

MATERIAL SAFETY DATA SHEET

Version No: MSDS/Fluoro-AUS/DP-002

Effective date: 25th November 2019

FLUOROURACIL INJECTION 50 mg/mL, 5 mL, 10 mL, 20 mL, 50 mL and 100 mL

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

Product Name: Fluorouracil Injection, 50 mg/mL, 5 mL, 10 mL, 20 mL, 50 mL and 100 mL

Sponsor	Manufacturer-1	Manufacturer-2
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	Intas Pharmaceuticals Ltd. Plot No. 5, 6 and 7, Pharmed, Near Matoda Village, Ahmedabad-382 213, Gujarat, India

SECTION 2 – COMPOSITION, INFORMATION ON INGREDIENTS

Active: fluorouracil

Inactive: sodium hydroxide, hydrochloric acid, water for Injections

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Fluorouracil	51-21-8	200-085-6	Muta. Cat.2;R46 Repr. Cat.2;R60-61 Xn;R22	5
Sodium hydroxide	1310-73-2	215-185-5	C;R35	**
Hydrochloric acid	7647-01-0	231-595-7	Skin Corr.1B (H314) STOT SE 3 (H335)	**
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

SECTION 3 – HAZARDS IDENTIFICATION

Appearance: Colorless solution

Signal Word: DANGER

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Statement of Hazard:

May damage fertility or the unborn child.
May cause genetic defects.

Additional Hazard Information:

Short Term: May be absorbed through the skin and cause systemic effects. Active ingredient may be harmful if swallowed.

Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on blood and blood forming organs.

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:

Toxic to reproduction, Category 2
Mutagenic: Category 2

EU Hazard Symbols:



EU Risk Phrases:

R46 - May cause heritable genetic damage.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

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

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.

SECTION 4 – EMERGENCY AND FIRST AID MEASURES

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

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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 3 – Hazards Identification and/or Section 11 - Toxicological Information.

SECTION 5 – FIRE FIGHTING MEASURES

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

Hazardous Combustion Products: Carbon monoxide, carbon dioxide, nitrogen oxides and fluorine-containing compounds

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

Fire / Explosion Hazards: Not flammable.

SECTION 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 the spill if it is safe to do so. Soak up with inert absorbent material and dispose of as hazardous waste.

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.

SECTION 7 – HANDLING AND STORAGE

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General Handling: Restrict access to work area. Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). It is recommended that all operations be fully enclosed and no air recirculated. 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.

SECTION 8 – EXPOSURE CONTROLS/PERSONAL PROTECTION

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

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
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	: 5 ppm 8.0 mg/m ³
Cyprus OEL - TWA	: 5 ppm 8 mg/m ³
Czech Republic OEL - TWA	: 8 mg/m ³

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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	: 2 ppm 3.0 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
Portugal OEL - TWA	: 5 ppm 8 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
Switzerland OEL -TWAs	: 2 ppm 3.0 mg/m ³
Vietnam OEL - TWAs	: 5 mg/m ³

The purpose of the Occupational Exposure Band (OEB) classification system is to separate substances into different Hazard categories when the available data are sufficient to do so, but inadequate to establish an Occupational Exposure Limit (OEL). The OEB given is based upon an analysis of all currently available data; as such, this value may be subject to revision when new information becomes available.

Fluorouracil:

Occupational Exposure Band (OEB): OEB 5 (control exposure to <1µg/m³)

Engineering Controls: Engineering controls should be used as the primary means to control exposures. Keep airborne contamination levels below the exposure limits listed above in this section. It is recommended that all operations be fully enclosed and no air recirculated.

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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, disposable gloves (double suggested) are recommended if skin contact with drug product is possible and for bulk processing operations.

Eyes: Safety glasses or goggles

Skin: Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

Respiratory protection: If airborne exposures are within or exceed the Occupational Exposure Band (OEB) range, wear an appropriate respirator with a protection factor sufficient to control exposures to the bottom of the OEB range.

SECTION 9 – PHYSICAL AND CHEMICAL PROPERTIES

Physical State : Solution
Color : Colorless
Molecular Formula : Mixture
Molecular Weight : Mixture

SECTION 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.

SECTION 11 – TOXICOLOGY INFORMATION

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

Acute Toxicity:

Fluorouracil

Species	Route	End Point	Dose
Rat	Oral	LD 50	230 mg/kg
Rat	Para-periosteal	LD 50	245 mg/kg

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Mouse	Oral	LD 50	115 mg/kg
Mouse	Intravenous	LD 50	81 mg/kg

Sodium hydroxide

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

HYDROCHLORIC ACID:

Species	Route	End Point	Dose
Rat	Oral	LD 50	238-277 mg/kg

Irritation / Sensitization:

Sodium hydroxide

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

Repeated Dose Toxicity:

Fluorouracil

Duration	Species	Route	Dose	End Point	Target Organ
5 Week(s)	Dog	Oral	175 mg/kg	LOAEL	Bone marrow

Reproduction & Developmental Toxicity:

Fluorouracil

Study Type	Species	Route	Dose	End Point	Effect(s)
Embryo / Fetal Development	Mouse	Intraperitoneal	10 - 40 mg/kg/day	LOAEL	Teratogenic
Embryo / Fetal Development	Rat	Intraperitoneal	12 - 37 mg/kg	LOAEL	Teratogenic
Embryo / Fetal Development	Hamster	Intraperitoneal	3 - 9 mg/kg	LOAEL	Teratogenic, Fetotoxicity
Embryo / Fetal Development	Monkey	Intramuscular	40 mg/kg	NOAEL	Not Teratogenic
Reproductive & Fertility-Males	Mouse	Intraperitoneal	25 - 50 mg/kg	LOAEL	Fertility

Genetic Toxicity:

Fluorouracil

Study Type	Cell Type/Organism	Result
<i>In Vivo</i> Chromosome Aberration	Rat Spermatogonia	Positive
Sister Chromatid Exchange	Human Lymphocytes	Positive
Chromosome Aberration	Chinese Hamster Ovary (CHO) cells	Positive
Sister Chromatid Exchange Chinese	Hamster Ovary (CHO) cells	Positive
<i>In Vivo</i> Micronucleus	Mouse	Positive

HYDROCHLORIC ACID:

Study Type	Cell Type/Organism	Result
Bacterial Mutagenicity (Ames)	Salmonella	Negative

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

Fluorouracil

IARC: Group 3 (Not Classifiable)

HYDROCHLORIC ACID

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.

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

EU Indication of danger:

Toxic to reproduction, Category 2

Mutagenic: Category 2

EU Risk Phrases:

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R60 - May impair fertility.

R61 - May cause harm to the unborn child.

OSHA Label: DANGER

May damage fertility or the unborn child.

May cause genetic defects.

Canada - WHMIS: Classifications

WHMIS hazard class:

D2a very toxic materials



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

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

Fluorouracil:

CERCLA/SARA 313 Emission reporting	:	1.0 %
CERCLA/SARA - Section 302 Extremely Hazardous	:	500 lb
TPQs	:	10000 lb
CERCLA/SARA - Section 302 Extremely Hazardous Substances EPCRA RQs	:	500 lb
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	:	200-085-6

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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
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 5 Schedule 6
EU EINECS/ELINCS List	:	231-595-7

SECTION 16 – OTHER DATA

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.

R46 - May cause heritable genetic damage.

R60 - May impair fertility.

R61 - May cause harm to the unborn child.

Sources of data: Information from published literature.

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