Product Name: Bumetanide Injection

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address
Hospira Inc.
275 North Field Drive
Lake Forest, Illinois USA
60045

Emergency Telephone
CHEMTREC: North America: 800-424-9300;
International 1-703-527-3887; Australia (02) 8014 4880

Hospira, Inc., Non-Emergency
224-212-2000

Product Name
Bumetanide Injection

Synonyms
3-(butylamino)-4-phenoxy-5-sulfamoylbenzoic acid; 3-(Aminosulfonyl)-5-(butylamino)-4-phenoxybenzoic acid.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Bumetanide

Chemical Formula
C_{17}H_{20}N_{2}O_{5}S

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include sodium chloride, ammonium acetate, and edetate disodium. Sodium hydroxide is added to adjust the pH.

<table>
<thead>
<tr>
<th>Component</th>
<th>Approximate Percent by Weight</th>
<th>CAS Number</th>
<th>RTECS Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl Alcohol</td>
<td>1</td>
<td>100-51-6</td>
<td>DN3150000</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>0.025</td>
<td>28395-03-1</td>
<td>DG4910000</td>
</tr>
</tbody>
</table>

3. HAZARD INFORMATION

Carcinogen List

<table>
<thead>
<tr>
<th>Substance</th>
<th>IARC</th>
<th>NTP</th>
<th>OSHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl Alcohol</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

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.

4. FIRST AID MEASURES

Eye contact
Remove from source of exposure. Flush with copious amounts of water. If
irritation persists or signs of toxicity occur, seek medical attention. Provide
symptomatic/supportive care as necessary.

Skin contact
Remove from source of exposure. Flush with copious amounts of water. If
irritation persists or signs of toxicity occur, seek medical attention. Provide
symptomatic/supportive care as necessary.

Inhalation
Remove from source of exposure. If signs of toxicity occur, seek medical
attention. Provide symptomatic/supportive care as necessary.

Ingestion
Remove from source of exposure. If signs of toxicity occur, seek medical
attention. Provide symptomatic/supportive care as necessary.

5. 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.

6. 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.

7. HANDLING AND STORAGE

Handling
No special handling required under conditions of normal product use.

Storage
No special storage required for hazard control. For product protection, follow
storage recommendations noted on the product case label, the primary
container label, or the product insert.

Special Precautions
No special precautions required for hazard control.
8. EXPOSURE CONTROLS/PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Component</th>
<th>Type</th>
<th>mg/m³</th>
<th>ppm</th>
<th>µg/m³</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl Alcohol</td>
<td>AIHA WEEL</td>
<td>N/A</td>
<td>10</td>
<td>N/A</td>
<td>8-hr TWA</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>Hospira EEL</td>
<td>N/A</td>
<td>N/A</td>
<td>2</td>
<td>8hr TWA</td>
</tr>
</tbody>
</table>

**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 (N95 or 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.

9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Appearance/Physical State</th>
<th>Solid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Clear, colorless to slightly yellow solution</td>
</tr>
<tr>
<td>Odor</td>
<td>NA</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH:</td>
<td>7.0</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point Range:</td>
<td>NA</td>
</tr>
<tr>
<td>Evaporation Rate:</td>
<td>NA</td>
</tr>
<tr>
<td>Flammability (solid, gas):</td>
<td>NA</td>
</tr>
<tr>
<td>Upper/Lower Flammability or Explosive Limits:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Pressure:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Density:</td>
<td>NA</td>
</tr>
<tr>
<td>Specific Gravity:</td>
<td>NA</td>
</tr>
<tr>
<td>Solubility:</td>
<td>Bumetanide is slightly soluble in water; soluble in alkaline solutions</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water:</td>
<td>NA</td>
</tr>
<tr>
<td>Auto-ignition temperature:</td>
<td>NA</td>
</tr>
<tr>
<td>Decomposition temperature:</td>
<td>NA</td>
</tr>
</tbody>
</table>
Product Name: Bumetanide Injection

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.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity
Not determined for the product formulation. Information for the ingredients is as follows:

