SAFETY DATA SHEET

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

Contact information

General

United Therapeutics Corporation
CORPORATE HEADQUARTERS
1040 Spring Street, Silver Spring, MD 20910

RESEARCH TRIANGLE PARK (RTP) OFFICES
55 T.W. Alexander Drive - P.O. Box 14186, RTP, NC 27709

Main: +1 (877) 522-2950 *(Available 8 am - 5 pm EST)*
Fax: +1 (919) 485-8352
E-mail: druginformation@unither.com

Emergency telephone number

Chemtrec *(24-hour availability)*:
+1 (800) 424-9300 (USA and Canada)
+1 (703) 527-3887 (International; collect calls accepted)

Product identifier

Dinutuximab (for injection)

Synonyms

For dinutuximab:
Immunoglobulin G1, anti-(ganglioside GD2) (human-Mus musculus monoclonal ch14.18 heavy chain) disulfide with human-Mus musculus monoclonal ch14.18 light chain, dimer;
Chimeric monoclonal antibody ch14.18;
Chimeric MOAB 14.18;
Human/murine anti-GD2 monoclonal antibody;
Chimeric anti-GD2;
Chimeric mAb 14.18

Trade names

Unituxin®

Chemical family

Mixture - contains a monoclonal antibody

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

Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/ mixture packaged in final form for patient use

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Globally Harmonized System [GHS] Not classified

Label elements

GHS hazard pictogram None required

GHS signal word None required

GHS hazard statements None required

GHS precautionary statements None required

Other hazards Dinutuximab is a chimeric (mouse - human) monoclonal antibody used in combination therapy for treatment of pediatric patients with neuroblastoma. It causes death of melanoma and neuroblastoma cells through both antibody-dependent cell-mediated cytotoxicity and complement-dependent cytotoxicity. The most commonly reported adverse effects observed with dinutuximab use included pain, pyrexia, thrombocytopenia, lymphopenia, infusion reactions, hypotension, hyponatremia, increased alanine aminotransferase, anemia, vomiting, diarrhea, hypokalemia, capillary leak syndrome, neutropenia, urticaria, hypoalbuminemia, increased aspartate aminotransferase, and hypocalcemia.

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).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Dinutuximab	1363687-32-4	N/A	<1%	STOT-R2:H373

Note The ingredients listed above are considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

SECTION 4 - FIRST AID MEASURES …continued

Immediate Medical Attention Needed	Yes. If exposed or concerned: Get medical advice/attention.
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	If swallowed, call a physician immediately. 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.

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	In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If substance is released or spilled, cordon off spill area. Take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe dust.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	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 with an appropriate solvent (see Section 9).
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid contact with eyes, skin and other mucous membranes. Wash thoroughly after handling. Avoid breathing vapor/mist/spray.
Conditions for safe storage including any incompatibilities	Store at 2-8 °C. Keep container tightly closed. Keep away from moisture.
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note Dispose of broken vials/syringes in a sharps container.

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Dinutuximab	United Therapeutics	OEL	70 μg/m^3

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Exposure/Engineering controls	None required for normal handling of packaged product. If handling bulk solution: Control exposures to below the OEL. Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at mist/aerosol/spray-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling. High-energy operations such as spraying or fluidizing should be done within an approved emission control or containment system.
Respiratory protection	None required for normal handling of packaged product. If vials are crushed or broken: choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine handling tasks, an approved and properly fitted air-purifying respirator with appropriate HEPA filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a powered air-purifying respirator equipped with appropriate HEPA filters or combination filters or a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where a lower level of respiratory protection may not provide adequate protection.
Hand protection	None required for normal handling of packaged product. Wear nitrile or other impervious gloves if skin contact with mixture is possible.
Skin protection	None required for normal handling of packaged product. 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	Should not be required during normal handling of packaged product. In case of spill, do not release to drains. Avoid release to the environment.
Other protective measures	Should not be required during normal handling of material.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Solution in single-dose vials
Color	Clear, colorless
Odor	No information identified.
Odor threshold	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

pH	No information identified.
Melting point/ freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
Flash point	Not applicable.
Evaporation rate	No information identified.
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	Soluble in water
Solvent solubility	No information identified.
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	Not applicable.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	Not applicable.
Oxidizing properties	Not applicable.
Other information	
Molecular weight	Not applicable (Mixture)
Molecular formula	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable under recommended handling and storage conditions.

SECTION 10 - STABILITY AND REACTIVITY …continued

Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	Avoid excessive heat. Avoid contact with moisture or water.
Incompatible materials	No information identified.
Hazardous decomposition products	None under normal use conditions.

SECTION 11 - TOXICOLOGICAL INFORMATION

Information on toxicological effects

Route of entry May be absorbed by inhalation and ingestion.

Acute toxicity

Compound	Type	Route	Species	Dose
Dinutuximab	--	--	--	--

Irritation/Corrosion No studies identified.

Sensitization No studies identified.

STOT-single exposure In a combined cardiovascular and respiratory safety pharmacology in male monkeys administered a single IV infusion dose of dinutuximab at 14 mg/kg, increases in blood pressure and heart rate were observed in test article-treated monkeys. In a single dose toxicity study in monkeys administered dinutuximab by IV infusion at 10.5 or 21 mg/kg, test article-related findings included swelling of the genitals (foreskin) at both dose levels during infusion lasting for approximately 2 hours post dose and vomiting within 30 minutes after infusion at the high dose only.

STOT-repeated exposure/Repeat-dose toxicity In a 28-day repeat dose toxicity study in rats, doses of ≥5 mg/kg/day (all doses tested) for 4 days followed by a 3-day dose-free period repeated for 4 weeks resulted in adverse effects on the liver, hematopoietic system, adrenals, and spleen. A NOAEL was not determined.

Reproductive toxicity No studies identified.

Developmental toxicity No studies identified.

Genotoxicity No studies identified.

Carcinogenicity No studies identified.

Aspiration hazard No data available.

Human health data See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Dinutuximab	--	--	--

Persistence and Degradability No data available.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment No data available.

Other adverse effects No data available.

Note The environmental characteristics of this product/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 Based on the available data, this substance is not regulated as an environmental hazard or listed as 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	Not listed
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	Not applicable.
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; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT -

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued	Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System
Issue Date	11 July 2016
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.