1. Product Information

Product Name : Bumetanide Injection, USP 1 mg/4 mL & 2.5 mg/10 mL (0.25 mg/mL)

Chemical Family: Mixture

Intended use: Indicated for the treatment of edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome.

Details of the manufacturer:

MSN Laboratories Private Limited.

Formulation Division, Unit - II,

Sy No 1277 & 1319 to 1324

Nandigama Village & Mandal

Ranga Reddy Dist

Telangana State, India.

PIN 509228

Phone: +91 40 3044 9200

2. Hazards Identification

Emergency Overview:

Bumetanide Injection is a solution containing bumetanide, a loop diuretic with a rapid onset and short duration of action. Clinically, bumetanide is used to treat edema associated with congestive heart failure, hepatic and renal disease. In the workplace, this material should be considered a potent drug and potentially irritating to the eyes and respiratory tract. Based on clinical use, possible target organs include the kidneys, cardiovascular system, and ears (hearing).

Occupational Exposure Potential:

Information on the absorption of this product via inhalation or skin contact is not available. Avoid liquid aerosol generation and skin contact.

Signs and Symptoms:

None known from occupational exposure. In clinical use, the most frequent adverse effects include muscle cramps, dizziness, hypotension, headache, nausea, and encephalopathy (in patients with pre-existing liver disease). Less common adverse effects include impaired hearing, pruritus, electrocardiogram changes, weakness, hives, abdominal pain, arthritic pain, musculoskeletal pain, rash and vomiting.

Medical Conditions Aggravated by Exposure:

Pre-existing allergy to sulfonamides (in clinical use, patients allergic to sulfonamides may show hypersensitivity to bumetanide); pre-existing renal, cardiovascular, gastrointestinal ailments; pre-existing hearing impairment.

3. Composition / Information on Ingredients

C.A.S. No : : 28395-03-1

Molecular Formula : $C_{17}H_{20}N_2O_5S$

Molecular Weight : 364.42 g/mol

Chemical Name : 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoic acid

4. First Aid Measures

Description of First Aid Measures

Eye Contact: Rinse thoroughly with plenty of water, also under the eyelids. If irritation occurs or persists, get medical attention.

Skin Contact: Wash off immediately with soap and plenty of water If skin irritation persists, call a physician.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Move to fresh air. If discomfort occurs, get medical attention.

5. Emergency Overview

Major Health Hazards: No major health hazards are known.

6. Fire Fighting Measures

Flammability:

None anticipated for this aqueous product.

Fire & Explosion Hazard:

None anticipated for this aqueous product.

Extinguishing media:

As with any fire, use extinguishing media appropriate for primary cause of fire.

Special Fire Fighting Procedures:

No special provisions required beyond normal fire fighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.

7. Accidental Release Measures

Spill Cleanup and Disposal:

Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Absorb the liquid with suitable material and clean affected area with soap and water. Dispose of spill materials according to the applicable federal, state, or local regulations.

8. Handling and Storage

Handling:

No special handling required under conditions of normal product use.

Storage:

Store at 20 to 25°C (68 to 77°F), excursions permitted to 15° - 30°C (59° - 86°F) [See USP Controlled Room Temperature]. Protect from light.

Special Precautions:

No special precautions required for hazard control.

9. Exposure Controls/Personal Protection

Personal protective equipment:

Respiratory protection:

Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N95or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Skin protection:

If skin contact with the product formulation is likely, the use of latex or nitrile gloves is recommended.

Eye protection:

Eye protection is normally not required during intended product use. However, if eye contact is likely to occur, the use of chemical safety goggles (as a minimum) is recommended.

Engineering Controls:

Engineering controls are normally not needed during the normal use of this product.

10. Physical and Chemical Properties

Physical State: Liquid

Color: Clear, colorless to slightly yellow solution

Odor: NA

Odor Threshold: NA

pH: 7.0

Melting point/Freezing point: NA

Initial Boiling Point/Boiling Point Range: NA

Evaporation Rate: NA

Flammability (solid, gas): NA

Upper/Lower Flammability or Explosive Limits: NA

Vapor Pressure: NA

Vapor Density: NA

Specific Gravity: NA

Solubility: Bumetanide is slightly soluble in water; soluble in alkaline solutions

Partition coefficient: n-octanol/water: NA

Auto-ignition temperature: NA

Decomposition temperature: NA

11. Stability and Reactivity

Reactivity:

Not determined.

Chemical Stability:

Stable under standard use and storage conditions.

Hazardous Reactions:

Not determined.

Conditions to avoid:

Not determined.

Incompatibilities:

Not determined.

