

SAFETY DATA SHEET

PRODUCT NAME: PRIMAXIN® I.V.**Page: 1/7****Revision 23-Jul-2008**

1. Product and Company Identification

Manufactured/Supplied by MERCK & CO., INC.
One Merck Drive
Whitehouse Station, NJ 08889-0100
(908) 423-1000

Emergency Telephone Number: 1-732-594-5555

Label Name PRIMAXIN® I.V.
Chemical Name Complex chemical mixture.
Synonyms Imipenem and Cilastatin Sodium for Injection; TIENAM[®] I.V.
Material Product Number 3514; 3515; 3516; 3517; 3551; 3552; 3666
NDC# 0006-3514-58;
NDC# 0006-3516-59;
NDC# 0006-3517-75;
NDC# 0006-3551-58;
NDC# 0006-3552-59;
NDC# 0006-3666-59

Intended Use Finished pharmaceutical product - broad spectrum antibacterial agent for intravenous administration.

2. Composition/Information on Ingredients

<u>Component</u>	<u>Molecular Formula</u>	<u>Molecular weight</u>	<u>CAS Number</u>	<u>Percent (%)</u>
IMIPENEM	C ₁₂ H ₁₇ N ₃ O ₄ S·H ₂ O	317.37	74431-23-5	48.9
CILASTATIN SODIUM	C ₁₆ H ₂₅ N ₂ O ₅ Na	380.43	81129-83-1	49.4
SODIUM BICARBONATE	C-H-O ₃ .Na	84.01	144-55-8	1.6

EC Label Harmful
R36- Irritating to eyes.
R42/43- May cause sensitization by inhalation and skin contact.

3. Hazards Identification

Appearance Near white to white powder. Solutions of PRIMAXIN I.V. range from colorless to yellow.

Label Text WARNING!
FINISHED PHARMACEUTICAL PRODUCT.
ANTIBACTERIAL AGENT (ANTIBIOTIC).
MAY CAUSE EYE IRRITATION.
MAY CAUSE ALLERGIC RESPIRATORY AND SKIN REACTION.

Emergency Overview

Avoid contact with eyes. Do not breathe dust. Avoid prolonged or repeated contact with skin. Keep container closed. Use only with adequate ventilation. Wash thoroughly after handling.

Potential Health Effects

See Section 11 for detailed information.

4. First Aid Measures

Eye Contact

In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention.

Skin Contact

In case of contact, immediately flush skin with plenty of water while removing contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

Inhalation

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Ingestion

Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Get medical attention if symptoms appear.

Notes to physician

Overdosage may result in seizures, ataxia, clonic convulsions, hypotension, decreased activity and bradypnea. Treat symptomatically and supportively. Hypersensitivity (anaphylactic) reactions require immediate treatment with epinephrine.

For additional guidance refer to the current prescribing information or the local poison control center.

5. Fire Fighting Measures

Flash Point

Not applicable.

Flammable Limits (% in air)

Not applicable.

Autoignition Temperature

IMIPENEM 454°C (849.2°F)
CILASTATIN SODIUM 410°C (770°F)

Oxidizing Properties

Not available.

Combustibility Information

Not available.

Dust Explosivity Information

IMIPENEM Explosion characteristics - Strong
Kst = 248 bar m/sec, Pmax = 8.6 bar.
Easily ignitable dust.
Minimum Ignition Energy (MIE)
3 mJ < MIE < 10 mJ Without induction
Minimum Ignition Energy (MIE)
MIE < 3 mJ With induction
Minimum Ignition Temperature (MIT)
450 C < MIT < 460 C

Shock Sensitivity

Not available.

Fire/Explosion Hazards

May present an explosion hazard when material is suspended in air in confined areas or equipment and subjected to spark, heat or flame.

IMIPENEM In the Burner Flame Application, material melted and burned in hot liquid fires, generating black smoke and flammable vapors and leaving behind a slight carbon char residue.

CILASTATIN SODIUM Powder self ignites at 770°F. Sample melts and burns in a hot liquid fire producing dark gray smoke and flammable vapors. Can form an explosive mixture with air in dusty conditions.

