SAFETY DATA SHEET

Piperacillin and Tazobactam for Injection USP

Section 1. Chemical Product and Company Information	
Product	Piperacillin and Tazobactam for Injection, USP
Chemical Name(s):	**Piperacillin:** (2S, 5R, 6R)-6-[(R)-2-(4-ethyl-2,3-dioxo-1- piperazine-carboxamido)-2-phenylacetamido]-3,3-dimethyl-7- oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate **Tazobactam:** (2S, 3S, 5R)-3-methyl-7-oxo-3-(1H-1,2,3- triazol-1-ylmethyl)-4-thia-1-azabicyclo[3.2.0]heptane-2- carboxylate-4,4-dioxide
Synonym	PipTaz, Zosyn
CAS Number	Piperacillin sodium: 59703-84-3; Tazobactam sodium: 89785-84-2
RTECS #	N/F
Trade Name	Zosyn
Chemical Formula	Piperacillin sodium: $C_{23}H_{26}N_5NaO_7S$; Tazobactam sodium $C_{10}H_{11}N_4NaO_5S$
Contact Information	Apollo Pharmaceuticals USA Inc. 4400 PGA Blvd. Suite 102, Palm Beach Gardens, FL 33410, USA Tel.: (561) 469-9058, Fax: (561) 727 8943
Emergency Phone Number	National Poison Control 1-800-222-1222

Section 2: Hazards Identification

Hazard pictograms (GHS-US):

Potential Acute Health Effects: May be harmful in case of skin contact (irritant), of eye contact (irritant), and inhalation.

Potential Chronic Health Effects: Piperacillin and Tazobactam for Injection is a drug used to treat bacterial infections. It may cause allergic reactions in individuals with a history of penicillin hypersensitivity or a history to multiple allergens. The most common effects may include diarrhea, headache, constipation, nausea, insomnia, rash, vomiting, dyspepsia, pruritus, stool changes, fever, agitation, pain, moniliasis, hypertension, dizziness, abdominal pain, chest pain, edema, anxiety, rhinitis, and dyspnea.

Carcinogenic Effects: Long-term carcinogenicity studies in animals have not been conducted with piperacillin/tazobactam, piperacillin, or tazobactam. This material is not considered to be a carcinogen by IARC, NIP or OSHA.

Mutagenic Effects: Not available

Teratogenic Effects: Animal studies have failed to reveal evidence of fetal toxicity or teratogenicity.

Developmental Toxicity: Classified development toxin (possible). The substance may be toxic to kidneys. Repeated or prolonged exposure to the substance can produce target organ damage.

Adverse effects: Not available

Section 3: Composition and Information on Ingredients

Principle Components:

Name	CAS #	% by Weight
Piperacillin sodium	59703-84-3	2 - 4 g/vial
Tazobactam sodium	89785-84-2	0.25 - 0.5 g/vial

Section 4. First Aid Measures

General: Remove from exposure. Remove contaminated clothing. For treatment advice, seek guidance from an occupational health physician or other licensed health-care provider familiar with workplace chemical exposure. If person is not breathing give artificial respiration. If breathing is difficult give oxygen. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention. Obtain medical attention.

Inhalation: If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, administer oxygen. Seek medical attention immediately.

Skin contact: In case of contact, immediately wash skin with plenty of water and soap for at least 15 minutes. Remove contaminated clothing and shoes. Wash clothes and thoroughly clean shoes before reuse. Seek medical attention immediately.

Eye contact: Check for and remove any contacts lenses. Immediately flush eyes with plenty of water for at least 15 minutes. Seek medical attention immediately.

Ingestion: DO NOT induce vomiting unless directed to do so by a medical professional. Never give anything by mouth to an unconscious person. Loosen tight clothing such as tie, collar and/or belt. Seek medical attention immediately.

Notes to physician: See product package insert for complete information.

Overdose Treatment: Treatment of overdose should be symptomatic and supportive. Administer activated charcoal with sorbitol to decrease absorption. For acidosis, administer sodium bicarbonate. Monitor fluids and electrolyte status. Correct fluid and electrolyte disturbance. Hemodialysis may be of benefit.

Section 5. Fire-fighting Measures

Flammability of the product: May combust at high temperatures.
Combustion Products: May include but are not limited to: Carbon oxides, nitrogen oxides and other noxious gases or vapors in case of incomplete combustion.

Unusual Fire and Explosion Hazards: Product is not expected to present a fire hazard.

Extinguishing Media and instruction:

Small fire: Use water spray, dry chemical, carbon dioxide or foam, as appropriate for surrounding fire and materials. **Large fire:** Use water spray, fog or foam, DRY chemical or carbon dioxide. May use type ABC multi-purpose extinguisher. DO NOT use water jet.

Protective equipment & precautions for firefighters: As with all fires, evacuate personnel to a safe area and fight fire from a safe distance. Use water spray to cool any closed containers exposed to the fire. Under fire conditions it emits toxic fumes. DO NOT breath fumes. Firefighters should wear self-contained breathing apparatus and protective clothing.

