1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

Product Identifier
Material Name: Methotrexate Injection, USP (Hospira, Inc.)

Trade Name: Not established
Chemical Family: Mixture

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against
Intended Use: Pharmaceutical product used as Antineoplastic

Details of the Supplier of the Safety Data Sheet
Hospira, A Pfizer Company
275 North Field Drive
Lake Forest, Illinois 60045
1-800-879-3477

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Hospira UK Limited
Horizon
Honey Lane
Hurley
Maidenhead, SL6 6RJ
United Kingdom

Emergency telephone number:
ChemSafe (24 hours): +44 (0)208 762 8322

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture
GHS - Classification
Germ Cell Mutagenicity: Category 2
Reproductive Toxicity: Category 1A

Label Elements

Signal Word: Danger
Hazard Statements:
H360D - May damage the unborn child
H341 - Suspected of causing genetic defects

Precautionary Statements:
P202 - Do not handle until all safety precautions have been read and understood
P281 - Use personal protective equipment as required
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations
3. COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Hazardous</th>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>59-05-2</td>
<td>200-413-8</td>
<td>Acute Tox.3 (H301)</td>
<td>2.5</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Repr.1A (H360D)</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Muta.2 (H341)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>1310-73-2</td>
<td>215-185-5</td>
<td>Skin Corr.1A (H314)</td>
<td>**</td>
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<td>Hydrochloric Acid</td>
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<td>231-595-7</td>
<td>STOT SE 3 (H335)</td>
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<td></td>
<td></td>
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<td>Press. Gas</td>
<td>**</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Acute Tox. 3 (H331)</td>
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<table>
<thead>
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<tr>
<td>Water for Injection</td>
<td>7732-18-5</td>
<td>231-791-2</td>
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<tr>
<td>Sodium chloride</td>
<td>7647-14-5</td>
<td>231-598-3</td>
<td>Not Listed</td>
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</tbody>
</table>

Additional Information:  
* Proprietary  
** to adjust pH  
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.  
In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the CLP/GHS abbreviations mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Description of First Aid Measures  
Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.  
Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
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: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed
Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.
Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed
Notes to Physician: None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture
Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.
Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters
During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures
Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions
Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up
Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.
Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling
Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

Conditions for Safe Storage, Including any Incompatibilities
Storage Conditions: Store as directed by product packaging.
Specific end use(s): Pharmaceutical drug product Antineoplastic
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters
Refer to available public information for specific member state Occupational Exposure Limits.

Methotrexate
Pfizer OEL TWA-8 Hr: 2 µg/m³

Sodium hydroxide
ACGIH Ceiling Threshold Limit: 2 mg/m³
Australia PEAK 2 mg/m³
Austria OEL - MAKs 2 mg/m³
Bulgaria OEL - TWA 2.0 mg/m³
Czech Republic OEL - TWA 1 mg/m³
Estonia OEL - TWA 1 mg/m³
France OEL - TWA 2 mg/m³
Greece OEL - TWA 2 mg/m³
Hungary OEL - TWA 2 mg/m³
Japan - OELs - Ceilings 2 mg/m³
Latvia OEL - TWA 0.5 mg/m³
OSHA - Final PELS - TWAs: 2 mg/m³
Poland OEL - TWA 0.5 mg/m³
Slovakia OEL - TWA 2 mg/m³
Slovenia OEL - TWA 2 mg/m³
Sweden OEL - TWAs 1 mg/m³
Switzerland OEL - TWA 2 mg/m³

Hydrochloric Acid
ACGIH Ceiling Threshold Limit: 2 ppm
Australia PEAK 5 ppm
Austria OEL - MAKs 5 ppm
Belgium OEL - TWA 5 ppm
Bulgaria OEL - TWA 5 ppm
Cyprus OEL - TWA 5 ppm
Czech Republic OEL - TWA 8 mg/m³
Estonia OEL - TWA 5 ppm
Germany - TRGS 900 - TWAs 2 ppm
Germany (DFG) - MAK 2 ppm
Greece OEL - TWA 5 ppm
Hungary OEL - TWA 7 mg/m³
Ireland OEL - TWAs 5 ppm
Italy OEL - TWA 5 ppm

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Engineering Controls:** Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

**Personal Protective Equipment:**

Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

**Hands:**

Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)

**Eyes:**

Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

**Skin:**

Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)

**Respiratory protection:**

Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL (e.g. particulate respirator with a full mask, P3 filter). (Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.)

---

**Material Name:** Methotrexate Injection, USP (Hospira, Inc.)

**Sodium chloride**

<table>
<thead>
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<th>Country</th>
<th>OEL - Ceilings</th>
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</tr>
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<tr>
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<tr>
<td>Malta OEL - TWA</td>
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<td>Netherlands OEL - TWA</td>
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<tr>
<td>Slovenia OEL - TWA</td>
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</tr>
<tr>
<td>Spain OEL - TWA</td>
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<td>7.6 mg/m³</td>
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<td>Switzerland OEL -TWAs</td>
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<td>Vietnam OEL - TWAs</td>
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**Version:** 1.0

**Revision date:** 13-Sep-2016
### 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
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<th>Property</th>
<th>Value</th>
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<tr>
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<td>Decomposition Temperature (°C):</td>
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<td>Vapor Pressure (kPa)</td>
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<td>Evaporation Rate (Gram/s):</td>
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<td>Vapor Pressure (kPa):</td>
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<tr>
<td>Relative Density</td>
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<td>Viscosity</td>
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<td>Flammability:</td>
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<tr>
<td>Autoignition Temperature (Solid) (°C):</td>
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<td>Flammability (Solids):</td>
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<td>Flash Point (Liquid) (°C):</td>
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<tr>
<td>Upper Explosive Limits (Liquid) (% by Vol.):</td>
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</tr>
<tr>
<td>Lower Explosive Limits (Liquid) (% by Vol.):</td>
<td>No data available</td>
</tr>
</tbody>
</table>

