MATERIAL SAFETY DATA SHEET

Version No: MSDS/Bus-AUS/DP-001 **Effective Date:** 11th September 2019

Busulfan Injection, 6 mg/mL, 10 mL

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

Product Name: Busulfan Injection, 6 mg/mL, 10 mL

Sponsor	Manufacturer
Accord Healthcare Pty Ltd Level 24, 570 Bourke Street Melbourne, VIC, 3000, Australia	Intas Pharmaceuticals Limited. Plot Numbers 457 and 458 Sarkhej-Bavla Highway Matoda, Sanand, Ahmedabad-382 210, India

SECTION 2 – COMPOSITION, INFORMATION ON INGREDIENTS

Active: Busulfan.

Inactive: Dimethylacetamide, Macrogol 400.

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Busulfan	55-98-1	200-250-2	Repr. 1B (H360FD) Carc. 1B (H350) Muta. 1B (H340)	< 1
N,N-DIMETHYLACETAMIDE	127-19-5	204-826-4	Repr. 1B (H360D) Acute Tox. 4 (H312) Acute Tox. 4 (H332) Eye Irrit. 2A (H319)	30 - 35
Polyethylene glycol	25322-68-3	Not Listed	Not Listed	*

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

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

SECTION 3 - HAZARDS IDENTIFICATION

Classification of the Substance or Mixture:

GHS – Classification

Serious Eye Damage/Eye Irritation	-	Category 2A
Germ Cell Mutagenicity	-	Category 1B
Reproductive Toxicity	-	Category 1B
Carcinogenicity	-	Category 1B

Label Elements:

Signal Word: Danger

Hazard Statements:

H319	:	Causes serious eye irritation
H350	:	May cause cancer
H360FD	:	May damage fertility. May damage the unborn child.
H340	:	May cause genetic defects

Precautionary Statements:

P201	-	Obtain special instructions before use
P202	-	Do not handle until all safety precautions have been read and understood
P264	-	Wash hands thoroughly after handling
P280	-	Wear protective gloves/protective clothing/eye protection/face protection
P308 + P313	-	IF exposed or concerned: Get medical attention/advice
P337 + P313	-	If eye irritation persists: Get medical advice/attention
P405	-	Store locked up

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 - 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: No data available

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 CO2, extinguishing powder, foam, or water.

Specific 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 mists) may fuel fires/explosions.

Advice for Fire-Fighters: During all firefighting 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.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Cleanup 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 product used as Antineoplastic

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

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

N,N-DIMETHYLACETAMIDE

ACGIH Threshold Limit Value (TWA)	:	10 ppm
ACGIH - Biological Exposure Limit	:	30 mg/g creatinine
ACGIH - Skin Absorption Designation	:	Skin - potential significant contribution to overall exposure by the cutaneous route
Australia TWA	:	10 ppm 36 mg/m^3
Austria OEL - MAKs	:	10 ppm 36 mg/m^3
Belgium OEL - TWA	:	10 ppm 36 mg/m^3
Bulgaria OEL - TWA	:	10 ppm 36 mg/m^3
Cyprus OEL - TWA	:	10 ppm 36 mg/m^3
Czech Republic OEL - TWA	:	30 mg/m^3

Denmark OEL - TWA	:	10 ppm 36 mg/m^3
Estonia OEL - TWA	:	10 ppm 36 mg/m^3
Finland OEL - TWA	:	10 ppm 36 mg/m^3
France OEL - TWA	:	2 ppm 7.2 mg/m^3
Germany - TRGS 900 - TWAs	:	10 ppm 36 mg/m^3
Germany (DFG) - MAK	:	10 ppm 36 mg/m^3
Germany - Biological Exposure Limit:	:	30 mg/g
Greece OEL - TWA	:	10 ppm 36 mg/m^3
Hungary OEL - TWA	:	36 mg/m^3
Ireland OEL - TWAs	:	10 ppm 36 mg/m^3
Italy OEL - TWA	:	10 ppm 36 mg/m^3
Latvia OEL - TWA	:	10 ppm 36 mg/m^3
Lithuania OEL - TWA	:	10 ppm 36 mg/m^3
Luxembourg OEL - TWA	:	10 ppm 36 mg/m^3
Malta OEL - TWA	:	10 ppm 36 mg/m^3
Netherlands OEL - TWA	:	36 mg/m^3
OSHA - Final PELS - TWAs:	:	10 ppm 35 mg/m^3
OSHA - Final PELs - Skin Notations:	:	prevent or reduce skin absorption
Poland OEL - TWA	:	35 mg/m^3
Portugal OEL - TWA	:	10 ppm 36 mg/m^3
Romania OEL - TWA	:	10 ppm 36 mg/m^3
Romania - Biological Exposure Limit:	:	30 µg/g Creatinine
Russia OEL - TWA	:	1 mg/m^3
Slovakia OEL - TWA	:	10 ppm 36 mg/m^3
Slovenia OEL - TWA	:	10 ppm 36 mg/m^3
Spain OEL - TWA	:	10 ppm 36 mg/m^3
Spain - Biological Exposure Limit:	:	30 mg/g Creatinine
Sweden OEL - TWAs	:	10 ppm

