

SAFETY DATA SHEET

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

Contact information

General



The Medicines Company
8 Sylvan Way, Parsippany, NJ 07054
Main: +1 (973) 290-6000 or +1 (800) 388-1183 (toll free)
Fax: +1 (973) 656-9898
E-mail: medical.information@themedco.com

Emergency telephone number

+1(888) 977-6326 (*Available at all times*)

Product identifier	Meropenem-Vaborbactam
Synonyms	vaborbactam was previously identified as RPX7009
Trade names	Vabomere
Chemical family	Mixture containing a beta-lactam.
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical product/Formulated pharmaceutical product packaged in final form and intended for the final user; indicated for the treatment of certain types of bacterial infections.
Note	The physical, chemical and ecological properties of this material and/or its ingredients have not been fully characterized. This SDS will be revisited as more data become available.

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]	Respiratory sensitizer - Category 1. Skin sensitizer - Category 1. Irritant (eye) - Category 2.
Label elements	

SECTION 2 - HAZARDS IDENTIFICATION ...continued

GHS hazard pictogram



GHS signal word

Danger

GHS hazard statements

H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled. H317 - May cause allergic skin reaction. H319 - Causes serious eye irritation.

GHS precautionary statements

P261 - Avoid breathing dust. P272 - Contaminated work clothing should not be allowed out of the workplace. P280 - Wear protective gloves/eye protection/face protection. P302 + P352 - IF ON SKIN: Wash with plenty of soap and water. P304 + P340 - IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention. P342 + P311 - If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician. P362 - Take off contaminated clothing and wash before reuse. P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P337 + P313 - If eye irritation persists: Get medical advice/attention.

Other hazards

Meropenem-vaborbactam is a combination of the carbapenem antibiotic meropenem and the beta-lactamase inhibitor vaborbactam. It is indicated for intravenous (IV) treatment of severe Gram-negative bacterial infections, including those resistant to other antibacterial drugs. Adverse effects reported in clinical trials included headache, infusion site reactions, lethargy, dizziness, diarrhea, and nausea.

Meropenem is a beta-lactam antibiotic. Beta-lactam antibiotics have been strongly associated with respiratory and skin sensitization in the workplace.

Note

This mixture is classified as hazardous 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

<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ ELINCS#</u>	<u>Amount</u>	<u>GHS Classification</u>
Meropenem trihydrate	119478-56-7	642-885-1	40-50%	SS1: H317; RS1: H334
Vaborbactam	1360457-46-0	807-463-5	30-40%	Not classified
Sodium carbonate	497-19-8	207-838-8	20-30%	EI2: H319

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS ...continued

Note The ingredients listed above are considered hazardous or are an active ingredient. See Section 16 for full text of EU and GHS classifications. Amounts are listed as ranges; the exact percentage of composition is withheld as a trade secret.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
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	Treat symptomatically and supportively. Epinephrine and supportive measures are recommended if the patient presents with anaphylactic symptoms.

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, and boron-, sulfur-, or sodium-containing compounds.
Flammability/Explosivity	No information identified. High concentrations of finely divided organic particles can explode if ignited.

SECTION 5 - FIREFIGHTING MEASURES ...continued

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 product is released or spilled, 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 If vials are broken or crushed, DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for 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 crushed or broken, dust containing drug substances may be released. Minimize dust generation and accumulation. Follow recommendations for handling bulk formulated/packaged pharmaceutical 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 temperatures (20-25°C).

Specific end use(s) Pharmaceutical.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

**Control Parameters/
Occupational Exposure
Limit Values**

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Meropenem trihydrate	--	--	--
Vaborbactam	--	--	--

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

**Control Parameters/
Occupational Exposure
Limit Values**

...continued

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Sodium carbonate	Czech Republic	TWA-8 HR	5 mg/m ³
	Czech Republic	Ceiling	10 mg/m ³
	Romania	TWA-8 HR	1 mg/mg ³
	Romania	STEL	3 mg/m ³

Exposure/Engineering controls

None required for normal handling of packaged product. If handling bulk product or vials are opened/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 dust-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling of powders. High-energy operations such as milling, particle sizing, 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 handling bulk product or vials are opened/crushed/broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly fitted air-purifying respirator with 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 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. If handling bulk product or vials are opened/crushed/broken: Wear nitrile or other impervious gloves if skin contact is possible. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Skin protection