Special Fire Procedures

Fire fighters should wear positive pressure self-contained breathing apparatus (SCBA) and full turnout gear.

Extinguishing Media

In case of fire, use water spray (fog), foam or dry chemicals.

Hazardous Decomposition Products

These products are carbon oxides, nitrogen oxides, sulfur oxides.

6. Accidental Release MeasuresPersonal Precautions

See Section 8 for Personal Protective Equipment. Immediately contact emergency personnel. Keep unnecessary personnel away. Follow all fire fighting procedures (Section 5).

Methods for cleaning up

If emergency personnel are unavailable vacuum or carefully scoop up spilled materials and place in an appropriate container for disposal. Avoid creating dusty conditions and prevent wind dispersal. Minimize contact of spilled material with soils to prevent runoff to surface waterways. **See Section 13 for Waste Disposal Information.**

7. Handling and StorageHandling

Avoid contact with eyes. Do not breathe dust. Avoid prolonged or repeated contact with skin. Keep container closed. Use only with adequate ventilation. Wash thoroughly after handling.

Storage

To prevent product degradation the dry powder should be stored at a temperature below 25°C (77°F). Avoid any contact with moisture. Keep container tightly closed.

8. Exposure Controls/Personal ProtectionExposure Guidelines

<u>Component</u>	<u>OSHA Permissible Exposure Limit (PEL)</u>	<u>ACGIH Threshold Limit Value (TLV)</u>	<u>Merck Exposure Control Limit (ECL) or PB-ECL Category</u>
IMIPENEM	Not established	Not established	5 mg/m ³ (TWA)
CILASTATIN SODIUM	Not established	Not established	5 mg/m ³ (TWA)
SODIUM BICARBONATE	Not established	Not established	Not established

Imipenem:

ADI = 50 mg/day

Wipe Test Criteria = Not Required

Cilastatin Sodium:ADI = 50 mg/day ECL = 5 mg/m³

Wipe Test Criteria = Not Required

Engineering Controls

None required with normal handling of finished product.

Use feasible engineering controls to minimize exposure to compound.

Personal Protective EquipmentEye/Face Protection

None required with normal handling of finished product.

Safety glasses with side shields. Where the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Skin Protection

None required with normal handling of finished product.

Disposable chemical resistant gloves.

Respiratory Protection

Use an appropriate approved air-purifying respirator equipped with HEPA cartridges/canisters where there is the potential for exceeding established occupational exposure limits or occupational exposure bands. When handling a compound in solution, a cartridge/canister appropriate for the solution may also be needed.

Use a positive pressure, air-supplied, pressure demand tight fitting respirator (e.g., SCBA or airline equipped with emergency escape bottle) where there is a potential for uncontrolled releases in excess of the respirator's capabilities, where exposure levels are unknown or where air-purifying respirators may not provide adequate protection.

Additional Protective Equipment

Work uniform or laboratory coat.

9. Physical and Chemical PropertiesAppearance

Near white to white powder. Solutions of PRIMAXIN I.V. range from colorless to yellow.

Odor/Threshold Limit

Slight sulfur-like odor.

pH

Acidic.

Boiling Point

Not applicable.

Melting Point

Not available.

Flash point

Not applicable.

Flammable Limits (% in air)

Not applicable.

Autoignition Temperature**IMIPENEM** 454°C (849.2°F)**CILASTATIN SODIUM** 410°C (770°F)

Solubility**IMIPENEM:**Sparingly soluble in water.**CILASTATIN SODIUM:**Very soluble in water.**SODIUM BICARBONATE:**Soluble in water.Partition Coefficient

Not available.

Specific Gravity

Not available.

Vapor Density

Not applicable.

Vapor Pressure

Not applicable.

Volatility Component

0% (w/w).

10. Stability and ReactivityStability

The product is stable.

Conditions to Avoid

Avoid any contact with moisture. Very hygroscopic material.

Incompatibility

None known.

Hazardous Polymerization

Will not occur.

Hazardous Decomposition Products

These products are carbon oxides, nitrogen oxides, sulfur oxides.

11. Toxicological InformationRoutes of Entry

Ingestion:

No.

Inhalation:

Yes.

Skin Contact:

No.

