SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

Product Identifier

Material Name: Imipenem and Cilastatin for Injection, USP (Hospira Inc.)

Trade Name: Imipenem and Cilastatin for Injection, USP
Chemical Family: Not determined

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Pharmaceutical product used as antibiotic agent

Details of the Supplier of the Safety Data Sheet

Hospira, A Pfizer Company
275 North Field Drive
Lake Forest, Illinois 60045
1-800-879-3477

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Hospira UK Limited
Horizon
Honey Lane
Hurley
Maidenhead, SL6 6RJ
United Kingdom
Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Respiratory Sensitization: Category 1
Skin Sensitization: Category 1

Label Elements

Signal Word: Danger
Hazard Statements:
H317 - May cause an allergic skin reaction
H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled

Precautionary Statements:
P261 - Avoid breathing dust/fume/gas/mist/vapors/spray
P272 - Contaminated work clothing must not be allowed out of the workplace
P280 - Wear protective gloves/protective clothing/eye protection/face protection
P284 - Wear respiratory protection
P304 + P340 - IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
P342 + P311 - If experiencing respiratory symptoms: Call a POISON CENTRE or doctor/physician
P302+ P352 - IF ON SKIN: Wash with plenty of soap and water
P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention
P362 - Take off contaminated clothing and wash before reuse
P501 - Dispose of contents/container in accordance with all local and national regulations

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.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Imipenem Monohydrate	64221-86-9	264-734-5	Resp Sens. 1 (H334) Skin Sens. 1 (H317)	49

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Sodium bicarbonate	144-55-8	205-633-8	Not Listed	<2
Cilastatin Sodium	82009-34-5	279-875-8	Not Listed	49

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

4. FIRST AID MEASURES

Description of First Aid Measures

Eye Contact: Flush eye(s) immediately with plenty of water. If irritation occurs or persists, get medical attention.

Skin Contact: Wash skin with soap and water. If skin irritation persists, call a physician.

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 exposed person to fresh air. Refer to a physician if subject experiences difficulty breathing. If breathing has stopped, a trained person should perform cardiopulmonary resuscitation (CPR) and seek immediate medical assistance.

Most Important Symptoms and Effects, Both Acute and Delayed

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

Medical Conditions Aggravated by Exposure: Allergies to cephalosporin antibiotics. People allergic to penicillins may exhibit cross reaction sensitivity.

Indication of the Immediate Medical Attention and Special Treatment Needed

Notes to Physician: None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire. May include oxides of sulfur, carbon, nitrogen and products of chlorine.

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters

During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

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 spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling

Minimize dust generation and accumulation. Avoid breathing dust. 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): No data available

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

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

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Sodium bicarbonate

Czech Republic OEL - TWA	5 mg/m^3
Latvia OEL - TWA	5 mg/m^3

The purpose of the Occupational Exposure Band (OEB) classification system is to separate substances into different Hazard categories when the available data are sufficient to do so, but inadequate to establish an Occupational Exposure Limit (OEL). The OEB given is based upon an analysis of all currently available data; as such, this value may be subject to revision when new information becomes available.

Imipenem Monohydrate

Pfizer Occupational Exposure Band (OEB):	OEB 1 - Sensitizer (control exposure to the range of 1000ug/m^3 to 3000ug/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).
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.)

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Powder in vial	**Color:**	White to off-white to slightly yellow
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:	6.5-8.5
Melting/Freezing Point (°C):	No data available
Boiling Point (°C):	No data available.

Partition Coefficient: (Method, pH, Endpoint, Value)
Imipenem Monohydrate
No data available
Cilastatin Sodium
No data available

9. PHYSICAL AND CHEMICAL PROPERTIES

Sodium bicarbonate
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

10. STABILITY AND REACTIVITY

Reactivity: No data available
Chemical Stability: Stable under normal conditions of use.
Possibility of Hazardous Reactions
- **Oxidizing Properties:** None
- **Conditions to Avoid:** Fine particles (such as dust and mists) may fuel fires/explosions.
- **Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers
- **Hazardous Decomposition Products:** Thermal decomposition products may include carbon monoxide, carbon dioxide, oxides of nitrogen, sulfur, hydrogen chloride and other chlorine- and sulfur-containing compounds.

