

# MATERIAL SAFETY DATA SHEET

Version No: MSDS/Metho-AUS/DP-003

Effective Date: 30<sup>th</sup> November 2019

## METHOTREXATE INJECTION, 50 MG/2 ML AND 1000 MG/10 ML

### SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

**Product Name:** Methotrexate Injection, 50 mg/2 mL and 1000 mg/10 mL

Sponsor	Manufacturer
Accord Healthcare Pty Ltd Level 24, 570 Bourke Street, Melbourne, VIC, 3000, Australia	Intas Pharmaceuticals Ltd. Plot No. 457, 458 Village-Matoda, Bavla Road, Ta. Sanand, Dist. Ahmedabad-382 210, Gujarat, India

### SECTION 2 – COMPOSITION, INFORMATION ON INGREDIENTS

**Active:** Methotrexate

**Inactive (50 mg/2 mL):** Sodium Chloride, Sodium Hydroxide, Water for Injection

**Inactive (1000 mg/10 mL):** Sodium Hydroxide, Water for Injection

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Methotrexate	59-05-2	200-413-8	Acute Tox.3 (H301) Repr.1A (H360D) Muta.2 (H341)	2.5
Sodium hydroxide	1310-73-2	215-185-5	Skin Corr.1A (H314)	**
Water for Injection	7732-18-5	231-791-2	Not Listed	*
Sodium chloride	7647-14-5	231-598-3	Not Listed	*

### SECTION 3 - HAZARDS IDENTIFICATION

**Classification of the Substance or Mixture:**

**GHS – Classification:**

Germ Cell Mutagenicity : Category 2  
Reproductive Toxicity : Category 1A

**Label Elements:**

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**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



**Other Hazards:** An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

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

## SECTION 4 - EMERGENCY & 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.

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## **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 3 – 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

## **SECTION 5 - FIRE FIGHTING MEASURES**

**Extinguishing Media:** Extinguish fires with CO<sub>2</sub>, 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.

## **SECTION 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.

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**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.

## SECTION 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

## SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

**Control Parameters:**

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

**Methotrexate:**

OEL TWA-8 Hr : 2 µg/m<sup>3</sup>

**Sodium hydroxide**

<b>ACGIH Ceiling Threshold Limit</b>	: 2 mg/m <sup>3</sup>
<b>Australia PEAK</b>	: 2 mg/m <sup>3</sup>
<b>Austria OEL - MAKs</b>	: 2 mg/m <sup>3</sup>
<b>Bulgaria OEL - TWA</b>	: 2.0 mg/m <sup>3</sup>
<b>Czech Republic OEL - TWA</b>	: 1 mg/m <sup>3</sup>
<b>Estonia OEL - TWA</b>	: 1 mg/m <sup>3</sup>
<b>France OEL - TWA</b>	: 2 mg/m <sup>3</sup>
<b>Greece OEL - TWA</b>	: 2 mg/m <sup>3</sup>
<b>Hungary OEL - TWA</b>	: 2 mg/m <sup>3</sup>
<b>Japan - OELs - Ceilings</b>	: 2 mg/m <sup>3</sup>
<b>Latvia OEL - TWA</b>	: 0.5 mg/m <sup>3</sup>
<b>OSHA - Final PELs - TWAs</b>	: 2 mg/m <sup>3</sup>

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Poland OEL - TWA : 0.5 mg/m<sup>3</sup>  
Slovakia OEL – TWA : 2 mg/m<sup>3</sup>  
Slovenia OEL - TWA : 2 mg/m<sup>3</sup>  
Sweden OEL - TWAs : 1 mg/m<sup>3</sup>  
Switzerland OEL -TWAs : 2 mg/m<sup>3</sup>

