MATERIAL SAFETY DATA SHEET

Version No: MSDS/Aza-AUS/DP-004 **Effective Date:** 14th October 2024

AZACITIDINE FOR INJECTION
100 MG/VIAL

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

Product Name: Azacitidine Accord Powder for Injection
100 mg/vial

Sponsor	Manufacturer
Accord Healthcare Pty Ltd Level 24, 570 Bourke Street, Melbourne, VIC, 3000, Australia Telephone: 1800 222 673 (hours 8:30am – 4:30pm)	Intas Pharmaceuticals Ltd. Plot No. 5, 6 and 7, Pharmez, Near Matoda Village, Ahmedabad-382 213, Gujarat, India

SECTION 2 – HAZARD(S) IDENTIFICATION

Classification of the Substance or Mixture:

GHS – Classification:

Germ Cell Mutagenicity	:	Category 2
Reproductive Toxicity	:	Category 1B
Carcinogenic	:	Category 1B
Acute toxicity - oral	:	Category 4
Specific Target Organ	:	Category 1
Toxicity (repeated exposure)	:	-
Aquatic toxicity (acute)	:	Category 1
Aquatic toxicity (chronic)	:	Category 1

Label Elements:

Signal Word: Danger

Hazard Statements:

H302	-	Harmful if swallowed
H341	-	Suspected of causing genetic defects
H350	-	May cause cancer

H360FD	-	May damage fertility. May damage the unborn child
H372	-	Causes damage to hematological and gastrointestinal systems through prolonged or repeated exposure
H400	-	Very toxic to aquatic life
H410	-	Very toxic to aquatic life with long-lasting effects

Precautionary Statements:

P201	-	Obtain special instructions before use
P202	-	Do not handle until all safety precautions have been read and understood
P260	-	Do not breathe dust
P264	-	Wash hands thoroughly after handling
P270	-	Do not eat, drink or smoke when using this product
P273	-	Avoid release to the environment
P280	-	Wear protective gloves/eye protection/face protection.
P281	-	Use personal protective equipment as required
P308 + P313	-	IF exposed or concerned: Get medical attention/advice
P301 + P312	-	IF SWALLOWED: Call a Poison Center or doctor/physician if you feel unwell
P330	-	Rinse mouth
P391	-	Collect spillage
P405	-	Store locked up
P501	-	Dispose of contents/container in accordance with all local and national regulations

Other Hazards: The most commonly occurring adverse effects with therapeutic use include hematological toxicity (*e.g.*, thrombocytopenia, anemia, neutropenia), fever, gastrointestinal effects (*e.g.*, nausea, vomiting, diarrhea, constipation), fatigue, injection site erythema, ecchymosis (skin discoloration caused by escape of blood into tissues from ruptured blood vessels). Other effects may include hypotension, shortness of breath, liver/kidney toxicity and electrolyte abnormalities. Post marketing reports of interstitial lung disease and tumor lysis syndrome may also be azacitidine-related.

Note: This mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA). See Section 16 for full text of EU and GHS classifications.

SECTION 3 – COMPOSITION / INFORMATION ON INGREDIENTS

Active: Azacitidine.

Inactive: Mannitol, Water for Injection.

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Azacitidine	320-67-2	206-280-2	ATO4: H302; Carc1B: H350; STOT-R1: H372; RT1B: H360FD; GCM2:	50

			H341; AA1: H400; CA1: H410	

Ingredient(s) listed above are considered dangerous/hazardous. The remaining components are non-dangerous/not hazardous and/or present at amounts below reportable limits.

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

SECTION 4 - FIRST AID MEASURES

Description of Necessary First Aid Measures:

Eye Contact: If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.

Skin Contact: Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.

Ingestion: Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.

Inhalation: Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.

Symptoms Caused by Exposure: See Sections 3 and 11.

Medical Attention and Special Treatment: Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

SECTION 5 - FIRE FIGHTING MEASURES

Suitable Extinguishing Media: Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.

Special Hazards Arising from the Substance or Mixture: No information identified. May emit carbon monoxide, carbon dioxide, and oxides of nitrogen.

Special Protective Equipment and Precautions for Fire-Fighters: Wear full protective clothing and a self-contained breathing apparatus with a full face piece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

Fire / Explosion Hazards: Not considered to be a fire hazard. No explosivity data available. High concentrations of finely divided airborne organic particles can potentially explode if ignited.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures: If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe dust.

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: If vials are broken or crushed, DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leakproof container suitable for disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.

Reference to other sections: See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for Safe Handling: If vials are crushed or broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Follow recommendations for handling bulk formulated/packaged cytotoxic pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Wash thoroughly after handling. Avoid breathing dust.