### 10. STABILITY AND REACTIVITY

- **Reactivity:** No data available
- **Chemical Stability:** Stable under normal conditions of use.
- **Possibility of Hazardous Reactions**
  - **Oxidizing Properties:** No data available
  - **Conditions to Avoid:** Fine particles (such as dust and mists) may fuel fires/explosions.
  - **Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers
  - **Hazardous Decomposition Products:** No data available

### 11. TOXICOLOGICAL INFORMATION

**Information on Toxicological Effects**

- **General Information:** The information included in this section describes the potential hazards of the individual ingredients.
- **Short Term:** May be absorbed through the skin and cause systemic effects.
11. TOXICOLOGICAL INFORMATION

Long Term: The use of this drug during pregnancy has resulted in birth defects. Animal studies have shown a potential to cause adverse effects on the fetus.

Known Clinical Effects: Adverse effects associated with therapeutic use include gastrointestinal disturbances such as nausea, dyspepsia, and vomiting and gastrointestinal irritation. Effects on blood and blood-forming organs have also occurred.

Acute Toxicity: (Species, Route, End Point, Dose)

Sodium chloride
- Rat Oral LD50 3000 mg/kg
- Mouse Oral LD50 4000 mg/kg

Sodium hydroxide
- Mouse IP LD50 40 mg/kg

Methotrexate
- Rat Oral LD50 135 mg/kg
- Rat Sub-tenon injection (eye) LD50 6mg/kg
- Rat Intravenous LD50 14mg/kg
- Mouse Oral LD50 146mg/kg
- Not Specified Inhalation LC50 > 188ug/m³

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Sodium chloride
- Eye Irritation Rabbit Moderate
- Skin Irritation Rabbit Mild

Sodium hydroxide
- Eye Irritation Rabbit Severe
- Skin Irritation Rabbit Severe

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Methotrexate
- 4 Week(s) Rat Oral 5.6 mg/kg LOAEL Bone marrow, Liver
- 6 Week(s) Rat Oral 4.2 mg/kg LOAEL Bone Marrow, Liver

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Methotrexate
- Embryo / Fetal Development Mouse Oral 10 mg/kg/day NOAEL Not teratogenic
- Embryo / Fetal Development Mouse Oral 25-50 mg/kg/day LOAEL Teratogenic
- Embryo / Fetal Development Monkey Intravenous 30 mg/kg/day LOAEL Developmental toxicity
- Embryo / Fetal Development Rat Intraperitoneal 5 mg/kg LOAEL Fetotoxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)
11. TOXICOLOGICAL INFORMATION

Methotrexate

*In Vitro Chromosome Aberration* Human Lymphocytes Positive
*In Vitro Sister Chromatid Exchange* Mouse Positive
*Unscheduled DNA Synthesis* Human Lymphocytes Positive
*In Vivo Micronucleus* Mouse Positive

**Carcinogen Status:** None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

**Hydrochloric Acid**

IARC: Group 3 (Not Classifiable)

**Methotrexate**

IARC: Group 3 (Not Classifiable)

12. ECOLOGICAL INFORMATION

**Environmental Overview:** Environmental properties have not been thoroughly investigated. Releases to the environment should be avoided.

**Toxicity:** No data available

**Persistence and Degradability:** No data available

**Bio-accumulative Potential:** No data available

**Mobility in Soil:** No data available

13. DISPOSAL CONSIDERATIONS

**Waste Treatment Methods:** Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.
15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

**Methotrexate**
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: developmental toxicity 1/1/1989
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
- EU EINECS/ELINCS List: 200-413-8

**Sodium hydroxide**
- CERCLA/SARA 313 Emission reporting: Not Listed
- CERCLA/SARA Hazardous Substances and their Reportable Quantities: 1000 lb, 454 kg
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
- EU EINECS/ELINCS List: 215-185-5

**Hydrochloric Acid**
- CERCLA/SARA 313 Emission reporting: 1.0 %
- CERCLA/SARA Hazardous Substances and their Reportable Quantities: 5000 lb, 2270 kg
- CERCLA/SARA - Section 302 Extremely Hazardous Substances EPCRA RQs: 500 lb
- CERCLA/SARA - Section 302 Extremely Hazardous Substances: 5000 lb
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
- EU EINECS/ELINCS List: 231-595-7

**Water for Injection**
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- REACH - Annex IV - Exemptions from the obligations of Register: Present
- EU EINECS/ELINCS List: 231-791-2

**Sodium chloride**
- CERCLA/SARA 313 Emission reporting: Not Listed
15. REGULATORY INFORMATION

<table>
<thead>
<tr>
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</tbody>
</table>

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Acute toxicity, oral-Cat.3; H301 - Toxic if swallowed
Acute toxicity, inhalation-Cat.3; H331 - Toxic if inhaled
Skin corrosion/irritation-Cat.1A; H314 - Causes severe skin burns and eye damage
Reproductive toxicity-Cat.1A; H360D - May damage the unborn child
Specific target organ toxicity, single exposure; Respiratory tract irritation-Cat.3; H335 - May cause respiratory irritation
Germ cell mutagenicity-Cat.2; H341 - Suspected of causing genetic defects

Data Sources: Publicly available toxicity information. Safety data sheets for individual ingredients. Pfizer proprietary drug development information.

Revision date: 13-Sep-2016


Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet