

SAFETY DATA SHEET

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

Contact information

General



Par Sterile Products
870 Parkdale Road, Rochester, M.I. 48307
T: +1 (800) 828-9393
F: +1 (201) 829-9222
E-mail: drugsafety@parpharm.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	Ethacrynate Sodium for Injection, USP
Synonyms	None identified
Trade names	None identified
Chemical family	Mixture - contains a sodium salt of ethacrynic acid, which is a unsaturated ketone derivative of an aryloxyacetic acid.
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical mixture product packaged in final form for patient use. Used as a diuretic.
Note	The physical, chemical, toxicological and ecological properties of this product/mixture 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. Please consult the prescribing/packaging information. The classification and labeling listed below is for bulk Ethacrynate Sodium Injection.
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 Contains ethacrynate sodium, which is used as a diuretic at doses ranging from 50 to 200 mg. Excessive diuresis may cause fluid and electrolyte imbalances, which may cause symptoms such as thirst, weakness, dizziness, confusion, muscle cramps, and nausea. Hearing loss has been also been reported with clinical use.

Note This mixture does not meet criteria for classification under GHS as implemented by Regulation EC No 1272/2008 (EU CLP) and Hazard Communication Standard No. 1910.1200 (US OSHA). Nevertheless, it should be handled with caution as it is pharmacologically active.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ ELINCS#</u>	<u>Amount</u>	<u>GHS Classification</u>
Ethacrynate sodium	6500-81-8	N/A	25-50%	ATO4; H302

Note The ingredient(s) listed above are considered hazardous. The remaining components are non-dangerous/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 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.

SECTION 4 - FIRST AID MEASURES ...continued

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.

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, hydrochloric acid, or other chlorine- and sodium- containing compounds.
Flammability/Explosivity	No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially 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.

SECTION 6 - ACCIDENTAL RELEASE MEASURES ...continued

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	Avoid breathing dust. 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.
Conditions for safe storage including any incompatibilities	Store at controlled room temperature 20 to 25° C (68 to 77 degree (See USP Controlled Room Temperature).
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note Dispose of broken vials in a sharps container.

**Control Parameters/
Occupational Exposure
Limit Values**

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Ethacrynate sodium	--	--	--

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 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

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

Respiratory protection ...continued	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. Double gloves should be considered. When the material is dissolved or 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.
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

Appearance	Lyophilized cake or powder for reconstitution
Color	White
Odor	No information identified.
Odor threshold	No information identified.
pH	5.0 to 7.0
Melting point/ freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
Flash point	Not applicable.
Evaporation rate	Not applicable.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued

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 water
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 weight	325.12 (ethacrynate sodium)
Molecular formula	C ₁₃ H ₁₁ Cl ₂ NaO ₄ (ethacrynate sodium)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	No information identified.
Possibility of hazardous reactions	No information identified.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note No toxicology data for the product/mixture were identified. The following data describe the active ingredient and/or the individual ingredients where applicable.

Information on toxicological effects

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

Acute toxicity

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
Ethacrynate sodium	LD ₅₀	Oral	Rat	1000 mg/kg
	LD ₅₀	Oral	Mice	627 mg/kg
	LD ₅₀	Intravenous (IV)	Mice	175 mg/kg

Irritation/Corrosion No information identified.

Sensitization No information identified.

STOT-single exposure Ototoxicity (hearing loss) was reported in guinea pigs following a single IV dose of 60 mg/kg ethacrynate sodium.

STOT-repeated exposure/Repeat-dose toxicity Ethacrynic acid given orally to mice at dose of 100 mg/kg/day for 21 days decreased blood sugar and liver phosphorylase levels and increased liver glycogen levels.

Reproductive toxicity No reproductive effects were reported in rat and mouse studies. Doses were unspecified.

Developmental toxicity No developmental effects were reported in long-term rat and mouse studies. Doses were unspecified. In a rat teratogenicity study, decreased fetal body weights were reported at 100 mg/kg/day, but not at 20 mg/kg/day.

Genotoxicity No studies identified.

Carcinogenicity Ethacrynate sodium was non-carcinogenic in a lifetime rat study. Additional details were not identified. None of the components 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>
Ethacrynate sodium	--	--	--

Persistence and Degradability Ethacrynate sodium is likely to persist in the environment.

SECTION 12 - ECOLOGICAL INFORMATION ...continued

Bioaccumulative potential	Ethacrynate sodium is not likely to bioaccumulate.
Mobility in soil	No data identified.
Results of PBT and vPvB assessment	Not performed.
Other adverse effects	Ethacrynate sodium is not inherently toxic to aquatic organisms. Details were not identified.
Note	The environmental characteristics of this mixture have not been fully investigated. The above data are for the active ingredient and/or any other ingredient(s) where applicable. 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.
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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 product/mixture is not regulated as an environmental hazard or a marine pollutant.
Special precautions for users	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.
WHMIS classification	Not classified.
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.
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	21 August 2015
Revisions	Updated product identifier in Section 1.

SECTION 16 - OTHER INFORMATION ...continued

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.