Conditions for Safe Storage, Including any Incompatibilities: Store as directed by product packaging and away from incompatible materials.

Specific end use(s): Pharmaceutical product used as Antineoplastic.

SECTION 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters – Exposure Standards, Biological Monitoring:

Azacitidine:

OEL TWA-8 Hr : 1 $\mu g/m^3$

DNELs/PNECs

PNEC (water) : 1.2 µg/L
PNEC (microorganism) : >1000 µg/L
PNEC (groundwater) : 73 µg/L

Appropriate Engineering Controls: If handling bulk product or vials are crushed/broken: Open handling should not be performed when handling potent substances or substances of unknown toxicity. Control exposures to below the OEL (if available). Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

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: Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Eyes: Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

Skin: Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

Respiratory protection: If handling bulk product or vials are crushed/broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly worn powered air-purifying respirator equipped with HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.

Environmental Exposure: Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.

Other protective measures: Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	Lyopholized powder/Lyopholized powder in vial
Colour	:	White to off-white
Odour	:	No data available
Odour Threshold	:	No data available
Solvent Solubility	:	Insoluble in acetone, ethanol, and methyl ethyl ketone; Soluble in dimethylsulfoxide (azacitidine)
Water Solubility	:	14 mg/mL (azacitidine)
pH	:	No data available
Melting/Freezing Point (°C)	:	~225-230°C (azacitidine)
Boiling Point and boiling range (°C)	:	No data available
Partition Coefficient (*n-octanol/water*)	:	-0.1-0.2 at pH 2 and 12 (25°C) (azacitidine)
Decomposition Temperature (°C)	:	No data available
Evaporation Rate (Gram/s)	:	No data available
Vapour Pressure (kPa)	:	No data available
Vapour Density (g/ml)	:	No data available
Relative Density	:	No data available
Viscosity	:	No data available
Auto-ignition Temperature (Solid) (°C)	:	No data available
Flammability (Solids, Gas)	:	No data available
Flash Point (Liquid) (°C)	:	No data available
Upper Flammability or Explosive Limits (Liquid) (% by Vol.)	:	No data available
Lower Flammability or Explosive Limits (Liquid) (% by Vol.)	:	No data available

SECTION 10 - STABILITY AND REACTIVITY

Reactivity: No data available.

Chemical Stability: Rapid decomposition in neutral or alkaline solutions; pharmacological stability not guaranteed beyond expiration date imprinted on package.

Conditions to Avoid: Avoid extreme temperatures. Avoid direct sunlight.

Incompatible Materials and Possible Hazardous Reactions: No data available.

Hazardous Decomposition Products: No data available.

SECTION 11 – TOXICOLOGICAL INFORMATION

The information included in this section describes the potential hazards of the active ingredient, azacitidine.

Information on Toxicological Effects:

Likely Routes of Exposure: May be absorbed by inhalation, skin contact and ingestion.

Acute Toxicity:

Species	Route	End Point	Dose
Mouse	Oral	LD50	572 mg/kg
Mouse	IV	LD50	~117 mg/kg
Rat	IV	LD50	~51 mg/kg
Dog	IV	Approximate lethal dose	~13.3 mg/kg

Irritation/Corrosion: Mild skin irritation was observed when a 9% solution of azacitidine was topically applied to rabbits.

Sensitization: No data available.

STOT-single exposure: Single IV administration of azacitadine to dogs at doses of 3.32 and 6.65 mg/kg caused only reversible hematological changes and liver enzyme increases.

STOT-repeated exposure/Repeat Dose Toxicity: Repeat-dose toxicity studies have been conducted in mice, dogs and monkeys. The main target organs of toxicity were the bone marrow, liver, kidney, lymphoid tissue, and the gastrointestinal tract.

14-day oral study, dog: Maximum tolerated dose (MTD) = 0.2 mg/kg/day.
10-day (5 days x 2 cycles) IV study, dog: MTD = 0.55 mg/kg/day.

14-day IV study, monkey: A dose of 2.2 mg/kg/day caused mortality, while 1.1 mg/kg/day caused leukopenia, anemia, elevated liver enzymes and increased BUN.

Reproduction Toxicity: In rodents treated with low intraperitoneal (IP) doses, azacitidine has produced adverse effects on male reproduction and fertility, including decreased testes/ epididymis weights, decreased sperm counts and decreased pregnancy rates.

Development Toxicity: Azacitidine produces dose-dependent embryotoxicity/embryolethality and teratogenicity in rodents after IP administration of doses as low as 1-2 and 0.5 mg/kg, respectively.

Genetic Toxicity: Azacitidine was a weak mutagen in several bacterial systems. It was both mutagenic and clastogenic in mammalian cell systems. Additionally, it induced mitotic recombination and mutations in *Drosophila*. Azacitidine did not induce dominant lethal mutations in mice.

Carcinogen Status: Azacitidine has shown carcinogenic potential in rodents following IP administration. Azacitidine has been classified by the International Agency for Research on Cancer (IARC) as an IARC Group 2A carcinogen (probably carcinogenic to humans). According to NTP, azacitidine is reasonably anticipated to be a human carcinogen. Azacitidine is also listed as a carcinogen under OSHA.

Aspiration hazard: No data available.

Human health data: See "Section 2 - Other Hazards".

SECTION 12 – ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided.

Ecotoxicity:

Type	Species	Concentration
EC50	Activated sludge	>100,000 µg/L
EC50/72h	Algae	~0.1-1.0 mg/L
NOEC (growth rate reduction)	Algae	31 µg/L
EC50/72h (growth rate reduction)	Desmodesmus subspicatus	9.6 mg/L
NOEC (growth rate reduction)	Desmodesmus subspicatus	0.53 mg/L
NOEC/21 days (reproduction)	Daphnia magna	730 µg/L
NOEC (Fish early life stage test)	Fathead minnow	1000 µg/L
NOEC/7 day (growth inhibition)	Lemna minor	0.068 mg/L
EC50/7d (growth rate reduction)	Lemna minor	1.8/2 mg/L (frond numbers/wet weight)

Persistence and Degradability: Azacitidine is biodegradable, but does not meet the criteria for "rapid biodegradability".

Bio-accumulative Potential: Based on the octanol/water partition coefficient, azacitidine is unlikely to bioaccumulate.

Mobility in Soil: Azacitidine is not stable in water. It is not expected to significantly adhere to sediment.

Adsorption coefficient (Koc): <33 L/kg.

Results of PBT and vPvB assessment: Not performed.

Other Adverse Effects: No data available.

SECTION 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.

SECTION 14 - TRANSPORTATION INFORMATION

Based on the available data, this packaged product is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG. It is exempt because it is packaged in either single packages or inner packaging in combination packages containing net quantities of less than 5 kg/5 L (IMDG Code 2.10.2.7; ICAO Special Instruction A197, 49CFR 171.4(c)(2)).

Shipment may be regulated if contents are removed from inner packaging and combined into containers exceeding 5 L or 5 kg.

The following regulations apply to the bulk product:

UN number: UN3077

UN proper shipping name: Azacitidine

Transport hazard classes and packing group: Hazard Class - 9; Packing Group III.

US DOT shipping description:
UN/ID Number - UN3077;
Proper Shipping Name - Environmentally Hazardous Substance, Solid, n.o.s. (contains azacitidine);
Hazard Class - 9;
Packing Group III. (exceptions from Environmentally Hazardous Substance marking exists for certain package sizes)

Sealed articles containing less than 5 kg of product can be shipped as Not Regulated under the provisions of 49 CFR 171.4.

IATA/ICAO shipping description:
UN/ID Number - UN3077;
Proper Shipping Name - Environmentally Hazardous Substance, Solid, n.o.s. (contains azacitidine);
Hazard Class - 9;
Packing Group III. (exceptions from Environmentally Hazardous Substance marking exists for certain package sizes)

Sealed articles containing less than 5 kg of product can be shipped as Not Regulated per Special Provision A197.

IMDG shipping description:
UN/ID Number - UN3077;
Proper Shipping Name - Environmentally Hazardous Substance, Solid, n.o.s. (contains azacitidine);
Hazard Class - 9;

Packing Group III. (exceptions from Marine Pollutant marking exists for certain package sizes) (Marine Pollutant)

Sealed articles containing less than 5 kg of product can be shipped as Not Regulated per Code 2.10.2.7.

IMDG marine pollutant: Azacitidine

ADR Shipping Description:
UN/ID Number - UN3077;
Proper Shipping Name - Environmentally Hazardous Substance, Solid, n.o.s. (contains azacitidine);
Hazard Class - 9;
Packing Group III.

Sealed articles containing less than 5 kg of product can be shipped as Not Regulated per Special Provision 375.

Canadian TDG:
UN/ID Number - UN3077;
Proper Shipping Name - Environmentally Hazardous Substance, Solid, n.o.s. (contains azacitidine);
Hazard Class - 9;
Packing Group III. (exceptions from Environmentally Hazardous Substance marking exists for certain package sizes)

Sealed articles containing less than 5 kg of product can be shipped as Not Regulated per Schedule 1.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code: Not applicable.

