SAFETY DATA SHEET

SECTION 1 : IDENTIFICATION

Product Name:	**Flumazenil Injection, USP**
Manufacturer Name:	Fresenius Kabi USA, LLC
Address:	Three Corporate Drive Lake Zurich, Illinois 60047
General Phone Number:	(847) 550-2300
Customer Service Phone Number:	(888) 386-1300
Health Issues Information:	(800) 551-7176
SDS Creation Date:	January 08, 2009
SDS Revision Date:	February 19, 2024

SECTION 2 : HAZARD(S) IDENTIFICATION

Signal Word:	Not applicable.
Hazard Statements:	Not applicable.
Precautionary Statements:	Not applicable.
Emergency Overview:	This product is intended for therapeutic use only when prescribed by a physician. Potential adverse reactions from prescribed doses and overdoses are described in the package insert.
Route of Exposure:	Inhalation Ingestion Eye contact Skin Absorption. Injection.
Potential Health Effects:	
Eye:	Contact with eyes may cause irritation.
Signs/Symptoms:	Therapeutic doses of flumazenil has been associated with the occurrence of seizures and are most frequent in patients who have been on benzodiazepines for long-term sedation or in overdose cases where patients are showing signs of serious cyclic antidepressant overdose. Side effects from therapeutic doses may include: hypoventilation, resedation, headache, dizziness, fatigue, agitation, emotional lability, injection site pain, increased sweating, abnormal or blurred vision, arrhythmia, bradycardia, tachycardia, hypertension, and chest pain. May cause vasodilation. Signs and symptoms include: flushing of the face, sensation of heat, headache, itching, and gastrointestinal distress. Occupational exposure has not been fully investigated.
Aggravation of Pre-Existing Conditions:	Hypersensitivity to flumazenil, benzodiazepines, or any of the components of this product. Patients who have been given benzodiazepines for control of a potentially life-threatening condition and patients who are showing signs of serious cyclic antidepressant overdose should not receive flumazenil.

SECTION 3 : COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS#	Ingredient Percent	EC Num.
Flumazenil	78755-81-4	0.1 mg/mL	
Methylparaben	99-76-3	1.8 mg/mL	
Propylparaben	94-13-3	0.2 mg/mL	
Acetic Acid	64-19-7	0.01 %	
Edetate Disodium	139-33-3	0.01 %	
Sodium Chloride	7647-14-5	0.9 %	

SECTION 4 : FIRST AID MEASURES

Eye Contact:	Immediately flush eyes with plenty of water for at least 15 to 20 minutes. Ensure adequate flushing of the eyes by separating the eyelids with fingers. Get immediate medical attention.
Skin Contact:	Immediately wash skin with plenty of soap and water for 15 to 20 minutes, while removing contaminated clothing and shoes. Get medical attention if irritation develops or persists.

Inhalation:	If inhaled, remove to fresh air. If not breathing, give artificial respiration or give oxygen by trained personnel. Seek immediate medical attention.
Ingestion:	If conscious, flush mouth out with water immediately. Call a physician or poison control center immediately. Do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person.
Other First Aid:	For Adverse Event Information, please call (800) 551-7176.

SECTION 5 : FIRE FIGHTING MEASURES

Flash Point:	Not established.
Flash Point Method:	Not established.
Auto Ignition Temperature:	Not established.
Lower Flammable/Explosive Limit:	Not established.
Upper Flammable/Explosive Limit:	Not established.
Fire Fighting Instructions:	Evacuate area of unprotected personnel. Use cold water spray to cool fire exposed containers to minimize risk of rupture. Do not enter confined fire space without full protective gear. If possible, contain fire run-off water.
Extinguishing Media:	Use alcohol resistant foam, carbon dioxide, dry chemical, or water fog or spray when fighting fires involving this material. Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Protective Equipment:	As in any fire, wear Self-Contained Breathing Apparatus (SCBA), MSHA/NIOSH (approved or equivalent) and full protective gear.
Hazardous Combustion Byproducts:	Thermal decomposition products may include smoke and toxic fumes. Oxides of carbon, oxides of nitrogen and other organic substances may be formed. Other undetermined low molecular weight hydrocarbon compounds may be released in small quantities depending upon specific conditions of combustion.