## Sodium chloride:

Latvia OEL - TWA : 5 mg/m<sup>3</sup>  
Lithuania OEL - TWA : 5 mg/m<sup>3</sup>

## Exposure Controls:

**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.)

## SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Physical State : Solution  
Color : Clear Yellow

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**Odor** : No data available  
**Odor Threshold** : No data available  
**Molecular Formula** : Mixture  
**Molecular Weight** : Mixture  
**Solvent Solubility** : No data available  
**Water Solubility** : No data available  
**pH** : No data available  
**Melting/Freezing Point (°C)** : No data available  
**Boiling Point (°C)** : No data available

**Partition Coefficient:**

**Water for Injection** : No data available  
**Sodium chloride** : No data available  
**Sodium hydroxide** : No data available  
**Methotrexate** : No data available

**Decomposition Temperature (°C)** : No data available.  
**Evaporation Rate (Gram/s)** : No data available  
**Vapor Pressure (kPa)** : No data available  
**Vapor Density (g/ml)** : No data available  
**Relative Density** : No data available  
**Viscosity** : No data available

**Flammability:**

**Autoignition Temperature (Solid) (°C)** : No data available  
**Flammability (Solids)** : No data available  
**Flash Point (Liquid) (°C)** : No data available  
**Upper Explosive Limits (Liquid) (% by Vol.)** : No data available  
**Lower Explosive Limits (Liquid) (% by Vol.)** : No data available

## SECTION 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

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**Hazardous Decomposition Products:** No data available

## SECTION 11 - TOXICOLOGY 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.

**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:

#### Sodium chloride:

Species	Route	End Point	Dose
Rat	Oral	LD50	3000 mg/kg
Mouse	Oral	LD50	4000 mg/kg

#### Sodium hydroxide:

Species	Route	End Point	Dose
Mouse	IP	LD50	40 mg/kg

#### Methotrexate:

Species	Route	End Point	Dose
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/m <sup>3</sup>

**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:

#### Sodium chloride:

Study Type	Species	Severity
Eye Irritation	Rabbit	Moderate
Skin Irritation	Rabbit	Mild

#### Sodium hydroxide:

Study Type	Species	Severity
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Eye Irritation	Rabbit	Severe
Skin Irritation	Rabbit	Severe

## Repeated Dose Toxicity:

### Methotrexate:

Duration	Species	Route	Dose	End Point	Target Organ
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:

### Methotrexate:

Study Type	Species	Route	Dose	End Point	Effect(s)
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:

### Methotrexate:

Study Type	Cell Type/Organism	Result
<i>In Vitro</i> Chromosome Aberration	Human Lymphocytes	Positive
<i>In Vitro</i> Sister Chromatid Exchange	Mouse	Positive
Unscheduled DNA Synthesis	Human Lymphocytes	Positive
<i>In Vivo</i> 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)

## SECTION 12 - ENVIRONMENTAL IMPACT 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



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**Mobility in Soil:** No data available

## SECTION 13 - DISPOSAL INFORMATION

**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.

## SECTION 14 - TRANSPORTATION INFORMATION

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

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

## SECTION 15 - REGULATORY INFORMATION

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

### **Methotrexate:**

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

### **Sodium hydroxide:**

<b>CERCLA/SARA 313 Emission reporting</b>	: Not Listed
<b>CERCLA/SARA Hazardous Substances and their Reportable Quantities</b>	: 1000 lb 454 kg
<b>California Proposition 65</b>	: Not Listed
<b>Inventory - United States TSCA - Sect. 8(b)</b>	: Present
<b>Australia (AICS)</b>	: Present

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**Standard for the Uniform Scheduling for Drugs and Poisons** : Schedule 5  
Schedule 6  
**EU EINECS/ELINCS List** : 215-185-5

## 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  
**California Proposition 65** : Not Listed  
**Inventory - United States TSCA - Sect. 8(b)** : Present  
**Australia (AICS):** : Present  
**EU EINECS/ELINCS List** : 231-598-3

## SECTION 16 - OTHER DATA

### 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:** Information from published literature.

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