MATERIAL SAFETY DATA SHEET

Product Name: Tomudex® (Raltitrexed disodium for Injection)

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

| Manufacturer Name and Address | Hospira Inc.  
275 North Field Drive  
Lake Forest, Illinois USA  
60045 |
| Hospira Healthcare Corporation  
1111, Dr. Frederick-Philips Boulevard, Suite 450 & 600  
St-Laurent, Quebec Canada  
H4M 2X6 |
| 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 | Tomudex® (Raltitrexed disodium for Injection) |
| Synonyms | Raltitrexed Powder for Injection; N-{5-[3,4-Dihydro-2-methyl-4-oxoquinazolin-6-ylmethyl(methyl)amino]-2-thenoyl}-L-glutamic acid. |

2. COMPOSITION/INFORMATION ON INGREDIENTS

| Active Ingredient Name | Raltitrexed |
| Chemical Formula | C_{21}H_{22}N_{4}O_{6}S |
| Preparation | Non-hazardous ingredients include mannitol and dibasic sodium phosphate heptahydrate. Hazardous ingredients present at less than 1% include sodium hydroxide. |

<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>Raltitrexed</td>
<td>100</td>
<td>112887-68-0</td>
<td>MA1253250</td>
</tr>
</tbody>
</table>

3. HAZARD INFORMATION

<table>
<thead>
<tr>
<th>Substance</th>
<th>IARC</th>
<th>NTP</th>
<th>OSHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltitrexed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview

Tomudex® (Raltitrexed disodium for Injection) is a powder for solution for injection containing raltitrexed, a folate analog that inhibits thymidylate synthase, an enzyme involved in the synthesis of DNA. Clinically, raltitrexed is used in the treatment of advanced colorectal cancer and other solid cancers. This material is cytotoxic and in the workplace should be considered a possible eye irritant, a potential occupational reproductive hazard and potentially harmful to the fetus. Following an accidental over-exposure, possible target organs may include the gastrointestinal tract, bone marrow, liver, and fetus.

Occupational Exposure

Information on the absorption of this product via inhalation or skin contact is not available.
**Product Name: Tomudex® (Raltitrexed disodium for Injection)**

### Potential
Avoid liquid aerosol or dust generation; avoid skin contact. In the workplace, there is increasing evidence that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these agents if workplace exposures are not properly controlled. The actual risk in the workplace is not known.

### Signs and Symptoms
None known from occupational exposure. None anticipated from normal handling of intact container. In clinical use, raltitrexed produces mild to moderate bone marrow depression with leucopenia, anemia, and thrombocytopenia. The nadir of the white cell count usually occurs 7 to 14 days after treatment. Other adverse effects include gastrointestinal toxicity with nausea and vomiting, diarrhea, anorexia, weakness and malaise, fever, pain, headache, skin rashes, arthralgia, muscle cramps, weight loss, peripheral edema, alopecia, taste disturbance, and conjunctivitis. Mucositis and reversible increases in liver enzyme values may also occur.

### Medical Conditions Aggravated by Exposure
Pre-existing hypersensitivity to raltitrexed; pre-existing gastrointestinal, bone marrow or liver ailments; pregnancy.

### 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 product. However, most organic powders will combust at high temperatures. |
| Fire & Explosion Hazard | None anticipated for this product. As with all powders, avoid the creation of dusty atmospheres. |
| 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 firefighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus. |

### 6. ACCIDENTAL RELEASE MEASURES

| Spill Cleanup and Disposal | For spilled powder, isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Collect the spilled powder using techniques that minimize powder migration or the creation of airborne dust. Clean affected area with soap and water. Dispose of materials according to the applicable federal, state, or local regulations. If a spill occurs after reconstitution, absorb liquid with suitable material and clean affected area with |
Product Name: Tomudex® (Raltitrexed disodium for Injection)

soap and water. Absorb the liquid with an inert absorbent material (e.g. absorbent pad). Dispose of materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Raltitrexed is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastic agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic agents have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate. Consult your hygienist or safety professional for your site requirements.

Avoid ingestion, inhalation, skin contact, and eye contact. If handling a powder, precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilization of this antineoplastic agent. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is required when working with this material.