None required for normal handling of packaged product. If handling bulk product or vials are opened/crushed/broken: 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. If handling bulk product or vials are opened/crushed/broken: Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

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 this substance, 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	Vials containing a powder
Color	White to off-white or pale yellow
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
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)	No information identified.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified.
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	Soluble in aqueous solutions
Solvent solubility	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued

Partition coefficient (<i>n</i>-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	Avoid extreme temperatures.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

**Information on
toxicological effects**

Route of entry	Bulk product may be absorbed through inhalation, skin contact, or ingestion.
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SECTION 11 - TOXICOLOGICAL INFORMATION ...continued

Acute toxicity

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
Meropenem trihydrate	LD ₅₀	IV	Mouse	2650 mg/kg
	LD ₅₀	IV	Rat	2850 mg/kg
Vaborbactam	Maximum Tolerated Dose (MTD)	IV (bolus)	Rat	300 mg/kg
	LD ₅₀	Oral	Rat	4090 mg/kg
Sodium carbonate	LD ₅₀	Oral	Rat	4090 mg/kg
	LD ₅₀	Oral	Mouse	6600 mg/kg

Irritation/Corrosion	Sodium carbonate is an eye irritant. Data assessing reversibility of irritation were not identified.
Sensitization	No specific data were identified, though beta-lactam antibiotics (such as meropenem) are associated with respiratory and skin sensitization.
STOT-single exposure	High osmolality at 1000 mg/kg/day caused severe local effects in the acute bolus IV rat study of vaborbactam. Later studies were conducted by slow IV infusion.
STOT-repeated exposure/Repeat-dose toxicity	In 28-day IV rat studies, no significant effects were noted following administration of a mixture of 500 mg/kg/day meropenem and 1000 mg/kg/day vaboractam. In 28-day IV dog studies, no significant effects were noted following administration of a mixture of 500 mg/kg/day meropenem and 1000 mg/kg/day vaboractam.
Reproductive toxicity	No effects on male or female fertility were noted in rat reproductive toxicity studies for either meropenem or vaborbactam. Vaborbactam was administered at IV doses of up to 1000 mg/kg/day for 28 (male) or 14 (female) days prior to mating. Meropenem was administered for 11 weeks (male) or 2 weeks (female) prior to mating.
Developmental toxicity	No developmental toxicity was reported in rats or rabbits treated at IV doses of up to 1000 mg/kg/day vaboractam during organogenesis. No developmental toxicity was reported in rats or monkeys treated at IV doses of up to 750 or 360 mg/kg/day, respectively, during organogenesis.
Genotoxicity	Vaborbactam was negative in the Ames bacterial mutagenicity, human lymphocyte chromosomal aberration, and mouse micronucleus assays. Meropenem was negative in the Ames bacterial mutagenicity, mammalian cell mutagenicity (CHO HGPRT), mammalian cell cytogenic, and mouse micronucleus assays.
Carcinogenicity	No studies identified. None of the components of the 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

<u>Compound</u>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
Meropenem trihydrate	--	--	--
Vaborbactam	--	--	--
Sodium carbonate	EC ₅₀ /120h	Nitzschia	242 mg/L
	LC ₅₀ /96h	Lepomis macrochirus	300 mg/L [static]
	LC ₅₀ /96h	Pimephales promelas	310-1220 mg/L [static]
	EC ₅₀ /48h	Daphnia magna	265 mg/L

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 environmental characteristics of the formulated product have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods

Dispose of wastes by appropriately permitted chemical waste incinerator in accordance to prescribed federal, state, and local guidelines. 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 onsite 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.

SECTION 14 - TRANSPORT INFORMATION ...continued

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	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	RS1 - Respiratory Sensitizer Category 1. H334 - May cause allergic or asthmatic symptoms or breathing difficulty if inhaled. SS1 - Skin sensitizer Category 1. H317 - May cause an allergic skin reaction. EI2A - Eye irritant Category 2A. H319 - Causes serious eye irritation.
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

SECTION 16 - OTHER INFORMATION ...continued

**Abbreviations
...continued**

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

11 August 2017

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.