SAFETY DATA SHEET

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1 Product Identifier

TOPROL XL TABLETS

Details of the supplier of the safety data sheet : Melinta Therapeutics LLC.
44 Whippany Road, Suite 280, Morristown, NJ 07960
Main: +1 844-MED-MLNT (1-844-633-6568)
E-mail: medinfo@melinta.com

Telephone number Triumvirate: +1 (800) 966-9282 (24-hour availability)

Alternative Names

Metoprolol succinate CR Tablets
Metoprolol succinate extended-release tablets
Betaloc ZOK tablets

CAS No. : Not applicable

1.2 Relevant identified uses of the substance or mixture and uses advised against

Use of the Substance/Mixture : Beta-adrenergic receptor blocking agent used as an anti-hypertensive and anti-anginal.

SECTION 2. HAZARDS I D E N T I F I C A T I O N

GHS Classification

Skin corrosion/irritation	:	Category 2
Reproductive toxicity	:	Category 1A
Effects on or via lactation	:	
Acute aquatic toxicity	:	Category 3
Chronic aquatic toxicity	:	Category 3

GHS label elements

Hazard pictograms :



Signal word : Danger

Hazard statements :
H315 Causes skin irritation.
H360 May damage fertility or the unborn child.
H362 May cause harm to breast-fed children.
H412 Harmful to aquatic life with long lasting effects.

Precautionary statements :

Prevention:

P201 Obtain special instructions before use.

P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust or mist.
P264 Wash skin thoroughly after handling.
P273 Avoid release to the environment.
P280 Wear protective gloves.
P281 Use personal protective equipment as required.

Response:

P302 + P352 IF ON SKIN: Wash with plenty of soap and water.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P332 + P313 If skin irritation occurs: Get medical advice/ attention.
P362 Take off contaminated clothing and wash before reuse.

Disposal:

P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification

May cause eye irritation.
May form an explosible dust-air mixture if dispersed.
See Section 11.

SECTION 3. COMPOSITION / INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Hazardous components

Chemical name	CAS-No.	Concentration (% w/w)
Metoprolol succinate	98418-47-4	>= 20 - < 30

SECTION 4. FIRST AID MEASURES

If inhaled : Remove patient from exposure.
Obtain medical attention if ill effects occur.

In case of skin contact : Wash skin with water.
If symptoms (irritation or blistering) occur obtain medical attention.

In case of eye contact : Irrigate with eyewash solution or clean water, holding the eyelids apart, for at least 10 minutes.
Obtain medical attention if ill effects occur.

If swallowed : Wash out mouth with water and give 200-300ml of water to drink.
Do NOT induce vomiting as a First-Aid measure.
Obtain medical attention if ill effects occur.

Most important symptoms and effects, both acute and delayed : Refer to sections 2 and 11
Causes skin irritation.
May damage fertility or the unborn child.

May cause harm to breast-fed children.

Notes to physician : Symptomatic treatment and supportive therapy as indicated.
For further details consult the prescribing information.

SECTION 5. FIREFIGHTING MEASURES

Suitable extinguishing media : water spray, foam, dry powder or CO2.

Unsuitable extinguishing media : Avoid high pressure media which could cause the formation of a potentially explosible dust-air mixture.

Specific hazards during firefighting : If involved in a fire, it may burn and emit noxious and toxic fumes.

Special protective equipment for firefighters : A self-contained breathing apparatus and suitable protective clothing should be worn in fire conditions.
Prevent fire extinguishing water from contaminating surface water or the ground water system.

SECTION 6. ACCIDENTA RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures : Avoid dispersal of dust in the air.
Ensure suitable personal protection during removal of spillages.
See Section 8.

Environmental precautions : Prevent entry into drains, sewers or watercourses.
Collect spillage.

Methods and materials for containment and cleaning up : Transfer spilled tablets to a suitable container for disposal.
Wash the spillage area with water.
Avoid release to the environment.

See section 13.

SECTION 7. HANDLING AND STORAGE

Advice on safe handling : Avoid contact with skin and eyes.
Wash hands after use.
Minimize dust generation and accumulation.
The product may form flammable dust clouds in air, if dust from crushed tablets is allowed to accumulate.

Conditions for safe storage : Keep container tightly closed.

Recommended storage temperature : < 30 °C

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Metoprolol succinate	98418-47-4	TWA	0.5 mg/m3	COM; HYG

Engineering measures : The specific controls will depend on local circumstances and should be based on the risk assessment. Appropriate controls to reduce exposure may include engineering controls, for example ventilation, procedural controls and the use of personal protection equipment.

Prevent entry into drains, sewers or watercourses.
See Section 6 for environmental precautions.