Hazardous decomposition products:

Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx) and nitrogen oxides (NOx).

Hazardous Polymerization:

Not anticipated to occur with this product.

12. Toxicological Information

Acute toxicity: Not determined for the product formulation.

Aspiration Hazard: None anticipated from normal handling of this product.

Dermal Irritation/Corrosion: None anticipated from normal handling of this product.

Ocular Irritation/Corrosion: None anticipated from normal handling of this product. However, inadvertent contact of this product with eyes may produce irritation.

Dermal or Respiratory Sensitization: None anticipated from normal handling of this product. In clinical use, patients allergic to sulfonamides may show hypersensitivity to bumetanide.

Reproductive Effects: Reproduction studies were performed to evaluate general reproductive performance and fertility in rats at oral dosages of 10, 30, 60, or 100 mg/kg/day. The pregnancy rate was slightly decreased in the treated animals; however, the differences were small and not statistically significant. Bumetanide is neither teratogenic nor embryocidal in mice when given in dosages up to 3400 times the maximum human therapeutic dose. Bumetanide was shown to be nonteratogenic, but it has a slight embryocidal effect in rats when given in dosages of 3400 times the maximum human therapeutic dose, and in rabbits at dosages of 3.4 times the maximum human therapeutic dose. In one study, moderate growth retardation and increased incidence of delayed ossification of sternebrae were observed in rats at oral dosages of 100 mg/kg/ day (3400 times the maximum human therapeutic dose). These effects were associated with maternal weight reductions noted during dosing. No such adverse effects were observed at

30 mg/kg/day (1000 times the maximum human therapeutic dose). No fetotoxicity was observed at 1000 to 2000 times the human therapeutic dose. In rabbits, a dose-related decrease in litter size and an increase in resorption rate were noted at oral dosages of 0.1 mg/kg/day and 0.3 mg/kg/day (3.4 and 10 times the maximum human therapeutic dose). A slightly increased incidence of delayed ossification of sternebrae occurred at 0.3 mg/kg/day; however, no such adverse effects were observed at the dose of 0.03 mg/kg/day. The sensitivity of the rabbit to bumetanide parallels the marked pharmacologic and toxicologic effects of the drug in this species. Bumetanide was not teratogenic in the hamster at an oral dosage of 0.5 mg/kg/day (17 times the maximum human therapeutic dose). Bumetanide was not teratogenic when given intravenously to mice and rats at doses up to 140 times the maximum human therapeutic dose.

Mutagenicity: Bumetanide was not mutagenic in various strains of Salmonella typhimurium when tested in the presence or absence of an in vitro metabolic activation system.

Carcinogenicity: An 18-month study showed an increase in mammary adenomas of questionable significance in female rats receiving oral dosages of 60 mg/kg/day (2000 times a 2 mg human dose). A repeat study at the same doses failed to duplicate this finding.

Target Organ Effects: Based on clinical use, possible target organs include the kidneys, cardiovascular system, and ears (hearing). In cats, dogs, and guinea pigs, bumetanide has been shown to produce ototoxicity. In these test animals bumetanide was 5 to 6 times more potent than furosemide and, since the diuretic potency of bumetanide is about 40 to 60 times furosemide, it is anticipated that blood levels necessary to produce ototoxicity in patients will rarely be achieved.

13. Ecological Information

Aquatic Toxicity: Not determined for product.

Persistence/Biodegradability: Not determined for product.

Bioaccumulation: Not determined for product.

Mobility in Soil: Not determined for product.

14. Disposal Considerations

Waste Disposal:

All waste materials must be properly characterized. Further, disposal should be performed in accordance with the federal, state or local regulatory requirements.

Container Handling and Disposal:

Dispose of container and unused contents in accordance with federal, state and local regulations.

15. Transport Information

ADR/ADG/ DOT STATUS: Not regulated

IMDG STATUS: Not regulated

ICAO/IATA STATUS: Not regulated

Transport Comments: None

16. Regulatory Information

RCRA Status: Not Listed.

U.S. OSHA Classification: Target Organ Toxin Possible Irritant.

GHS Classification: In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user.

Hazard Class: Not Applicable

Hazard Category: Not Applicable

Signal Word: Not Applicable

Symbol: Not Applicable

Prevention: P260 - Do not breathe dust/fume/gas/mist/vapors/spray.

Hazard Statement: Not Applicable

Response: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention. Wash hands after handling.

17. Other Information

While the information herein is believed to be reliable, it is furnished without warranty of any kind. It shall be used only as a guide. We assume no liabilities from the use of this product or information contained herein.