Ecological information

12.1. Toxicity

Ecology - general : Harmful to aquatic organism, may cause long-term adverse effects in the aquatic environment, based on information available on the active ingredient: Metoprolol succinate:

Type and Species	*Value*
EC50 (Green algae) biomass	22.8 mg/L/72H
ErC50 (Green algae) (OECD 201)	58.3 mg/L/72H
NOEC (Green algae) growth rate (OECD 201)	7.5 mg/L/72H
EC50 (Daphnia magna) (OECD 202)	120 mg/L/48H

NOEC (Daphnia magna) (OECD 202)	30 mg/L/48H
LC50 (Rainbow trout) (OECD 203)	130 mg/L/96H
NOEC (Rainbow trout) (OECD 203)	32 mg/L/96H

12.2. Persistence and degradability

Persistence and degradability	Not readily biodegradable

12.3. Bioaccumulative potential

Bioaccumulative potential	The product has a low potential for bioaccumulation.

12.4. Mobility in soil

Ecology - soil	No additional information available

12.5. Other adverse effects

No additional information available

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste disposal recommendations : Dispose of contents/container in accordance with local/regional/international regulations. It is recommended that if permitted in your jurisdiction that the waste material be disposed of via high-temperature incineration.

Contaminated packaging: Empty container will retain product residue. Observe all hazard precautions.

SECTION 14: Transport information

In accordance with DOT

14.1 UN Number: Not applicable

14.2 UN Proper shipping name: Not applicable

Additional information

Other information : No supplementary information available.

Transport by sea

No additional information available

Air transport

No additional information available

SECTION 15: Regulatory information

15.1. US Federal regulations

TSCA Regulations (40 CFR 710): This product is a drug and ix exempt from the TSCA Regulation when manufactured, processed, or distributed in commerce for use as a drug.

CERCLA and SARA Regulations (40 CFR 302, 355, 370 and 372): This product does not contain any chemicals subject to applicable reporting requirements under these regulations.

Other Regulations Considered:

RCRA - Discarded product is not considered a “Hazardous Waste” under RCRA (40 CFR 261).

15.2. International regulations

CANADA

Not determined

EU-Regulations

Not determined

Classification according to Regulation (EC) No. 1272/2008 [CLP]

Not determined

Classification according to Directive 67/548/EEC or 1999/45/EC

Not determined

15.2.2. National regulations

No additional information available

15.3. US State regulations

California Proposition 65: This product does not contain a listed chemical.

SECTION 16: Other information

References : Available upon request

Other information : None.

Full text of classifications see Section 3:

Acute Tox. 4 (Oral)	Acute toxicity (oral) Category 4
Eye Irritant 2A	Eye Irritant Category 2A
Skin Irritant 2	Skin Irritant Category 2
Muta Cat 2	Germ Cell Mutagen Category 2
Carc Cat 2	Carcinogen Category 2
Repro Cat 2	Reproductive toxicity Category 2
STOT SE 3 RI	Specific Target Organ Toxicity – Single Exposure – Respiratory Irritant
STOT SE 3 Narc	Specific Target Organ Toxicity – Single Exposure – Narcotic effects

Full List of Acronyms used in SDS:

ACGIH - American Conference of Governmental Industrial Hygienists; ADNR – Regulation for the Carriage of Dangerous Substances on the Rhine (EU); ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; ATE – Acute Toxicity Estimate; CAS# - Chemical Abstract Services Number; CERCLA – Comprehensive Environmental Response, Compensation and Liability Act; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EC/EU – European Community/European Union; EC50 – Effective Concentration 50%; ErC50 – Effective Concentration (rate) 50%; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC – International Agency for Research on Cancer; IATA – International Air Transport Association; ICAO – International Civil Aviation Organization; IMDS – International Material Data System; LC50/LD50 – Lethal Concentration/Lethal Dose 50%; NOEC – No Observed Effect Concentration; OECD – Organisation for Economic Cooperation and Development; OSHA -Occupational Safety and Health Administration; PPE – Personal Protective Equipment; RCRA – Resource Conservation and Recovery Act; SARA – Superfund Amendments and Reauthorization Act; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TLV- Threshold Limit Value; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; UN – United Nations; WHMIS - Workplace Hazardous Materials Information System

Date of Preparation: January 5, 2016 Revision 1

SDS US (GHS HazCom 2012)

This SDS is intended to provide a brief summary of our knowledge and guidance regarding the use of this material in an industrial setting. It is not meant to be an all-inclusive document on worldwide hazard communication regulations. This information is offered in good faith. Each user of this material needs to evaluate the conditions of use and design the appropriate mechanisms to prevent employee exposures, property damage or release to the environment. Refer to Product Monograph for pharmaceutical use information.