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

Pfizer Inc
Pfizer Pharmaceuticals Group
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1-212-573-2222

Pfizer Ltd
Ramsgate Road
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ChemSafe (24 hours): +44 (0)208 762 8322
Contact E-Mail: pfizer-MSDS@pfizer.com

Material Name: Methotrexate Solution for Injection

<table>
<thead>
<tr>
<th>Trade Name:</th>
<th>Methoblastin; Maxtrex; Methotrexat; Lantarel; Trexan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Family:</td>
<td>Mixture</td>
</tr>
<tr>
<td>Intended Use:</td>
<td>Antineoplastic</td>
</tr>
</tbody>
</table>

2. HAZARDS IDENTIFICATION

Appearance: Clear yellow solution

Statement of Hazard: Non-hazardous in accordance with international standards for workplace safety.

Additional Hazard Information:

| Short Term:      | May be absorbed through the skin and cause systemic effects. May be harmful if swallowed. (based on components). |
| Long Term:       | Animal studies have shown a potential to cause adverse effects on the fetus. The use of this drug during pregnancy has resulted in birth defects. |
| 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. |

EU Indication of danger: Not classified

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

PZ00135
3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>59-05-2</td>
<td>200-413-8</td>
<td>Mut. Cat.3;R68</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr. Cat.1;R61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T;R25</td>
<td></td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>1310-73-2</td>
<td>215-185-5</td>
<td>C;R35</td>
<td>###</td>
</tr>
</tbody>
</table>

Additional Information:
* Proprietary
### as required.
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. 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.

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.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

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

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

General Handling:
Avoid contact with eyes, skin and clothing. Avoid breathing vapor or mist. Wash thoroughly after handling. Avoid open handling.

Storage Conditions:
Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

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

Sodium chloride
Latvia OEL - TWA
5 mg/m³
Lithuania OEL - TWA
5 mg/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

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.

Environmental Exposure Controls:
Refer to specific Member State legislation for requirements under Community environmental legislation.

Personal Protective Equipment:
Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

Hands:
Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.

Eyes:
Wear safety glasses or goggles if eye contact is possible.

Skin:
Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Respiratory protection: 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.

9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Physical State:</th>
<th>Solution</th>
<th>Color:</th>
<th>Clear Yellow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.
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

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients.

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

**Methotrexate**
- Rat Oral LD$_{50}$ 135 mg/kg
- Rat Sub-tenon injection (eye) LD$_{50}$ 6 mg/kg
- Rat Intravenous LD$_{50}$ 14 mg/kg
- Mouse Oral LD$_{50}$ 146 mg/kg
- Not Specified Inhalation LC$_{50}$ > 188 ug/m$^3$

**Sodium chloride**
- Rat Oral LD$_{50}$ 3000 mg/kg
- Mouse Oral LD$_{50}$ 4000 mg/kg

**Sodium hydroxide**
- Mouse IP LD$_{50}$ 40 mg/kg

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)
11. TOXICOLOGICAL INFORMATION

Methotrexate

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

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Species</th>
<th>Route</th>
<th>Dose</th>
<th>End Point</th>
<th>Effect(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryo / Fetal Development</td>
<td>Mouse</td>
<td>Oral</td>
<td>10 mg/kg/day</td>
<td>NOAEL</td>
<td>Not teratogenic</td>
</tr>
<tr>
<td>Embryo / Fetal Development</td>
<td>Mouse</td>
<td>Oral</td>
<td>25-50 mg/kg/day</td>
<td>LOAEL</td>
<td>Teratogenic</td>
</tr>
<tr>
<td>Embryo / Fetal Development</td>
<td>Monkey</td>
<td>Intravenous</td>
<td>30 mg/kg/day</td>
<td>LOAEL</td>
<td>Developmental toxicity</td>
</tr>
<tr>
<td>Embryo / Fetal Development</td>
<td>Rat</td>
<td>Intraperitoneal</td>
<td>5 mg/kg</td>
<td>LOAEL</td>
<td>Fetotoxicity</td>
</tr>
</tbody>
</table>

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Cell Type/Organism</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Vitro Chromosome Aberration</td>
<td>Human Lymphocytes</td>
<td>Positive</td>
</tr>
<tr>
<td>In Vitro Sister Chromatid Exchange</td>
<td>Mouse</td>
<td>Positive</td>
</tr>
<tr>
<td>Unscheduled DNA Synthesis</td>
<td>Human Lymphocytes</td>
<td>Positive</td>
</tr>
<tr>
<td>In Vivo Micronucleus</td>
<td>Mouse</td>
<td>Positive</td>
</tr>
</tbody>
</table>

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

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.

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

EU Indication of danger: Not classified

OSHA Label:
Non-hazardous in accordance with international standards for workplace safety.

Canada - WHMIS: Classifications

WHMIS hazard class:
D2a  very toxic materials

Methotrexate

California Proposition 65
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 chloride

Inventory - United States TSCA - Sect. 8(b)  Present
Australia (AICS):  Present
EU EINECS/ELINCS List  231-598-3

Sodium hydroxide

CERCLA/SARA Hazardous Substances and their Reportable Quantities:
Inventory - United States TSCA - Sect. 8(b)  Present
Australia (AICS):  Present
Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 5
EU EINECS/ELINCS List  215-185-5

Water for Injection

Inventory - United States TSCA - Sect. 8(b)  Present
Australia (AICS):  Present
REACH - Annex IV - Exemptions from the obligations of Register:
EU EINECS/ELINCS List  231-791-2

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

PZ00135
R25 - Toxic if swallowed.
R35 - Causes severe burns.
R60 - May impair fertility.
R68 - Possible risks of irreversible effects.

**Data Sources:** Pfizer proprietary drug development information. Safety data sheets for individual ingredients.

**Reasons for Revision:** Updated Section 7 - Handling and Storage. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 10 - Stability and Reactivity. Updated Section 4 - First Aid Measures.

**Prepared by:** Product Stewardship Hazard Communication
Pfizer Global Environment, Health, and Safety Operations

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**End of Safety Data Sheet**