MATERIAL SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
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New York, New York 10017
1-212-573-2222

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

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

Material Name: Methotrexate Solution for Injection (25 mg/ml and 100 mg/mL)

Trade Name: METHOTREXATE; MIANTREX
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as Antineoplastic

2. HAZARDS IDENTIFICATION

Appearance: Clear yellow solution
Signal Word: DANGER

Statement of Hazard:
Harmful if swallowed.
Suspected of causing genetic defects.
May damage the unborn child.

Additional Hazard Information:
Short Term: May be absorbed through the skin and cause systemic effects.
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:
Harmful
Toxic to reproduction: Category 1
Mutagenic: Category 3

EU Hazard Symbols:

EU Risk Phrases:
R22 - Harmful if swallowed.
R61 - May cause harm to the unborn child.
R68 - Possible risk of irreversible effects.

Australian Hazard Classification (NOHSC): Hazardous Substance. Non-Dangerous Goods.

2. HAZARDS IDENTIFICATION

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

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Methotrexate	59-05-2	200-413-8	Mut. Cat.3;R68 Repr. Cat.1;R61 T;R25	2.5-10
Sodium hydroxide	1310-73-2	215-185-5	C;R35	**
Hydrochloric Acid	7647-01-0	231-595-7	C;R35 T;R23	**

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Sodium chloride	7647-14-5	231-598-3	Not Listed	*
Water for Injection	7732-18-5	231-791-2	Not Listed	*

Additional Information: * Proprietary
** to adjust pH
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 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.

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/m^3

Sodium chloride

Latvia OEL - TWA	5 mg/m^3
Lithuania OEL - TWA	5 mg/m^3

Sodium hydroxide

ACGIH Ceiling Threshold Limit:	2 mg/m^3
Australia PEAK	2 mg/m^3
Austria OEL - MAKs	2 mg/m^3
Bulgaria OEL - TWA	2.0 mg/m^3
Czech Republic OEL - TWA	1 mg/m^3
Estonia OEL - TWA	1 mg/m^3
France OEL - TWA	2 mg/m^3
Greece OEL - TWA	2 mg/m^3
Hungary OEL - TWA	2 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Japan - OELs - Ceilings	2 mg/m^3
Latvia OEL - TWA	0.5 mg/m^3
OSHA - Final PELS - TWAs:	2 mg/m^3
Poland OEL - TWA	0.5 mg/m^3
Slovakia OEL - TWA	2 mg/m^3
Slovenia OEL - TWA	2 mg/m^3
Sweden OEL - TWAs	1 mg/m^3

Hydrochloric Acid

ACGIH Ceiling Threshold Limit:	2 ppm
Australia PEAK	5 ppm 7.5 mg/m^3
Austria OEL - MAKs	5 ppm 8 mg/m^3
Belgium OEL - TWA	5 ppm 8 mg/m^3
Bulgaria OEL - TWA	8.0 mg/m^3
Cyprus OEL - TWA	5 ppm 8 mg/m^3
Czech Republic OEL - TWA	8 mg/m^3
Estonia OEL - TWA	5 ppm 8 mg/m^3
Germany - TRGS 900 - TWAs	2 ppm 3 mg/m^3
Germany (DFG) - MAK	2 ppm 3.0 mg/m^3
Greece OEL - TWA	5 ppm 7 mg/m^3
Hungary OEL - TWA	8 mg/m^3
Ireland OEL - TWAs	5 ppm 8 mg/m^3
Italy OEL - TWA	5 ppm 8 mg/m^3
Japan - OELs - Ceilings	5 ppm 7.5 mg/m^3
Latvia OEL - TWA	5 ppm 8 mg/m^3
Lithuania OEL - TWA	5 ppm 8 mg/m^3
Luxembourg OEL - TWA	5 ppm 8 mg/m^3
Malta OEL - TWA	5 ppm 8 mg/m^3
Netherlands OEL - TWA	8 mg/m^3
Poland OEL - TWA	5 mg/m^3
Romania OEL - TWA	5 ppm 8 mg/m^3
Slovakia OEL - TWA	5 ppm 8.0 mg/m^3
Slovenia OEL - TWA	5 ppm 8 mg/m^3
Spain OEL - TWA	5 ppm 7.6 mg/m^3

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.

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.

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

Physical State:	Solution	**Color:**	Clear Yellow
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

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)

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

Methotrexate
Rat Oral LD50 135 mg/kg
Rat Sub-tenon injection (eye) LD50 6 mg/kg
Rat Intravenous LD50 14 mg/kg
Mouse Oral LD50 146 mg/kg
Not Specified Inhalation LC50 > 188 ug/m^3

Sodium hydroxide
Mouse IP LD50 40 mg/kg

11. TOXICOLOGICAL INFORMATION

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)

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.

Methotrexate
IARC: Group 3 (Not Classifiable)

Hydrochloric Acid
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 Symbol: T
EU Indication of danger: Harmful
Toxic to reproduction: Category 1
Mutagenic: Category 3

EU Risk Phrases:

R22 - Harmful if swallowed.
R61 - May cause harm to the unborn child.
R68 - Possible risk of irreversible effects.

EU Safety Phrases:

S23 - Do not breathe fumes/vapour/spray.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
DANGER
Harmful if swallowed.
Suspected of causing genetic defects.
May damage the unborn child.

Canada - WHMIS: Classifications

WHMIS hazard class:
D2a very toxic materials

15. REGULATORY INFORMATION

Methotrexate

California Proposition 65	developmental toxicity initial date 1/1/89
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:	1000 lb 454 kg
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 5 Schedule 6
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 TPQs	500 lb
CERCLA/SARA - Section 302 Extremely Hazardous Substances EPCRA RQs	5000 lb
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 5 Schedule 6
EU EINECS/ELINCS List	231-595-7

Water for Injection

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

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R25 - Toxic if swallowed.
R35 - Causes severe burns.
R61 - May cause harm to the unborn child.
R68 - Possible risks of irreversible effects.

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

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

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

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