SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

Contact information

General

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Product identifier	Treprostinil
Synonyms	Treprostinil Sodium; [[(1R,2R,3aS,9aS)-2,3,4,9,9a-hexahydro-2-hydroxy-1-[(3S0-3-hydroxyoctyl]-1H-benz[f] inden-5-yl]oxy]acetic acid
Trade names	Treprostinil Sodium Injection
Chemical family	Mixture - contains a prostacyclin analog
Relevant identified uses of the substance or mixture and uses advised against	Formulated pharmaceutical product/mixture packaged in final form for patient use; used for the treatment of pulmonary hypertension.
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product/mixture. Workers manufacturing this product/mixture should consult the SDS of each hazardous ingredient for hazard information and handling recommendations.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture	**Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada.** Consult prescribing/packaging information. **The classification and labeling listed below is for bulk drug product.**
Globally Harmonized System [GHS]	Not classified

SECTION 2 - HAZARDS IDENTIFICATION …continued

Label elements

GHS hazard pictogram	None required
GHS signal word	None required
GHS hazard statements	None required
GHS precautionary statements	None required

Other hazards

Treprostinil is a synthetic analog of the naturally occurring prostaglandin, prostacyclin. It is a direct vasodilator of pulmonary and systemic arterial vascular beds that also inhibits platelet aggregation, thereby alleviating pulmonary hypertension. This product is intended to be given IV. The most commonly reported adverse effects include infusion-site reactions, rash/itching, headache, jaw, chest, and back pain, infection/flu like symptoms, fever, weakness, gastrointestinal disturbances, hypotension, edema, dizziness, insomnia, anxiety, flushing, nose bleeds, throat irritation and/or pain, and runny nose. Direct contact with the skin may cause vasodilation resulting in significant redness and possibly a burning sensation.

Note

This mixture does not meet criteria for classification under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA). Nevertheless, it should be handled with caution as it contains a potent pharmaceutical compound.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Treprostinil sodium (Par)	289480-64-4	N/A	<2%	ATO3: H301; STOT-R1: H372; RT2: H361d

Note

The substance listed above is considered hazardous. The remaining components are not hazardous and/or present at amounts below reportable limits.

Amounts are listed as ranges; the exact percentage of composition is withheld as a trade secret. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	No. If exposed or concerned: Get medical advice/attention.

SECTION 4 - FIRST AID MEASURES …continued

Eye Contact	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.
Skin Contact	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion	Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.
Most important symptoms and effects, both acute and delayed	See Sections 2 and 11.
Indication of immediate medical attention and special treatment needed, if necessary	Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Specific hazards arising from the substance or mixture	No information identified. May emit carbon monoxide and carbon dioxide.
Flammability/ Explosivity	No explosivity or flammability data identified. As product is an aqueous solution, it is not expected to be flammable or explosive.
Advice for firefighters	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If vials are opened, crushed or broken, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe dust/mist/vapors/spray.
Environmental precautions	Do not empty into drains. Avoid release to the environment.

SECTION 6 - ACCIDENTAL RELEASE MEASURES…continued

Methods and material for containment and cleaning up	If vials are crushed or broken, DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	If vials are opened, crushed or broken, drug substance may be released. Minimize dust generation and accumulation. Follow recommendations for handling cytotoxic antineoplastic agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Wash thoroughly after handling. Avoid breathing dust.
Conditions for safe storage including any incompatibilities	Store at controlled room temperature 20°C to 25°C (68°F to 77°F).
Specific end use(s)	Pharmaceutical.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note	Wash hands, face and other potentially exposed areas immediately in the event of physical contact. Dispose of broken vials/syringes in a sharps container.

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Treprostinil sodium (Par)	--	--	--

Exposure/Engineering controls	None required for normal handling of packaged product. If handling bulk product and/or vials are open/crushed/broken: Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Utilize closed and sealed systems whenever possible. Solutions used for procedures where aerosolization may occur (e.g., spraying, pumping, open transfers,) must be handled using an engineered local exhaust ventilation (LEV) and/or enclosure or isolator system. Control the potential for spills and leaks by securing all connections. Use clean-in-place systems.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION…continued

