SAFETY DATA SHEET

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

Contact information

General

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Product identifier	Rolapitant Injection (1.8 mg/mL in 100-mL volume)
Synonyms	For rolapitant: SCH 619734; (5S)-8(S)-[[1(R)-[3,5-bis(trifluoromethyl)phenyl]ethoxy]methyl]-8-phenyl-1,7-diazaspiro[4.5]decan-2-one
Trade names	None identified
Chemical family	Mixture - contains a spirocyclic lactam
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/ mixture; being investigated to treat post-operative and chemotherapy-induced nausea and vomiting (PONV and CINV, respectively).
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the active pharmaceutical mixture.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture	**The classification and labeling listed below is for bulk drug product.**
Globally Harmonized System [GHS]	Not classified
Label elements	
GHS hazard pictogram	None required
GHS signal word	None required

SECTION 2 - HAZARDS IDENTIFICATION …continued

GHS hazard statements	None required
GHS precautionary statements	None required
Other hazards	Rolapitant is a highly selective neurokinin-1 (NK1) receptor antagonist that acts as an antiemetic drug. It was well-tolerated at high oral and intravenous (IV) doses in clinical trials. Common adverse effects (none of which appeared to be dose-dependent) included mild gastrointestinal disturbances, headache, dizziness, hypotension, and rash. Infusion-related reactions at the infusion site were also noted following IV treatment.
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 has not yet been fully tested.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Rolapitant hydrochloride monohydrate	914462-92-3	N/A	0.1-0.3 %	ATO4: H302

Note The substance(s) listed above are considered hazardous. The remaining components (primarily Water for Injection) are not hazardous and/or present at amounts below reportable limits. 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.
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.

SECTION 4 - FIRST AID MEASURES …continued

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.

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, carbon dioxide, oxides of nitrogen, hydrochloric acid, hydrofluoric acid and other chlorine- and fluorine-containing compounds.
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 material 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 mist/spray.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
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.

SECTION 6 - ACCIDENTAL RELEASE MEASURES …continued

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 breathing mist/spray.

Conditions for safe storage including any incompatibilities Store at USP controlled room temperature (22°C to 25°C) away from incompatible materials. Excursions are permitted at 15°C to 30°C. Avoid extreme temperatures.

Specific end use(s) No information identified.

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 in a sharps container.

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Rolapitant hydrochloride monohydrate	Tesaro	8-hour TWA	1.3 mg/m^3

Exposure/Engineering controls None required for normal handling. If handling bulk product and/or vials are crushed/broken: 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 aerosol-generating points. High-energy operations such as spraying should be done within an approved emission control or containment system.

Respiratory protection None required for normal handling. If handling bulk product and/or vials are crushed/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.

Hand protection Wear nitrile or other impervious gloves if skin contact is possible. When the material is suspended in an organic solvent, wear gloves that provide protection against the solvent.

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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Eye/face protection	None required for normal handling. 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	Translucent white liquid. Packaged in clear cyclic olefin polymer vials or clear glass vials.
Color	Translucent white
Odor	Odorless
Odor threshold	No information identified.
pH	7-8
Melting point/ freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.
Evaporation rate	No information identified.
Flammability (solid, gas)	Not applicable.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	Not applicable.
Vapor density	Not applicable.
Relative density	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Water solubility	Very slightly soluble (for rolapitant drug substance)
Solvent solubility	Freely soluble in DMSO and ethanol (for rolapitant drug substance); Soluble in acetone (for rolapitant drug substance)
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	As an aqueous solution, it is not expected to be explosive.
Oxidizing properties	No information identified.
Other information	
Molecular weight	Not applicable (Mixture)
Molecular formula	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	Stable under normal conditions.
Chemical stability	Stable under normal handling and storage conditions.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	See Section 5 - Hazardous combustion products.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note	**No data on product formulation. The following information is for rolapitant (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
Rolapitant hydrochloride monohydrate	LD_{50}	Oral	Rat (F)	>500 mg/kg
	LD_{50}	Oral	Rat (M)	>2000 mg/kg
	LD_{50}	IP	Rat (F)	>500 mg/kg
	LD_{50}	IP	Rat (M)	>1000 mg/kg

Irritation/Corrosion No data available.

Sensitization No data available.

STOT-single exposure Some mortality and non-specific clinical signs were observed in male and female rats treated orally with single doses of 2000 and 500 mg/kg, respectively.

STOT-repeated exposure/Repeat-dose toxicity In a 3-month repeated oral study with mice, minor liver effects (increased weight and centrilobular vacuolation) were noted in males at all doses tested (≥25 mg/kg/day) and in females at 75 mg/kg/day; increased uterine weights in females were reported at 150 mg/kg/day. An oral NOAEL of 25 mg/kg/day (target organ toxicity) was identified.

In 3- and 6-month repeated oral studies with rats, only minor, mild, and reversible changes (including increased liver weight and centrilobular hypertrophy, minimal thyroid follicular cell hypertrophy, and epididymal epithelial vacuolation) were noted at doses up to 100 mg/kg/day (a NOAEL for target organ toxicity). In a 2-week IV study, no adverse effects were reported in rats treated with up to 18 mg/kg/day (an IV NOAEL).

No adverse effects were reported in monkeys treated orally with up to 30 mg/kg/day for 9 months (considered a NOAEL). In a 1-month repeated oral study, clinical signs including convulsions were noted at doses of 60 mg/kg/day; however, a repeat study found no convulsions at oral doses up to 100 mg/kg/day. In a 2-week GLP study, no adverse effects were reported at IV doses up to 10 mg/kg/day (an IV NOAEL).

Reproductive toxicity Rolapitant did not impair male fertility in rats at oral doses up to 100 mg/kg/day. In females, a reversible decrease in corpora lutea number was noted at an oral dose of 5 mg/kg/day when given during early gestation (NOAEL = 1 mg/kg/day).

Developmental toxicity Rolapitant was not developmentally toxic to the offspring of rats and rabbits treated orally with doses up to 5 and 30 mg/kg/day, respectively. Higher doses were associated with maternal toxicity and related embryo/fetotoxic effects.

Genotoxicity Rolapitant was negative for genotoxicity *in vitro* (bacterial mutagenicity; chromosomal aberration assay in human peripheral blood lymphocytes) and *in vivo* (micronucleus assay in mice).

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Carcinogenicity Rolapitant was not carcinogenic in mice treated orally with up to 150 mg/kg/day in a bioassay. Although a slight (non-significant) increase in benign adrenal tumors and malignant thyroid tumors was observed in rats at doses of 50 and 100 mg/kg/day, respectively, these tumors were determined to be rat-specific and irrelevant to humans. 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
Rolapitant hydrochloride monohydrate	--	--	--

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.

SECTION 14 - TRANSPORT INFORMATION …continued

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 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.
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	ATO4 - Acute Toxicity (Oral) Category 4. H302 - Harmful if swallowed.
Sources of data	Information from published literature and internal company data.

SECTION 16 - OTHER INFORMATION …continued

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 - 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

6 May 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.