SECTION 6 : ACCIDENTAL RELEASE MEASURES

Personal Precautions:	Evacuate area and keep unnecessary and unprotected personnel from entering the spill area. Avoid personal contact and breathing vapors or mists. Use proper personal protective equipment as listed in Section 8.
Environmental Precautions:	Avoid runoff into storm sewers, ditches, and waterways.
Methods for containment:	Contain spills with an inert absorbent material such as soil, sand or oil dry.
Methods for cleanup:	Absorb spill with inert material (e,g., dry sand or earth), then place in a chemical waste container. After removal, flush spill area with soap and water to remove trace residue.

SECTION 7 : HANDLING and STORAGE

Handling:	When handling pharmaceutical products, avoid all contact and inhalation of vapor, mists and/or fumes. Use with adequate ventilation. Use only in accordance with directions.
Storage:	Store at controlled room temperature 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature].
Work Practices:	Facilities storing or utilizing this material should be equipped with an eyewash facility and a safety shower.
Hygiene Practices:	Wash thoroughly after handling. Avoid contact with eyes and skin. Avoid inhaling vapor or mist.

SECTION 8: EXPOSURE CONTROLS, PERSONAL PROTECTION

Engineering Controls:	General ventilation is sufficient if this product is being used in a controlled medical setting (clinic, hospital, medical office) for its sole intended parenteral (injection) purpose. Otherwise, use appropriate engineering control such as process enclosures, local exhaust ventilation, or other engineering controls including use of a biosafety cabinet / fume hood to control airborne levels below recommended exposure limits.
Eye/Face Protection:	Chemical splash goggles. Wear a face shield also when splash hazard exist.
Skin Protection Description:	Protective laboratory coat, apron, or disposable garment recommended.
Hand Protection Description:	Wear appropriate protective gloves. Consult glove manufacturer's data for permeability data. Nitrile rubber or natural rubber gloves are recommended.
Respiratory Protection:	No personal respiratory protective equipment is normally required when this product is being used/administered by a licensed healthcare practitioner (i.e. an end-user such as a clinician / doctor / nurse) for its sole intended parenteral (injection) purpose in a controlled medical setting. The need for respiratory protection will vary according to the airborne concentrations and environmental conditions. A NIOSH approved air-purifying respirator with an organic vapor cartridge or canister may be permissible under certain circumstances. Consult the NIOSH web site (http://www.cdc.gov/niosh/npptl/topics/respirators/) for a list of respirator types and approved suppliers.
Other Protective:	Consult with local procedures for selection, training, inspection and maintenance of the personal protective equipment.

EXPOSURE GUIDELINES

Acetic Acid :

Guideline OSHA:	PEL-TWA: 10 ppm

SECTION 9 : PHYSICAL and CHEMICAL PROPERTIES

Physical State:	Liquid solution.
Color:	Colorless.
Boiling Point:	Not established.
Melting Point:	Not established.
Solubility:	Slightly soluble in acidic aqueous solutions.
Vapor Density:	Not established.
Vapor Pressure:	Not established.
Percent Volatile:	Not established.
pH:	Approximately 4
Molecular Formula:	Mixture
Molecular Weight:	303.3
Flash Point:	Not established.
Flash Point Method:	Not established.
Auto Ignition Temperature:	Not established.

SECTION 10 : STABILITY and REACTIVITY

Chemical Stability:	Stable under normal temperatures and pressures.
Hazardous Polymerization:	Not reported.
Conditions to Avoid:	No conditions contributing to instability are known to exist for normal handling of this product.

SECTION 11 : TOXICOLOGICAL INFORMATION

Flumazenil :

Acute Toxicity:	LD50 IV Mouse: > 2.5 mg/kg
Teratogenicity:	Pregnancy Category C: Therapeutic use of flumazenil should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Other: Not applicable

Flumazenil :