		35 mg/m^3
Switzerland OEL -TWAs	:	10 ppm 35 mg/m^3
UK - Biological Exposure Limit:	:	100 mmol/mol creatinine

Polyethylene glycol

Austria OEL - MAKs	:	1000 mg/m^3
Germany - TRGS 900 - TWAs	:	1000 mg/m^3
Germany (DFG) - MAK	:	1000 mg/m^3 average molecular weight 200-600
Slovakia OEL - TWA	:	1000 mg/m^3
Slovenia OEL - TWA	:	1000 mg/m^3
Switzerland OEL -TWAs	:	1000 mg/m^3

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 gloves (e.g. Nitrile, etc.) are 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 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 half mask, P3 filter). (Respirators must meet the standards in accordance with EN140, EN143, ASTM F2704-10 or international equivalent.)

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Physical State	:	Solution
Color	:	Clear, colorless
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: (Method, pH, Endpoint, Value)		
N,N-DIMETHYLACETAMIDE	:	No data available
Polyethylene glycol	:	No data available
Busulfan	:	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
Flammablity:		
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 mists) may fuel fires/explosions.

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

Hazardous Decomposition Products: No data available

SECTION 11 - TOXICOLOGY INFORMATION

Information on Toxicological Effects Known Clinical Effects: Common adverse effects include seizure myelosuppression, cardiac tamponade, pulmonary dysfunction, fever, headache, loss of strength/exhaustion (prostration), increased heart rate (tachycardia), increase in blood pressure (hypertension), nausea, inflammation of the mouth (stomatitis), vomiting, loss of appetite (anorexia), insomnia, diarrhea, and anxiety. May cause adverse effects on the developing fetus.

Acute Toxicity:
N,N-DIMETHYLACETAMIDE:

Species	Route	End Point	Dose
Rabbit	Dermal	LD 50	2240 mg/kg
Rat	Inhalation	LC50 1H	8.81 mg/L

Busulfan:

Species	Route	End Point	Dose
Mouse	Oral	LD 50	120 mg/kg

Irritation / Sensitization:
Polyethylene glycol:

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

Reproduction & Development Toxicity:
Busulfan

Duration	Species	Route	Dose	End Point	Effect(s))
Embryo / Fetal Development	Rat	Oral	48 mg/kg/day	LOAEL	Teratogenic, Early embryonic development
Reproductive & Fertility	Rat	Oral	49 mg/kg/day	LOAEL	Fertility
Embryo / Fetal Development	Rabbit	Oral	32 mg/kg/day	LOAEL	Teratogenic, Fetotoxicity, Early embryonic development
Embryo / Fetal Development	Mouse	Oral	40 mg/kg/day	LOAEL	Teratogenic, Fetotoxicity, Early embryonic development

Genetic Toxicity:
Busulfan:

Study Type	Cell Type/Organism	Result
In Vivo Chromosome Aberration	Rat	Positive
Bacterial Mutagenicity (Ames)	*Salmonella*	Positive
In Vivo Direct DNA Damage	Rat Hepatocyte	Positive
Sister Chromatid Exchange	Human Lymphocytes	Positive
Unscheduled DNA Synthesis	Mouse	Positive

Carcinogen Status: See below

Busulfan:
IARC : Group 1 (Carcinogenic to Humans)
NTP : Known Human Carcinogen

SECTION 12 - ENVIRONMENTAL IMPACT INFORMATION

Environmental Overview: Environmental properties have not been investigated.

Toxicity: No data available

Persistence and Degradability: No data available

Bio-accumulative Potential: No data available

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:

Busulfan:

CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition 65	:	carcinogen 2/27/1987 developmental toxicity 1/1/1989
Australia (AICS)	:	Present
Standard for the Uniform Scheduling for Drugs and Poisons	:	Schedule 4
EU EINECS/ELINCS List	:	200-250-2

N,N-DIMETHYLACETAMIDE:

CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition 65	:	developmental toxicity 5/21/2010 male reproductive toxicity 5/21/10
Inventory - United States TSCA - Sect. 8(b)	:	Present
Australia (AICS)	:	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	:	Schedule 5 Schedule 6
REACH - Annex XVII - Restrictions on Certain Dangerous Substances	:	Use restricted. See item 30.
REACH - Toxic to Reproduction Category 2	:	Present
EU EINECS/ELINCS List	:	204-826-4

Polyethylene glycol:

CERCLA/SARA 313 Emission reporting	:	Not Listed
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 2 Schedule 3
EU EINECS/ELINCS List	:	Not Listed

SECTION 16 - OTHER DATA

Text of CLP/GHS Classification abbreviations mentioned in Section 3:

Carcinogenicity	-	Cat.1B
H350	-	May cause cancer
Germ cell mutagenicity	-	Cat.1B
H340	-	May cause genetic defects
Reproductive toxicity	-	Cat.1B
H360FD	-	May damage fertility. May damage the unborn child.
Acute toxicity, dermal	-	Cat.4
H312	-	Harmful in contact with skin
Acute toxicity, inhalation	-	Cat.4
H332	-	Harmful if inhaled
Serious eye damage/eye irritation	-	Cat.2A
H319	-	Causes serious eye irritation

Sources of data: Information from published literature.

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