Storage

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. For product protection, follow temperature and/or light storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions

Persons with known allergies to raltitrexed, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling open containers of this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

<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>Raltitrexed</td>
<td>Not Applicable</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>None Established</td>
</tr>
</tbody>
</table>

Respiratory protection

Respiratory protection is normally not needed during intended product use. However, if the generation of dusts or 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 (N99 or equivalent) is recommended under conditions where airborne dust or 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 intended use of this product.
Product Name: Tomudex® (Raltitrexed disodium for Injection)
9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State: Solid
Color: Sterile lyophilized pale yellow-brown to brown powder
Odor: NA
Odor Threshold: NA
pH: 6.9 TO 7.9 for reconstituted solution
Melting point/Freezing point: 170°C with decomposition
Initial Boiling Point/Boiling Point Range: NA
Evaporation Rate: NA
Flammability (solid, gas): NA
Upper/Lower Flammability or Explosive Limits:
Vapor Pressure: NA
Vapor Density: NA
Specific Gravity: NA
Solubility: NA
Partition coefficient: n-octanol/water: NA
Auto-ignition temperature: NA
Decomposition temperature: NA

10. 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), nitrogen oxides (NOx), and sulfur oxides (SOx).

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>
</tr>
</thead>
<tbody>
<tr>
<td>Raltitrexed</td>
<td>100%</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt;500</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>875-1249</td>
<td>mg/kg</td>
<td>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 with redness and discomfort.

Dermal or Respiratory Sensitization
None anticipated from normal handling of this product.

Reproductive Effects
Fertility studies in the rat indicate that raltitrexed can cause impairment of male fertility. In these studies, fertility returned to normal three months after dosing ceased. In developmental toxicity studies in animals, raltitrexed caused embryolethality and fetal abnormalities in pregnant rats. When this material was given to mice as a single intraperitoneal dosage of 15 mg/kg on gestational day 9, tail defects, cleft palate and other facial defects were noted.

Mutagenicity
Raltitrexed was not mutagenic in the Ames test or in supplementary tests using E. coli or Chinese hamster ovary cells. This material caused increased levels of chromosome damage in an in vitro assay of human lymphocytes. An in vivo micronucleus study in the rat indicated that at cytotoxic dose levels, this material may cause chromosome damage in the bone marrow.

Carcinogenicity
The carcinogenic potential of raltitrexed has not been evaluated.

Target Organ Effects
Following an accidental over-exposure, possible target organs may include the gastrointestinal tract, bone marrow, liver, and fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity
Not determined for product The no-observed-effect-concentration (NOEC)(96hr) = 1000 mg/L in Bluegill sunfish The NOEC(72hr) = 1000 mg/L in Rainbow trout The NOEC(96hr) = 320 mg/L The NOEC(14d) on cell density was 125 mg/L in green algae The NOEC(14d) on growth rate was 1000 mg/L in green algae The NOEC(21d) on cell density was 96 mg/L in blue-green algae The NOEC(21d) on growth rate was 48 mg/L in blue-green algae.

Persistence/Biodegradability
Not determined for product. Raltitrexed was not considered biodegradable.

Bioaccumulation
Not determined for product. Raltitrexed has a low potential for bioaccumulation.

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.
Product Name: Tomudex® (Raltitrexed disodium for Injection)

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>Raltitrexed</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 Possible Eye Irritant
 Classification Target Organ Toxin
 Reproductive Toxin

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.

EU Classification*

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

Classification(s): Not Applicable
Symbol: Not Applicable
Indication of Danger: Not Applicable
Risk Phrases: Not Applicable
Safety Phrases: S23 - Do not breathe vapor.
Product Name: Tomudex® (Raltitrexed disodium for Injection)

S24 - Avoid contact with skin.
S25 - Avoid contact with 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: 11/07/2011
Obsolete Date: 11/11/2010

Disclaimer:
The information and recommendations contained herein are based upon tests believed to be reliable. However, Hospira does not guarantee their accuracy or completeness NOR SHALL ANY OF THIS INFORMATION CONSTITUTE A WARRANTY, WHETHER EXPRESSED OR IMPLIED, AS TO THE SAFETY OF THE GOODS, THE MERCHANTABILITY OF THE GOODS, OR THE FITNESS OF THE GOODS FOR A PARTICULAR PURPOSE. Adjustment to conform to actual conditions of usage may be required. Hospira assumes no responsibility for results obtained or for incidental or consequential damages, including lost profits, arising from the use of these data. No warranty against infringement of any patent, copyright or trademark is made or implied.