RTECS Number:	NI2922170
Ingestion:	Oral - Rat LD50: 4200 mg/kg [Behavioral - Somnolence (general depressed activity) Behavioral - Tremor Behavioral - Rigidity (including catalepsy)] Oral - Mouse LD50: 1300 mg/kg [Behavioral - Somnolence (general depressed activity) Behavioral - Tremor Behavioral - Rigidity (including catalepsy)]
Other Toxicological Information:	Intravenous. - Rat LD50: 85 mg/kg [Behavioral - convulsions or effect on seizure threshold Behavioral - rigidity (including catalepsy)] Intravenous. - Mouse LD50: 143 mg/kg [Behavioral - convulsions or effect on seizure threshold Behavioral - rigidity (including catalepsy)] Intravenous. - Human TDLo: 0.014 mg/kg [Vascular - BP elevation not characterized in autonomic section Nutritional and Gross Metabolic - body temperature decrease] Subcutaneous - Mouse LDLo: >1 gm/kg [Details of toxic effects not reported other than lethal dose value] Subcutaneous - Rat TDLo: 21 mg/kg [Reproductive - Effects on Newborn - behavioral] Subcutaneous - Mouse TDLo: 220 mg/kg [Reproductive - Effects on Newborn - behavioral] Intraperitoneal. - Rat LD50: 1360 mg/kg [Details of toxic effects not reported other than lethal dose value] Intraperitoneal. - Mouse LD50: 4 gm/kg [Details of toxic effects not reported other than lethal dose value] Intraperitoneal. - Mouse TDLo: 5 mg/kg [Behavioral - changes in motor activity (specific assay) Behavioral - alteration of classical conditioning] Intraperitoneal. - Mouse TDLo: 5.6 mg/kg [Behavioral - antipsychotic] Intraperitoneal. - Mouse TDLo: 10 mg/kg [Behavioral - alteration of classical conditioning] Intraperitoneal. - Rat TDLo: 1 mg/kg [Behavioral - changes in psychophysiological tests] Intraperitoneal. - Mouse TDLo: 10 mg/kg [Behavioral - changes in psychophysiological tests] Intraperitoneal. - Rat TDLo: 3 mg/kg [Brain and Coverings - changes in surface EEG Behavioral - sleep] Intraperitoneal. - Rat TDLo: 10 mg/kg [Brain and Coverings - other degenerative changes]

Methylparaben :

RTECS Number:	DH2450000
Skin:	Administration onto the skin - Rabbit Standard Draize test.: 0.1 mL/24H Administration onto the skin - Rabbit Standard Draize test.: 0.5 mL/21D (Intermittent) Administration onto the skin - Rat TDLo: 374.92 gm/kg/13W (Intermittent) [Nutritional and Gross Metabolic - Weight loss or decreased weight gain Blood - Other changes]

Ingestion:	Oral - Mouse LD50: >8 gm/kg [Peripheral Nerve and Sensation - Flaccid paralysis without anesthesia (usually neuromuscular blockage) Behavioral - Ataxia] Oral - Mouse LD50: >8000 mg/kg [Behavioral - Ataxia] Oral - Rat LD50: 2100 mg/kg [Details of toxic effects not reported other than lethal dose value]
Other Toxicological Information:	Intravenous. - Mouse TDLo: 100 mg/kg [Vascular - shock Lungs, Thorax, or Respiration - respiratory depression] Intravenous. - Mouse TDLo: 2.5 mg/kg [Lungs, Thorax, or Respiration - tumors] Subcutaneous - Mouse TDLo: 165 mg/kg [Behavioral - ataxia Lungs, Thorax, or Respiration - respiratory depression] Subcutaneous - Mouse LD50: 1.2 gm/kg [Details of toxic effects not reported other than lethal dose value] Subcutaneous - Rat LD50: >500 mg/kg [Details of toxic effects not reported other than lethal dose value] Subcutaneous - Mouse TDLo: 49.5 mg/kg/3D (intermittent) [Related to Chronic Data - changes in uterine weight] Subcutaneous - Mouse TDLo: 165 mg/kg/3D (intermittent) [Reproductive - Maternal Effects - uterus, cervix, vagina Related to Chronic Data - changes in uterine weight] Intraperitoneal. - Mouse LD50: 960 mg/kg [Peripheral Nerve and Sensation - flaccid paralysis without anesthesia (usually neuromuscular blockage) Behavioral - somnolence (general depressed activity) Behavioral - ataxia] Intraperitoneal. - Mouse LD50: 125 mg/kg [Details of toxic effects not reported other than lethal dose value] Intraperitoneal. - Rat LD50: 960 mg/kg [Details of toxic effects not reported other than lethal dose value]

Propylparaben :

RTECS Number:	DH2800000
Ingestion:	Oral - Mouse LD50: 6332 mg/kg [Details of toxic effects not reported other than lethal dose value]
Other Toxicological Information:	Subcutaneous - Mouse LD50: 1650 mg/kg [Details of toxic effects not reported other than lethal dose value] Subcutaneous - Mouse TDLo: 51 mg/kg/3D (intermittent) [Related to Chronic Data - changes in uterine weight] Subcutaneous - Rat TDLo: 99 mg/kg/3D (intermittent) [Related to Chronic Data - changes in uterine weight] Subcutaneous - Mouse TDLo: 195 mg/kg/3D (intermittent) [Reproductive - Maternal Effects - uterus, cervix, vagina Related to Chronic Data - changes in uterine weight] Intraperitoneal. - Mouse LD50: 200 mg/kg [Details of toxic effects not reported other than lethal dose value]