Personal protective equipment

Respiratory protection : Use an air fed hood if the risk assessment does not support the selection of other protection.

Eye protection : Use safety glasses to protect against direct contact with the product if the risk assessment does not support the selection of other protection.

Skin and body protection : Use impervious clothing to protect against direct contact with the product or for repeated, excessive handling use full chemical protective suit if the risk assessment does not support the selection of other protection. Use impervious protective gloves to protect against direct contact with the product. If the product is dissolved or wetted use a glove material that is resistant to the solvent/liquid.

Protective measures : Decisions about whether the use of personal protective equipment (PPE) is appropriate as part of the control strategy should be based on the workplace risk assessment and should take account of local legislative requirements for selection and use. There are multiple factors that will affect the specific requirements such as amount and concentration of the material, duration of exposure, frequency of exposure, external environmental conditions, the task, the user etc.
All the information above should not be used in isolation and should be considered in the context of the workplace risk assessment on a case-by-case basis.

The recommended personal protective equipment (PPE) is based on preventing the potential adverse health effects from exposure to the active pharmaceutical ingredient (API). The risk of exposure to the API in the formulation/product needs to be taken into consideration.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	coated tablets
Color	:	white to off-white
Odor	:	No data available
Odor Threshold	:	No data available
pH	:	No data available
Melting point/range	:	No data available
Initial boiling point and boiling range	:	No data available
Flash point	:	No data available
Evaporation rate	:	No data available
Flammability (solid, gas)	:	No data available
Upper explosion limit	:	No data available
Lower explosion limit	:	No data available
Vapor pressure	:	No data available
Relative vapor density	:	No data available
Relative density	:	No data available
Solubility(ies)		
Water solubility	:	No data available
Solubility in other solvents	:	No data available
Partition coefficient: n-octanol/water	:	No data available
Auto-ignition temperature	:	No data available
Decomposition temperature	:	No data available
Viscosity		
Viscosity, dynamic	:	No data available
Viscosity, kinematic	:	No data available
Explosive properties	:	No data available
Oxidizing properties	:	No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity	:	No known reactivity hazard under normal conditions.
Chemical stability	:	Stable under normal conditions.
Possibility of hazardous reactions	:	None known.
Conditions to avoid	:	No conditions producing hazardous situations known.
Incompatible materials	:	None known.
Hazardous decomposition products	:	No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

11.1.1 Acute toxicity

Not classified based on available information.

Product:

Acute oral toxicity	:	Remarks: Low acute toxicity.
Acute inhalation toxicity	:	Remarks: May cause effects as described under single exposure. (STOT)
Acute dermal toxicity	:	Remarks: No information available.

Components:

Metoprolol succinate:

Acute oral toxicity	:	LD50 Oral (Rat): 2,000 - 3,750 mg/kg
Acute inhalation toxicity	:	Remarks: May cause effects as described under single Exposure (STOT)
Acute dermal toxicity	:	Remarks: No information available.

11.1.2 Skin corrosion/irritation

Causes skin irritation.

Product:

Remarks: Will cause skin irritation.

Components:

Metoprolol succinate:

Result: Irritating skin.

11.1.3 Serious eye damage/eye irritation

Not classified based on available information.

Product:

Remarks: No information available.

Components:

Metoprolol succinate:

Remarks: May cause eye irritation.
May cause excessive watering of the eye (lachrymation).

11.1.4 Respiratory or skin sensitization

Skin sensitization

Not classified based on available information.

Respiratory sensitization

Not classified based on available information.

Product:

Remarks: No information available.

Components:

Metoprolol succinate:

Remarks: Rare cases of skin sensitization have been reported.

11.1.5 Germ cell mutagenicity

Not classified based on available information.

Product:

Germ cell mutagenicity - Assessment : No information available.

Components:

Metoprolol succinate:

Germ cell mutagenicity - Assessment : There is no evidence of genotoxic potential in in vitro and in vivo tests.

11.1.6 Carcinogenicity

Not classified based on available information.

Product:

Carcinogenicity - Assessment : No information available.

Components:

Metoprolol succinate:

Carcinogenicity - Assesment : No evidence of carcinogenicity in animal studies.

11.1.7 Reproductive toxicity

May damage fertility or the unborn child.
May cause harm to breast-fed children.

Product:

Reproductive toxicity - Assessment	:	No information available.

Components:

Metoprolol succinate:

Reproductive toxicity - Assessment	:	Studies in animals have shown that repeated doses produce embryo/foeto toxic effects., By analogy with other beta- blockers, Positive evidence of adverse effects on development from human epidemiological studies., Foetal and neonatal toxicity in babies born to women receiving treatment during pregnancy has been reported. Effects on or via lactation

11.1.8 STOT - single exposure

Not classified based on available information.

Product:

Remarks: No information available.

Components:

Metoprolol succinate:

Exposure routes: Inhalation, Oral
Remarks: May cause lowering of blood pressure (resulting in dizziness, fatigue, and headache), change in heart rhythm and gastrointestinal disorders.

11.1.9 STOT - repeated exposure

Not classified based on available information.

Product:

Remarks: No information available.

Components:

Metoprolol succinate:

Remarks: May cause effects as described under single exposure. (STOT)

11.1.10 Aspiration toxicity

Not classified based on available information.

Components:

Metoprolol succinate:

No information available.

Further information

Product:

Remarks: This health hazard assessment is based on a consideration of the composition of this product.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Product:

Ecotoxicology Assessment

Chronic aquatic toxicity : Harmful to aquatic life with long lasting effects.
Remarks: No information on this formulation. The following information refers to Metoprolol succinate

Components:

Metoprolol succinate:

Toxicity to fish : LC50 (Oncorhynchus mykiss (rainbow trout)): 130 mg/l
Exposure time: 96 H
Test Type: static test
Method: OECD Test Guideline 203

NOEC (Oncorhynchus mykiss (rainbow trout)): 32 mg/l
Exposure time: 96 H
Test Type: static test
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): 120 mg/l
Exposure time: 48 H
Test Type: static test
Method: OECD Test Guideline 202

NOEC (Daphnia magna (Water flea)): 30 mg/l
Exposure time: 48 H
Test Type: static test
Method: OECD Test Guideline 202

Toxicity to algae : ErC50 (Selenastrum capricornutum (green algae)): 58.3 mg/l
Exposure time: 72 H
Test Type: Growth inhibition
Method: OECD Test Guideline 201

NOEC (Selenastrum capricornutum (green algae)): 7.5 mg/l
Exposure time: 72 H
Test Type: Growth inhibition
Method: OECD Test Guideline 201

Toxicity to bacteria : EC50 (Sewage sludge organisms): > 100 mg/l
Exposure time: 3 H
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Ecotoxicology Assessment

Chronic aquatic toxicity : Harmful to aquatic life with long lasting effects.

Persistence a n d degradability

Components:

Metoprolol succinate:

Biodegradability : Remarks: Not rapidly degradable.

Bioaccumulative potential

Components:

Metoprolol succinate:

Bioaccumulation : Remarks: The substance has low potential for bioaccumulation.

Mobility in soil

Components:

Metoprolol succinate:

Mobility : Remarks: Water solubility >= 1 mg/l.

Distribution among environmental compartments : Remarks: No information available.

Other adverse effects

No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal m e t h o d s

Waste from residues : Disposal should be in accordance with local, state or national legislation.
Waste, even small quantities, should never be poured down drains, sewers or water courses.
Dispose of contents/ container to an approved incineration plant.

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

SECTION 14. TRANSPORT INFORMATION

Not classified as dangerous in the meaning of transport regulations.

SECTION 15. REGULATORY INFORMATION

Safety, health, and environmental regulations/legislation specific for the substance or mixture

In order to comply with legal duties, it is necessary to consult local and national legislation.

Prohibition/Licensing Requirements	:	There is no applicable prohibition or notification/licensing requirements, including for carcinogens under Commonwealth, State or Territory legislation.

The components of this product are reported in the following inventories:

REACH	:	Not listed
DSL	:	This product contains the following components that are not on the Canadian DSL nor NDSL.
Metoprolol succinate		98418-47-4
AICS	:	Not listed
ENCS	:	Not listed
ISHL	:	Not listed
IECSC	:	Not listed
TCSI	:	Not listed
TSCA	:	Not On TSCA Inventory

SECTION 16. OTHER INFORMATION

Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; COM – In-house occupational exposure limit; CPR - Controlled Products Regulations; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; HYG – Analytical method for occupational exposure monitoring; IARC - International Agency for Research on Cancer; IATA
- International Air Transport Association; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organization for Standardization; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent

Bioaccumulative and Toxic substance; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorization and Restriction of Chemicals; SADT - Self- Accelerating Decomposition Temperature; SDS - Safety Data Sheet; Sen – Capable of causing respiratory sensitization; Sk – Can be absorbed through skin, thus contributing to systemic effects; STEL – Short-term exposure limit 15-minutes time-weighted average; TLV – Threshold Limit Value (ACGIH); TLV-C – Threshold Limit Value Ceiling limit (ACGIH); TSCA - Toxic Substances Control Act (United States); TWA – Long-term exposure limit 8h time-weighted average; UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

Further information

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information, and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal, and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.