Toxicity Data

<u>Component</u>	<u>Test</u>	<u>Species</u>	<u>Route</u>	<u>Result</u>
Imipenem/ Cilastatin Sodium (1:1)	LD50	Mouse	I.V.	751 to 1359 mg/kg
	LD50	Rat	I.V.	771 to 1583 mg/kg
Imipenem	LD50	Mouse	Oral	10000 mg/kg
	LD50	Mouse	I.V.	1650 mg/kg
	LD50	Rat	I.V.	1650 mg/kg
	Irrit.	Rabbit	Dermal	Non-irritating
	Irrit.	Rabbit	Ocular	Slightly irritating
Cilastatin Sodium	LD50	Rat	Oral	>10000 mg/kg
	LD50	Mouse	Oral	>10000 mg/kg
	Irrit.	Rabbit	Dermal	Non-irritating
Sodium Bicarbonate	Irrit.	Rabbit	Ocular	Moderately irritating
	LD50	Rat	Oral	4220 to 8000 mg/kg

Effects of Acute ExposureEye contact**IMIPENEM:**Slightly irritating to the eyes.**CILASTATIN SODIUM:**Moderately irritating to the eyes.Skin contact**IMIPENEM** Not absorbed through the skin. Non-irritating to intact skin in animal studies. May cause sensitization by skin contact.**CILASTATIN SODIUM**Non-irritating to intact skin.Inhalation**IMIPENEM:**May cause sensitization by inhalation.**CILASTATIN SODIUM**No known effects of over-exposure due to inhalation.Ingestion

Practically non-toxic if swallowed.

Effects of Chronic Exposure

In clinical studies, the most common effects that may be associated with Primaxin IV included fever, hypotension, seizures, dizziness, pruritis, urticaria, and somnolence.

IMIPENEM High intravenous doses in animal studies caused kidney damage and slight decreases in fetal body weight in rats and an increase in embryonic loss in monkeys. There was no other evidence of fetal harm observed in developmental toxicity studies. The compound was shown to be non-genotoxic *in vivo* and *in vitro* assays.

CILASTATIN SODIUM In a three-month intravenous toxicity study in rats at 20, 100, and 500 mg/kg/day, a slightly lowered body weight gain was observed in the highest dose group. No treatment-related effects on hematologic, serum biochemical, or urine parameters were observed.

Carcinogen Designation

Not listed as a carcinogen by OSHA, NTP or IARC.

Medical Conditions Aggravated by Overexposure:

Pre-existing hypersensitivity (anaphylactic) reactions to Beta-lactams (penicillins, cephalosporins, etc.), CNS disorders and compromised renal function.

12. Ecological InformationEnvironmental Effects

IMIPENEM Will not persist long enough to be harmful to aquatic organisms. Very rapidly degrades.

CILASTATIN SODIUM Not harmful to aquatic organisms.

Ecotoxicity Data

<u>Component</u>	<u>Species</u>	<u>Period</u>	<u>Result</u>
Imipenem	<i>Daphnia magna</i> (LC50)	48 hours	100 mg/L
Cilastatin Sodium	<i>Daphnia magna</i> (LC50)	48 hours	29700 mg/L

Environmental Fate

IMIPENEM Sparingly soluble in water. Hydrolyzes rapidly at room temperature, therefore will not persist in the environment.

13. Disposal ConsiderationsWaste Disposal Information

Avoid contact of spilled material and runoff with soil and surface waterways. Dispose of or treat all spill residues including contaminated soils following all applicable regulations.

14. Transport InformationShipping Description

<u>U.S. DOT</u>	Not regulated.
<u>IATA/ICAO</u>	Not regulated.
<u>IMO</u>	Not regulated.
<u>ADR/RID</u>	Not regulated.

15. Regulatory Information

U.S. Federal Regulations

Hazardous per OSHA Hazard Communication Standard criteria (29 CFR 1910.1200).

State Regulations

Not available.

International Regulations

Classified as Dangerous according to the Dangerous Substance Directive (DSD).

16. Other Information

Revisions: Effects of Chronic Exposure

Revision:

7/23/2008.

Date of Preparation

July 1999

Date of Previous Issue

19-Nov-2007

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7/23/2008.

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Disclaimer:

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