Acetic Acid :

RTECS Number:	AF1225000
Eye:	Eye - Rabbit Rinsed with water.: 5 mg/30S
Skin:	Administration onto the skin - Rabbit LD50: 1060 uL/kg [Details of toxic effects not reported other than lethal dose value] Administration onto the skin - Rabbit TDLo: 0.04 gm/kg/24H [Skin and Appendages - Primary irritation (After topical exposure)] Administration onto the skin - Rabbit Open irritation test: 525 mg Administration onto the skin - Rabbit Standard Draize test.: 50 mg/24H Administration onto the skin - Rat TDLo: 0.25 mg/kg [Gastrointestinal - Ulceration or bleeding from duodenum] Administration onto the skin - Mouse Unscheduled DNA synthesis: 79279 ug/kg Administration onto the skin - Mouse Mutation test systems : 1201 mg/kg
Inhalation:	Inhalation - Mouse LC50: 5620 ppm/1H [Sense Organs and Special Senses (Eye) - Conjunctive irritation Sense Organs and Special Senses (Eye) - effect, not otherwise specified Blood - Other changes]
Ingestion:	Oral - Rat LD50: 3310 mg/kg [Details of toxic effects not reported other than lethal dose value]
Other Toxicological Information:	Intravenous. - Mouse LD50: 525 mg/kg [Behavioral - convulsions or effect on seizure threshold] Subcutaneous - Rabbit LDLo: 600 mg/kg [Details of toxic effects not reported other than lethal dose value] Intraperitoneal. - Mouse TDLo: 50 mg/kg [Behavioral - analgesia] Intraperitoneal. - Mouse TDLo: 93.75 mg/kg [Behavioral - convulsions or effect on seizure threshold]

Edetate Disodium :

RTECS Number:	AH4375000
Eye:	Rabbit, not irritating.
Skin:	Rabbit, not irritating.
Inhalation:	Inhalation - Rat LOAEC 30 mg/m³/6 h (aerosol) (OECD Guideline 412) (ECHA)
Ingestion:	Oral - Rat LD50 2800 mg/kg (ECHA)
Other Toxicological Information:	Intravenous. - Mouse LD50 : 56 mg/kg (RTEC)

Sodium Chloride :

RTECS Number:	VZ4725000
Eye:	Eye - Rabbit Standard Draize test.: 10 mg [Moderate]
Skin:	Administration onto the skin - Rabbit LD50: >10 gm/kg [Details of toxic effects not reported other than lethal dose value] Administration onto the skin - Rabbit Standard Draize test.: 50 mg/24H [mild] Administration onto the skin - Rabbit Standard Draize test.: 500 mg/24H [mild]
Inhalation:	Inhalation - Rat LC50: >42 gm/m3/1H [Details of toxic effects not reported other than lethal dose value]
Ingestion:	Oral - Mouse LD50: 4 gm/kg [Details of toxic effects not reported other than lethal dose value] Oral - Rat LD50: 3000 mg/kg [Details of toxic effects not reported other than lethal dose value]

