SAFETY DATA SHEET

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

<table>
<thead>
<tr>
<th>Par Sterile Products</th>
<th>Emergency telephone number (Chemtrec):</th>
</tr>
</thead>
<tbody>
<tr>
<td>870 Parkdale Road</td>
<td>1-(800) 424-9300 (US and Canada)</td>
</tr>
<tr>
<td>Rochester, M.I. 48307</td>
<td>1-(703) 527-3887 (collect calls accepted)</td>
</tr>
<tr>
<td>T: +1 (800) 828-9393</td>
<td></td>
</tr>
<tr>
<td>F: +1 (201) 829-9222</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:drugsafety@parpharm.com">drugsafety@parpharm.com</a></td>
<td></td>
</tr>
</tbody>
</table>

Product identifier: Colistimethate for Injection, USP

Synonyms: Coly-Mycin® M Parenteral (sterile colismethate sodium, USP); Sodium colistin methanesulfonate

Trade names: Coly-Mycin® M Parenteral

Chemical family: Polypeptide; lyophilized

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

Bulk formulated pharmaceutical product/ Formulated pharmaceutical product packaged in final form for patient use. Used for the treatment of infections.

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

Issue Date: 14 August 2014

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. Please consult the prescribing/packaging information. The classification and labelling listed below is for bulk drug product (colistimethate, lyophilized).

Regulation (EC) 1272/2008 [GHS]: Specific Target Organ Toxicity (repeated exposure) - Category 1. Reproductive Toxicity - Category 2.


Label elements:
SECTION 2 - HAZARDS IDENTIFICATION …continued

CLP/GHS hazard pictogram

**CLP/GHS signal word**

Danger

**CLP/GHS hazard statements**

H372 - Causes damage to the liver, kidneys, and spleen through prolonged or repeated exposure. H361d - Suspected of damaging the unborn child.

**CLP/GHS precautionary statements**

P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P281 - Use personal protective equipment as required. P308 + P313 - If exposed or concerned: get medical advice/attention. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

**Other hazards**

Colistimethate is an antibacterial agent indicated for the treatment of infections caused by gram-negative bacteria. It is intended for intravenous (IV) or intramuscular (IM) administration, at doses of 2.5 to 5 mg/kg (175 to 350 mg for a 70-kg individual). Adverse effects reported with clinical use include transient neurological disturbances (paresthesia, numbness, tingling, itchiness, vertigo/dizziness, slurred speech), nephrotoxicity, difficulty breathing, gastrointestinal discomfort (including potentially serious infections with *C. difficile*), rash, and fever.

Colistimethate has also been formulated for inhaled administration (by a dry powder inhaler) for patients with infections secondary to cystic fibrosis. Preliminary clinical data indicate that significant systemic absorption by inhalation may occur in some individuals.

**US Signal word**

Warning

**US Hazard overview**

Can cause transient neurological effects. May cause damage to the liver, kidneys, and spleen based on animal data. Possible developmental hazard - may cause adverse developmental effects (based on animal data). Substance not yet fully tested.

**Note**

This product is classified as dangerous/hazardous according to directives 67/548/EEC, 1999/45/EC, Regulation EC No 1272/2008 (EU CLP) and applicable US regulations. The GHS classifications are based on Regulation EC 1272/2008 (EU CLP).
### SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS #</th>
<th>EINECS/ELINCS#</th>
<th>Amount</th>
<th>EU Classification</th>
<th>GHS Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colismethate Sodium</td>
<td>8068-28-8</td>
<td>232-516-9</td>
<td>100%</td>
<td>Harmful - Xn: R48/20, R63</td>
<td>STOT R1: H372; RT2: H361d</td>
</tr>
</tbody>
</table>

**Note**
The ingredients listed above are considered hazardous or are the active ingredient. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of EU and GHS classifications. The EU classification is based on Directive 67/548/EEC and the CLP/GHS classification is based on Regulation (EC) 1272/2008.

### 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**  
Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. Refer to current prescribing information or to local poison control information centers.
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 toxic fumes of carbon monoxide, carbon dioxide, oxides of nitrogen, and sulfur-containing compounds.

**Flammability/Explosivity**
No information identified. High concentrations of finely divided organic particles can explode if ignited.

**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**
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**
Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust. Wash thoroughly after handling.