Special remarks on fire hazard: Not available

Special remarks on explosion hazard: Not available

Section 6. Accidental Release Measures

Release to land:
Small Spill: Use appropriate tools to put the spilled solid in a convenient waste disposal container. A high efficiency vacuum may be used to collect spillage. AVOID breathing dust. Finish cleaning by spreading water and soap on the contaminated spill site and dispose of according to local, state, and federal regulations.

Large Spill: Use a shovel to put the material into a convenient waste disposal container. Sweep up or vacuum with caution to avoid generation of dust during clean-up. AVOID breathing dust. Finish cleaning by spreading water and soap on the contaminated surface and clean surface thoroughly to remove residual contamination. Collect in suitable container labelled appropriately for disposal. For proper waste disposal, see section 13 of the SDS.

Release to air: Avoid raising dust or mist. Clean up spill immediately. Wash with water/detergent solution after material pick up is complete. If dust is generated, wear a disposable dust respirator (N95), and reduce exposures by ventilating area. If breathing becomes difficult, give oxygen. Remove to fresh air.

Release to Water: Refer to local water authority; drain disposal is not recommended.

Protective equipment: Keep unnecessary personnel away. Wear latex or nitrile gloves, safety glasses, and a disposable dust mask (N95), wear protective coveralls and shoe covers for large spills.

Section 7. Handling and Storage

Handling: As a general rule, when handling Piperacillin and Tazobactam for Injection, USP, avoid inhalation, contact with eyes, skin and clothing. Avoid prolonged or repeat exposure.
Keep locked up. Keep away from heat, sources of ignition and oxidizing agents. Empty containers pose a fire risk, evaporate the residue under a fume hood. DO NOT ingest. DO NOT breathe dust. Wear suitable protective clothing. Use only in accordance with directions.

Storage: Keep container tightly closed. Keep container in a cool, dry, well ventilated area (see USP CRT storage conditions). Store at 68° to 77°F (20° to 25°C); excursions permitted between 59° and 86°F (15° and 30°F). Refer to label instructions to ensure product integrity.

Incompatibilities: No material to be especially mentioned. However, keep away from strong oxidizing agents and bases.

Section 8. Exposure Control / Personal Protection

Engineering Controls: Use process enclosure, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operation generates dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Protective chemical safety glasses. Lab coat or protective suit and gloves. Protecting mask or dust respirator. Be sure to use an approved/ certified respirator or equivalent. **In case of Large Spill:** Protective chemical splash goggles with full protective suit. Protective mask on dust respirator. Boots and chemical-resistant gloves. Protect all exposed skin. A self-contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Respiratory Protection: Under normal use, respirators are not required. If dusts are generated, use a disposable mask (N95). Personnel wearing respirators should be fit tested and approved for respirator use, under OSHA Respiratory Protection Standard 29 CFR 1910.134.

Exposure limit: Not Established

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Section 9. Physical and chemical properties	
Physical appearance: Solid powder	**Evaporation rate:** Not Established
Color: White to off-white	**Flammability:** Not Established
Molecular Weight:	**Upper Flammable Limit:** Not Established
Piperacillin Sodium – 539.54 g/mole	**Lower Flammable Limit:** Not Established
Tazobactam Sodium – 322.28 g/mole	**Vapor Pressure:** Not Established
Taste: Not available	**Vapor Density:** Not Established
Odor: Odorless	**Relative Density:** Not Established
Odor Threshold: Not available	**Partition Coefficient:** Not Established
pH: 5.0 – 7.0	**Auto-Ignition Temperature:** Not Established
Melting Point: 311°F (155°C)	**Decomposition Temperature:** Not Established
Freezing Point: Not Established	**Viscosity:** Not Established
Boiling Point: Not Established	**Dispersion Properties:** Not Established
Flash Point: Not Established	**Solubility:** Very Soluble in water

Section 10. Stability and reactivity

Reactivity: Stable under normal conditions.

Chemical stability: Stable. No dangerous reactions are known to occur under conditions of normal use.

Possibility of hazardous reaction: Hazardous polymerization is not anticipated to occur with this product.

Conditions to avoid: Store away from strong oxidizers and strong bases.

Incompatible materials: There are no materials to be especially noted.

Hazardous decomposition products: During thermal decomposition, it may emit irritating and/or toxic fumes of carbon dioxide, nitrogen oxides or sulfur oxides.

Corrosivity: Non-corrosive in presence of glass.

Polymerization: Not known to occur.

Section 11. Toxicological information

Routes of exposure: Absorbed through skin, eye contact, inhalation and ingestion.

Symptoms: Individuals with a history of penicillin hypersensitivity or a history of sensitivity to multiple allergens should avoid contact. The most common effects may include diarrhea, headache, constipation, nausea, insomnia, rash, vomiting, dyspepsia, pruritus, stool changes, fever, agitation, pain, moniliasis, hypertension, dizziness, abdominal pain, chest pain, edema, anxiety, rhinitis, and dyspnea.