<table>
<thead>
<tr>
<th>Ingredient(s)</th>
<th>Percent</th>
<th>Test Type</th>
<th>Route of Administration</th>
<th>Value</th>
<th>Units</th>
<th>Species</th>
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</thead>
<tbody>
<tr>
<td>Bumetanide</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt;6000</td>
<td>mg/kg</td>
<td>Rat, Mouse, Rabbit</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4624</td>
<td>mg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>350</td>
<td>mg/kg</td>
<td></td>
</tr>
<tr>
<td>Bumetanide</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>&gt;200</td>
<td>mg/kg</td>
<td>Rat, Mouse, Rabbit</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70</td>
<td>mg/kg</td>
<td></td>
</tr>
<tr>
<td>Benzyl Alcohol</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>1040 - 2500</td>
<td>mg/kg</td>
<td>Rat, Mouse, Rabbit</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Guinea Pig</td>
</tr>
<tr>
<td>Benzyl Alcohol</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>53</td>
<td>mg/kg</td>
<td>Rat, Mouse</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>324</td>
<td>mg/kg</td>
<td></td>
</tr>
<tr>
<td>Benzyl Alcohol</td>
<td>100</td>
<td>LD50</td>
<td>Dermal</td>
<td>2000</td>
<td>mg/kg</td>
<td>Rabbit</td>
</tr>
<tr>
<td>Benzyl Alcohol</td>
<td>100</td>
<td>LC50</td>
<td>Inhalation</td>
<td>&gt;500</td>
<td>mg/m3</td>
<td>Rat, Mouse</td>
</tr>
</tbody>
</table>

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.
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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.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Not determined for product.

LC50(96 hr) = 460 mg/L in Pimephales promelas for benzyl alcohol
LC50 = 640 mg/L in Leuciscus idus for benzyl alcohol
EC50(24 hr) = 400 mg/L in Daphnia magna for benzyl alcohol
EC50 = 95 mg/L in Chlorella pyrenoidosa for benzyl alcohol

Persistence/Biodegradability

Not determined for product.

Benzyl alcohol was degraded over 90% in a 28-day biodegradation assay in sewage sludge.

Bioaccumulation

Not determined for product.

Mobility in Soil

Not determined for product.
13. 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.

14. TRANSPORTATION INFORMATION

ADR/ADG/DOT STATUS: Not regulated
IMDG STATUS: Not regulated
ICAO/IATA STATUS: Not regulated
Transport Comments: None

15. REGULATORY INFORMATION

USA Regulations

<table>
<thead>
<tr>
<th>Substance</th>
<th>TSCA Status</th>
<th>CERCLA Status</th>
<th>SARA 302 Status</th>
<th>SARA 313 Status</th>
<th>PROP 65 Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl Alcohol</td>
<td>Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

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.

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.
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Get medical attention if you feel unwell.

**EU Classification**
*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance Bumetanide*

Classification(s): Not Applicable
Symbol: Not Applicable
Indication of Danger: Not Applicable
Risk Phrases: Not Applicable
Safety Phrases: S23 - Do not breathe vapor.  
S24/25 - Avoid contact with skin and eyes.  
S37/39 - Wear suitable gloves and eye/face protection.

**16. OTHER INFORMATION:**

Notes:
ACGIH TLV American Conference of Governmental Industrial Hygienists – Threshold Limit Value  
CAS Chemical Abstracts Service Number  
CERCLA US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act  
DOT US Department of Transportation Regulations  
EEL Employee Exposure Limit  
IATA International Air Transport Association  
LD50 Dosage producing 50% mortality  
NA Not applicable/Not available  
NE Not established  
NIOSH National Institute for Occupational Safety and Health  
OSHA PEL US Occupational Safety and Health Administration – Permissible Exposure Limit  
Prop 65 California Proposition 65  
RCRA US EPA, Resource Conservation and Recovery Act  
RTECS Registry of Toxic Effects of Chemical Substances  
SARA Superfund Amendments and Reauthorization Act  
STEL 15-minute Short Term Exposure Limit  
TSCA Toxic Substance Control Act  
TWA 8-hour Time Weighted Average

MSDS Coordinator: Hospira GEHS  
Date Prepared: 09/02/2011  
Obsolete Date: 10/21/2008

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