**Conditions for safe storage including any incompatibilities**
Store at 20-25° C (68-77°F) and protect from light.

**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.

Control Parameters/
Occupational Exposure
Limit Values

<table>
<thead>
<tr>
<th>Compound</th>
<th>Issuer</th>
<th>Type</th>
<th>OEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colismethate Sodium</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Exposure/Engineering controls

Control exposures to below the OEL (if available). 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 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

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

Wear nitrile or other impervious gloves if skin contact is possible. When the material is diluted 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.

Eye/face protection

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.

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

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Powder</td>
</tr>
<tr>
<td>Color</td>
<td>White to pale yellow</td>
</tr>
<tr>
<td>Odor</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Odor threshold</td>
<td>No information identified.</td>
</tr>
<tr>
<td>pH</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Flash point</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Upper/lower flammability or explosive limits</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Vapor density</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Relative density</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Water solubility</td>
<td>Soluble.</td>
</tr>
<tr>
<td>Solvent solubility</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Partition coefficient (n-octanol/water)</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No information identified.</td>
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<tr>
<td>Decomposition temperature</td>
<td>No information identified.</td>
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<tr>
<td>Viscosity</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>No information identified.</td>
</tr>
</tbody>
</table>

Other information
SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Molecular weight 1750
Molecular formula \( \text{C}_{58}\text{H}_{105}\text{N}_{16}\text{Na}_{5}\text{O}_{28}\text{S}_{5} \)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity No information identified.
Chemical stability No information identified.
Possibility of hazardous reactions No information identified.
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 May be absorbed by inhalation, skin contact and ingestion.

Acute toxicity

<table>
<thead>
<tr>
<th>Compound</th>
<th>Type</th>
<th>Route</th>
<th>Species</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colistimethate Sodium</td>
<td>LD\text{50}</td>
<td>Oral</td>
<td>Rat</td>
<td>5450 mg/kg</td>
</tr>
</tbody>
</table>

Irritation/Corrosion No local irritation was reported with IV administration of reconstituted solution
Sensitization No studies identified.
STOT-single exposure No studies identified.
STOT-repeated exposure/Repeat-dose toxicity An IM dose of 60 mg/kg/day colistimethate sodium for 30 days was lethal to rats. Convulsions were also reported at this dose. In a 6-month study, IP injections of ≥ 10 mg/kg/day caused dose-dependent mortality in rats. Target organs of toxicity included the kidneys, liver, and spleen.
Reproductive toxicity There were no adverse effects on fertility or reproduction in rats at doses of 9.3 mg/kg/day. Additional details were not identified.

Developmental toxicity Colistimethate sodium given IM during organogenesis to rabbits at 4.15 and 9.3 mg/kg caused foot malformations in approximately 3% of the fetuses. Increased resorptions occurred at 9.3 mg/kg. No adverse developmental effects were reported at these doses in rats. Additional details were not identified.

Genotoxicity The weight of evidence indicates that colistimethate is not likely to be genotoxic.
SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Carcinogenicity  
No studies identified. This substance is not listed by NTP, IARC, ACGIH or OSHA as a carcinogen.

Aspiration hazard  
No studies identified.

Human health data  
See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

<table>
<thead>
<tr>
<th>Toxidity</th>
<th>Compound</th>
<th>Type</th>
<th>Species</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colismethate Sodium</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Additional toxicity information  
No data available.

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 this substance 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 substance is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

UN number  
None assigned.
SECTION 14 - TRANSPORT INFORMATION

- 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 a marine pollutant.
- Special precautions for users: Substance not fully tested - avoid exposure.
- 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 complies with the requirements under US, EU and GHS (EU CLP - Regulation EC No 1272/2008) guidelines. Consult your local/regional authorities for more information.
- Chemical safety assessment: Not conducted.
- OSHA Hazardous: Yes. Warning. Can cause transient neurological effects. May cause damage to the liver, kidneys, and spleen based on animal data. Possible developmental hazard - may cause adverse developmental effects (based on animal studies).
- WHMIS classification: Not required. Drugs are not subject to WHMIS. This substance has been classified in accordance with the hazard criteria of the Controlled Products Regulations and the SDS contains all of the information required by those regulations.
- 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 R phrases and EU Classifications: Xn - Harmful. R48/20 - Danger of serious damage to health by prolonged exposure through inhalation.
SECTION 16 - OTHER INFORMATION …continued

**Full text of H phrases, P phrases and GHS classification**

STOT-R1 - Specific Target Organ Toxicity Following Repeat Exposure Category 1. H372 - Causes damage to liver, kidneys, and spleen through prolonged or repeated exposure. RT2 - Reproductive toxicity Category 2. H361d - Suspected of damaging the unborn child.

**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; 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

**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.