Short term: Hazardous in cases of inhalation. Hazardous in case of skin contact (irritant). Symptoms such as skin rash, diarrhea, nausea, vomiting or rash are commonly observed.

Long term: Exposure may result in blood and lymphatic system disorder, leading to infections. May cause damage to the following organs: Kidneys.

Reproductive toxicity: Animal studies have failed to reveal evidence of fetal toxicity or teratogenicity. There are no controlled data in human pregnancies. However, Piperacillin is excreted into human milk in small amounts. Material crosses the placenta and is excreted in human milk. May be harmful to pregnant women and their babies. May be harmful to breastfed babies. There are no data on the excretion of Tazobactam into human milk.

FDA Pregnancy Category: B

Toxicity to animals:

Component	Type	Route	Species	Dosage
Piperacillin sodium	LD_{50}	Oral	Rat	>10 g/kg
Piperacillin sodium	LD_{50}	Oral	Mice	>10 g/kg
Piperacillin sodium	LD_{50}	Intravenous	Rat	2260 mg/kg
Piperacillin sodium	TD_{Lo}	Intravenous	Woman	2180 mg/kg/6 days
Piperacillin sodium	TD_{Lo}	Intramuscular	Woman	960 mg/kg/3 days
Piperacillin sodium	LD_{50}	Intraperitoneal	Mice	9770 mg/kg
Piperacillin sodium	LD_{50}	Subcutaneous	Mice	>10 g/kg
Piperacillin sodium	LD_{50}	Intravenous	Mice	4900 mg/kg
Piperacillin sodium	LD_{50}	Intravenous	Dog	>6 g/kg
Piperacillin sodium	LD_{50}	Intravenous	Monkey	>4 g/kg
Tazobactam sodium	LD_{50}	Oral	Mice	>5,000 mg/kg
Tazobactam sodium	LD_{50}	Oral	Rat	>5,000 mg/kg
Tazobactam sodium	LD_{50}	Intravenous	Mice	>5,000 mg/kg
Tazobactam sodium	LD_{50}	Intravenous	Rat	>5,000 mg/kg

Measures of toxicity: Not available

Additional reproductive health and toxicity data is available from the National Institute for Occupational Safety and Health (NIOSH) and/or Registry of Toxic Effects of Chemical Substance (RTECS).

Section 12. Ecological information

Ecotoxicity:
Microorganism: Minimum inhibitory concentration (MIC) >1000 mg/l for 3 test species.
Pseudomonas MIC=250 mg/l Daphnia: LC50 / 48h/daphnia >8.5 mg/l NOEC=8.5 mg/l

Bioaccumulation potential: Not available

Products of biodegradation: Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise. Stable at pH 7 and below. At pH 9, half-life = 29h

Toxicity of the products of biodegradation: The product itself and its products of degradation are not toxic.

Section 13. Disposal Information

Waste classification: Non-Hazardous

Waste from residues/unused products: Dispose of waste in accordance with all applicable federal, state and local laws.

Waste Disposal: Dispose of waste in accordance with all applicable federal, state and local laws.

Section 14. Transport Information

DOT Classification: Not a DOT controlled material (United States).
UN Number: Not available
UN Shipping name: Not available
Transport hazard class: Not available
Packing Group: Not available
Environmental hazard: Not available
Transport in bulk: Not available
Special precautions needed with transport: Not available

Section 15 Regulatory Information

Federal and State Regulations:
U.S. Regulations:
TSCA - No CERCLA - Not on this list
SARA 302 – Not on this list
SARA 311 - Not on this list
SARA 312 – Not on this list
SARA 313 – Not on this list
OSHA Substance Specific – No
Other Classifications:
WHMIS (Canada): Not controlled under WHMIS (Canada).
DSCL (EEC): R36/38-Irritating to eyes and skin. R61- may cause harm to the unborn child.
HMIS (U.S.A.):
Health Hazard: 2
Fire Hazard: 0
Reactivity: 0
Personal Protection: E

National Fire Protection Association (U.S.A.):
Health: 2
Flammability: 1
Reactivity: 0
US OSHA Classification: Possible Sensitizer, Target Organ Toxin, Possible Irritant

Section 16. Additional Information

References: Not available
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Prepared & Approved by: Apollo Pharmaceuticals USA Inc. Quality Department & Safety Committee

The above information is believed to be accurate and represents the best information currently available to Apollo Pharmaceuticals USA Inc. The use of this product should be through or under the direction of a physician or a registered healthcare practitioner. This SDS does not address therapeutic use of this material. Apollo Pharmaceuticals USA Inc. makes no warranties, 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. In no event should Apollo Pharmaceuticals USA Inc. be liable for any claim, loss, or damage of any third party, even if Apollo Pharmaceuticals USA Inc. has been advised of the possibility of such damages to occur.