Environmental hazards: Based on the available data, this substance is regulated as an environmental hazard or a marine pollutant.

Special precautions for users: Avoid release to the environment.

SECTION 15 - REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture
This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.

Azacitidine:

TSCA status	**:**	Not Listed
SARA 313	**:**	Not Listed
California Proposition 65	**:**	Azacitidine is listed as a carcinogen
Poisons Schedule	**:**	Not Listed
Additional information	**:**	Azacitidine is listed as a hazardous drug by NIOSH

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications:

ATO4	-	Acute Toxicity (Oral) Category 4.
Carc1B	-	Carcinogenicity Category 1B.
STOT-R1	-	Specific Target Organ Toxicity Following Repeat Exposure Category 1.
RT1B	-	Reproductive toxicity Category 1B.
GCM2	-	Germ Cell Mutagenicity Category 2.
AA1	-	Acute aquatic toxicity Category 1.
CA1	-	Chronic Aquatic Toxicity Category 1.
H302	-	Harmful if swallowed.
H341	-	Suspected of causing genetic defects.
H350	-	May cause cancer.
H360FD	-	May damage fertility. May damage the unborn child.
H372	-	Causes damage to hematological and gastrointestinal systems through prolonged or repeated exposure.
H400	-	Very toxic to aquatic life.
H410	-	Very toxic to aquatic life with long lasting effects.

Abbreviations:

ACGIH	:	American Conference of Governmental Industrial Hygienists
AICS	:	Australian Inventory of Chemical Substances
AIHA	:	American Industrial Hygiene Association
ANSI	:	American National Standards Institute
CAS	:	Number Chemical Abstract Service Registry Number
CERCLA	:	Comprehensive Environmental Response Compensation and Liability Act
CHAN	:	Chemical Hazard Alert Notice
CHEMTREC	:	Chemical Transportation Emergency Center
DOT	:	Department of Transportation
DSL	:	Domestic Substances List
ECHA	:	European Chemicals Agency
EINECS	:	European Inventory of Existing Commercial Chemical Substances
ELINCS	:	European List of Notified Chemical Substances
EPA	:	Environmental Protection Agency
GHS	:	Globally Harmonized System of Classification and Labelling of Chemicals
HEPA	:	High Efficiency Particulate Air (Filter)
HMIS	:	Hazardous Materials Identification System
IARC	:	International Agency for Research on Cancer
ICAO/IATA	:	International Civil Aviation Organization/International Air Transport
IMO	:	International Maritime Organization
KOW	:	Octanol/Water Partition Coefficient
LEL	:	Lower Explosive Limit
MSDS	:	Material Safety Data Sheet
MSHA	:	Mine Safety and Health Administration
NA	:	Not Applicable, except in Section 14 where NA = North America
NE	:	Not Established

NADA	:	New Animal Drug Application
NAIF	:	No Applicable Information Found
NCI	:	National Cancer Institute
NDSL	:	Non-Domestic Substances List
NFPA	:	National Fire Protection Association
NIOSH	:	National Institute for Occupational Safety and Health
NPDES	:	National Pollutant Discharge Elimination System
NOS	:	Not Otherwise Specified
NTP	:	National Toxicology Program
OSHA	:	Occupational Safety and Health Administration
OEL	:	Occupational Exposure Limit
PEL	:	Permissible Exposure Limit (OSHA)
RCRA	:	Resource Conservation and Recovery Act
RQ	:	Reportable Quantity
RTECS	:	Registry of Toxic Effects of Chemical Substances
SARA	:	Superfund Amendments and Reauthorization Act
SDS	:	Safety Data Sheet
STEL	:	Short Term Exposure Limit
TLV	:	Threshold Limit Value (ACGIH)
TPQ	:	Threshold Planning Quantity
TSCA	:	Toxic Substances Control Act
TWA	:	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	:	Upper Explosive Limit
UN	:	United Nations
USP	:	United States Pharmacopeia
WEEL	:	Workplace Environmental Exposure Level (AIHA)
WHMIS	:	Workplace Hazardous Materials Information System

Data Sources: Information from published literature.

The information above is believed to be accurate and represents the best information currently available to us. However, we make no warranty of merchantability or any other warranty, express or implied, with respect to such information, and we assume no liability resulting from its use. Users should make their own investigations to determine the suitability of the information for their particular purposes. In no event shall INTAS be liable for any claims, losses, or damages of any third party or for lost profits or any special, indirect, incidental, consequential or exemplary damages, howsoever arising, even if INTAS has been advised of the possibility of such damages.