Other Toxicological Information:	Intravenous. - Mouse LD50: 645 mg/kg [Details of toxic effects not reported other than lethal dose value] Intravenous. - Rabbit LDLo: 1100 mg/kg [Behavioral - convulsions or effect on seizure threshold Behavioral - muscle contraction or spasticity Cardiac - other changes] Intravenous. - Guinea pig LDLo: 300 mg/kg [Details of toxic effects not reported other than lethal dose value] Intravenous. - Mouse TDLo: 2.1 mg/kg [Vascular - other changes Blood - hemorrhage Skin and Appendages - dermatitis, irritative (after systemic exposure)] Intravenous. - Rabbit LDLo: 1.5 mg/kg [Details of toxic effects not reported other than lethal dose value] Intravenous. - Rabbit TDLo: 0.04 mg/kg [Vascular - other changes Blood - hemorrhage Skin and Appendages - dermatitis, irritative (after systemic exposure)] Subcutaneous - Rat LDLo: 3500 mg/kg [Behavioral - irritability] Subcutaneous - Mouse LD50: 3 gm/kg [Details of toxic effects not reported other than lethal dose value] Subcutaneous - Guinea pig LDLo: 2160 mg/kg [Details of toxic effects not reported other than lethal dose value] Subcutaneous - Rabbit TDLo: 0.04 mg/kg [Vascular - other changes Skin and Appendages - dermatitis, irritative (after systemic exposure)] Subcutaneous - Mouse TDLo: 1900 mg/kg [Reproductive - Effects on Embryo or Fetus - fetal death] Subcutaneous - Mouse TDLo: 1900 mg/kg [Reproductive - Specific Developmental Abnormalities - musculoskeletal system] Subcutaneous - Mouse TDLo: 2500 mg/kg [Reproductive - Effects on Embryo or Fetus - fetotoxicity (except death, e.g., stunted fetus)] Subcutaneous - Mouse TDLo: 13440 mg/kg [Reproductive - Fertility - abortion] Intraperitoneal. - Mouse LD50: 2602 mg/kg [Details of toxic effects not reported other than lethal dose value] Intraperitoneal. - Rat LD50: 2600 mg/kg [Details of toxic effects not reported other than lethal dose value] Intraperitoneal. - Rat LDLo: 3.72 gm/kg [Behavioral - tremor Behavioral - convulsions or effect on seizure threshold] Intraperitoneal. - Rat TDLo: 1710 mg/kg [Reproductive - Effects on Embryo or Fetus - fetotoxicity (except death, e.g., stunted fetus) Reproductive - Effects on Embryo or Fetus - fetal death Reproductive - Specific Developmental Abnormalities - musculoskeletal system] Intraperitoneal. - Rat TDLo: 10 gm/kg [Reproductive - Effects on Newborn - behavioral] Intraperitoneal. - Rat Cytogenetic analysis: 2338 mg/kg

SECTION 12 : ECOLOGICAL INFORMATION

Ecotoxicity:	No ecotoxicity data was found for the product.
Environmental Stability:	No environmental information found for this product.
Edetate Disodium :	
Ecotoxicity:	Guppy (Poecilia reticulata) LC50 (96hr) 320 mg/L (OECD SIDS) Zebra fish (Danio rerio) NOEC (35d) >= 25.7 mg/L (OECD Guideline 210 , GLP) (TS : Ethylenediamintetraacetic acid, calcium disodium complex) Water flea (Daphnia magna) EC50 (48hr) 140 mg/L, NOEC (21d) 25 mg/L (EEC Guideline XI/681/86, GLP) (TS : Ethylenediaminetetraacetic acid, disodium salt) Green algae (Scenedesmus quadricauda) NOEC (24 d) 200 mg/L (ECHA)

SECTION 13 : DISPOSAL CONSIDERATIONS

Waste Disposal:	Dispose of in accordance with Local, State, Federal and Provincial regulations.

SECTION 14 : TRANSPORT INFORMATION

DOT Shipping Name:	Not Regulated.
DOT UN Number:	Not Regulated.

SECTION 15 : REGULATORY INFORMATION

Methylparaben :	
TSCA Inventory Status:	Listed
EINECS Number:	202-785-7
Canada DSL:	Listed
Propylparaben :	
TSCA Inventory Status:	Listed
EINECS Number:	202-307-7
Canada DSL:	Listed
Acetic Acid :	
TSCA Inventory Status:	Listed
EINECS Number:	200-580-7
Canada DSL:	Listed
Canada IDL:	Identified under the Canadian Hazardous Products Act Ingredient Disclosure List: 0.1%.6(51)
Edetate Disodium :	

TSCA Inventory Status:	Listed
EINECS Number:	205-358-3
Canada DSL:	Listed

Sodium Chloride :

TSCA Inventory Status:	Listed
EINECS Number:	231-598-3
Canada DSL:	Listed

SECTION 16 : ADDITIONAL INFORMATION

HMIS Ratings:

HMIS Health Hazard:	1
HMIS Fire Hazard:	0
HMIS Reactivity:	0
HMIS Personal Protection:	C

SDS Creation Date:	January 08, 2009
SDS Revision Date:	February 19, 2024
SDS Revision Notes:	Overall SDS review - no changes to formulation. Added the word 'USP' to product name. Added HMIS ratings for Health, Flammability, Reactivity, and Personal Protective Equipment (PPE).
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