Respiratory protection	None required for normal handling of packaged product. If handling bulk product and/or vials are open/crushed/broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required when performing aerosol generating operations. An airline respirator or self-contained breathing apparatus (SCBA) and disposable outerwear is required for spill cleanup.
Hand protection	None required for the normal handling of packaged product. Wear nitrile or other impervious gloves if skin contact with tablets is possible.
Skin protection	Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.
Eye/face protection	None required for normal handling of packaged product. Wear safety glasses with side shields if eye contact is likely, e.g., during clean up of large spill. Base the choice of protection on the job activity and potential for contact with eyes and face.
Environmental Exposure Controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
Other protective measures	Wash hands in the event of contact with tablets, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Sterile solution in glass vials
Color	Clear
Odor	No information identified.
Odor threshold	No information identified.
pH	6.0-8.0
Melting point/ freezing point	90°C-100°C
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.
Evaporation rate	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Flammability (solid, gas)	Not applicable.
Upper/lower flammability or explosive limits	Not applicable.
Vapor pressure	No information identified
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	No information identified.
Solvent solubility	No information identified.
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.
Other information	
Molecular formula	Not applicable (Mixture)
Molecular weight	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Chemically stable; pharmacological stability not guaranteed beyond expiration date imprinted on package.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note **No data on product formulation. The following information is for treprostinil (the active ingredient) and other ingredients, where applicable.**

Information on toxicological effects

Route of entry May be absorbed by inhalation, skin contact and ingestion.

Acute toxicity

Compound	Type	Route	Species	Dose
Treprostinil sodium (Par)	LD_{50}	Oral	Rat	92 mg/kg
	LD_{50}	IV	Rat	56 mg/kg

Irritation/Corrosion No studies identified.

Sensitization No studies identified.

STOT-single exposure No studies identified.

STOT-repeated exposure/Repeat-dose toxicity For treprostinil, toxicity studies were carried out in rats and dogs for up to 6 months in duration at doses up to 450 and 200 ng/kg/min (648 and 288 µg/kg/day), respectively, administered *via* continuous SC infusion. The primary adverse effects included injection-site reactions, reversible redness of the extremities, and minimal changes in white blood cell counts, bilirubin, and organ/body weights. IH administration of treprostinil to rats and dogs for up to 3 months resulted in various respiratory tract lesions. Rats also developed cardiac changes. A NOAEL for dogs was 107 µg/kg/day. In rats, effects were seen at doses as low as 7 µg/kg/day; NOAEL was not identified.

Reproductive toxicity Treprostinil had no effect on reproduction in rats given SC doses up to 450 ng/kg/min (648 µg/kg/day) or 10 mg/kg/day (route presumed oral). A 32% reduction in pregnancy rate was noted in females treated with 20 mg/kg/day (route presumed oral).

Developmental toxicity No evidence of fetal toxicity was noted in rats following continuous SC infusions of 900 ng/kg/min (1296 µg/kg/day). An increase in post-implantation loss and fetal mortality was noted in rats treated with ≥10 mg/kg/day; NOAELs for maternal and fetal toxicity were 5 mg/kg/day (route presumed oral). In rabbits, SC doses ≥150 ng/kg/min (216 µg/kg/day) were associated with increases in skeletal variations and maternal toxicity. Decreased fetal weights and external tissue and skeletal malformations were noted at 0.5 and ≥1.5 mg/kg/day, respectively; NOAELs for maternal and fetal toxicity were 0.5 mg/kg/day (route presumed oral).

Genotoxicity Treprostinil was not genotoxic *in vitro* (Ames bacterial reverse mutation assay, mouse lymphoma forward mutation assay) or *in vivo* (rat micronucleus test).

Carcinogenicity Oral administration of treprostinil diolamine to mice for 26 weeks at doses up to 20 mg/kg/day did not increase the incidence of tumors. None of the components of this mixture present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.

Aspiration hazard No data available.

Human health data See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Treprostinil sodium (Par)	--	--	--

Persistence and Degradability No data available.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment Not performed.

Other adverse effects No data available.

Note The ecological characteristics of this mixture have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

UN number None assigned.

UN proper shipping name None assigned.

Transport hazard classes and packing group None assigned.

Environmental hazards This product/mixture is not regulated as an environmental hazard or a marine pollutant.

Special precautions for users Due to lack of data, avoid release to the environment.

SECTION 14 - TRANSPORT INFORMATION …continued

Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	Not listed.
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	H301 - Toxic if swallowed. ATO3 - Acute Toxicity (Oral) Category 3. H372 - Causes damage to lungs through prolonged or repeated exposure. STOT-R1 - Specific Target Organ Toxicity Following Repeat Exposure Category 1. H361d - Suspected of damaging the unborn child. RT2 - Reproductive toxicity Category 2.
Sources of data	Information from published literature and internal company data.
Abbreviations	ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PBT - Persistent, Bioaccumulative, and Toxic; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued	Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
Issue Date	2 July 2019
Revisions	This is the first version of this SDS.
Disclaimer	The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions. No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.