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects

General Information: The information included in this section describes the potential hazards of the individual ingredients.

Short Term: Individuals who are sensitive to beta lactam antibiotics, both penicillins and cephalosporins, may experience contact or systemic hypersensitivity and anaphylaxis upon exposure to this drug. Respiratory reactions may be characterized by rhinitis, sneezing, scratchy throat, oral mucosal edema, laryngeal mucosal edema, coughing, shortness of breath, wheezing, and chest pain. Asthma like reactions occur with acute exposures in sensitized patients.

Known Clinical Effects: Ingestion of this material may cause effects similar to those generally seen in clinical use of antibiotics including gastrointestinal irritation, vomiting, transient diarrhea, nausea, and abdominal pain. The most common adverse effects reported with clinical use were diarrhea, nausea, rash, and vomiting. Adverse effects associated with therapeutic use include seizure, dizziness, itching sensation (pruritus), hives, redness and swelling of the skin (urticaria), fever.

Acute Toxicity: (Species, Route, End Point, Dose)

Imipenem Monohydrate
Rat Oral LD50 > 5000 mg/kg
Rat IV LD50 1972mg/kg

Cilastatin Sodium
Rat IV LDlo 1583 mg/kg

11. TOXICOLOGICAL INFORMATION

Mouse IV LDmin. 1359mg/kg

Sodium bicarbonate
Rat Oral LD50 4220 mg/kg
Mouse Oral LD50 3360mg/kg
Rat Inhalation LC50 > 900mg/m^3

Irritation / Sensitization: (Study Type, Species, Severity)

Sodium bicarbonate
Eye Irritation Rabbit Minimal
Skin Irritation Rabbit Slight

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Imipenem Monohydrate
Embryo / Fetal Development Rat Intravenous900 mg/kg/day NOAEL Not teratogenic
Embryo / Fetal Development Rabbit Intravenous 60 mg/kg/day

Cilastatin Sodium
Embryo / Fetal Development Rabbit Intravenous300 mg/kg/day NOAEL No effects at maximum dose
Embryo / Fetal Development Rat Subcutaneous 1000 mg/kg/day NOAEL No effects at maximum dose

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Imipenem Monohydrate
Mammalian Cell Mutagenicity Negative
Bacterial Mutagenicity (Ames) Negative

Cilastatin Sodium
Bacterial Mutagenicity (Ames) Negative

Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

Product Level Toxicity Data
Acute toxicity

Species	Route	End Point	Dose
Rat	Intravenous	LD50	771:1583
Mouse	Intravenous	LD50	751:1359

Reproduction & Development Toxicity

Study Type	Species	Route	Dosage (mg/kg/day)	End Point	Effect(s)
Reproductive & Fertility	Rat	Intravenous	80	NOAEL	No effects at maximum dose
Reproductive & Fertility	Rat	Subcutaneous	320	NOAEL	No effects at maximum dose

11. TOXICOLOGICAL INFORMATION

Embryo/Fetal Development	Rabbit	Intravenous	80	NOAEL	Not teratogenic
Embryo/Fetal Development	Rabbit	Subcutaneous	320	NOAEL	Not teratogenic

Genetic Toxicity

Study Type	Cell Type / Organism	Result
Mammalian Cell Mutagenicity	Not specified	Negative
Unscheduled DNA Synthesis	Not specified	Negative
In Vivo Cytogenetics	Mouse	Negative

12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been thoroughly investigated. Releases to the environment should be avoided.

Toxicity:
Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Sodium bicarbonate
Daphnia magna (Water Flea) EC50 48 Hours 2350 mg/L
Lepomis macrochirus (Bluegill Sunfish) LC50 96 Hours 8250 mg/L
Gambusia affinis (Mosquitofish) LC50 96 Hours 7550 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential: No data available

Mobility in Soil: No data available

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.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

Sodium bicarbonate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	205-633-8

Cilastatin Sodium

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	279-875-8

Imipenem Monohydrate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	264-734-5

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Sensitization, skin-Cat.1; H317 - May cause an allergic skin reaction
Sensitization, respiratory-Cat.1; H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled

Data Sources: Pfizer proprietary drug development information. Publicly available toxicity information.

Revision date: 04-Aug-2016
Product Stewardship Hazard Communication

Prepared by: Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet