MATERIAL SAFETY DATA SHEET

1. PRODUCT IDENTIFICATION

Product Name Oxaliplatin Injection USP 50mg/10ml vial, 100 mg/20 ml vial and 200 mg/40 ml vial.

Company Name Sun Pharmaceutical Industries Ltd.
Acme Plaza, Andheri-Kurla Road, Andheri (E)
Mumbai – 400 059, INDIA

2. COMPOSITION AND INGREDIENTS

	For 50 mg/10 ml vial	**For 100 mg/20 ml vial**	**For 200 mg/40 ml vial**
CHEMICAL NAME	Percent	Percent	Percent
Oxaliplatin USP	0.50%	0.50%	0.50%
Water for Injection USP	q.s. To 10 ml	q.s. To 20 ml	q.s. To 40 ml

3. HAZARDS IDENTIFICATION

WARNING: The drug substance Oxaliplatin is mutagenic, cytotoxic, neurotoxic and fetotoxic. The drug substance is a possible carcinogen and a severe eye irritant.

NIOSH HAZARDOUS DRUG ALERT: Oxaliplatin injection is an antineoplastic agent and is considered a Hazardous Drug according to the NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. Health care workers who prepare or administer hazardous drugs or who work in areas where these drugs are used should follow specific handling guidelines in order to prevent exposure to these agents in the air or on work surfaces, clothing, medical equipment, or patient urine or feces. See Section 8 for specific handling guidance from the NIOSH Alert for use in the health care setting.

Signs and Symptoms of Overexposure : Anticipated signs of overexposure include nausea, vomiting, diarrhea, peripheral neurotoxicity (with cold sensitivity and rare laryngeal dysesthesias, sensation of difficulty with breathing or swallowing), and possible myelosuppression (low blood counts). Mucositis (sore mouth, or soreness of other mucous membranes) and transient elevation of liver enzymes have been observed. As with other platinum compounds allergic reactions have been observed. In therapeutic use very rare anaphylactoid reactions (severe, possibly life-threatening allergic reactions) have been observed.

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3. HAZARDS IDENTIFICATION Continued..

OSHA chemical hazards according to 29 CFR 1910.1200 for Oxaliplatin pure drug substance: Mutagen, possible carcinogen, cytotoxic, fetotoxic, cardiotoxic, neurotoxic, and irritant.

European Regulation Information for the pure drug substance Oxaliplatin:

T: TOXIC
R60: May impair fertility
R61: May cause harm to the unborn child
R64: May cause harm to breastfed babies.
R68: Possible risk of irreversible effects.
R40: Limited evidence of a carcinogenic effect.
R48/23/24/25 Toxic: Danger of serious damage to health by prolonged exposure through inhalation and if swallowed.
R42/43: May cause sensitization by inhalation and skin contact.

4. FIRST AID MEASURES

Eye Contact: The drug substance Oxaliplatin is a severe eye irritant. In case of contact with the product solution, flush eyes with water for at least 15 minutes. Seek medical attention immediately.

Skin Contact: If the product solution comes in contact with skin and clothing, remove contaminated clothing and wash thoroughly with running water for at least 15 minutes. Use soap if available. Seek medical attention if irritation develops.

Ingestion: In case of acute overdose by ingestion, seek immediate medical attention or contact the appropriate poison control center in your respective country for further instructions.

Inhalation: The product solution could be inhaled if liquid is aerosolized. If inhaled, remove to fresh air. Seek medical attention.

Note To Physicians: Advise physician that the drug substance in this product is an organo-platinum, antineoplastic agent. The compound is mutagenic, and based on the characteristics of the compound, may be carcinogenic.

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5. FIRE FIGHTING MEASURES

This product is mainly composed of water and therefore presents no fire or explosion hazard.

However, the following information would apply if the material were involved in a significant fire.

Products of Combustion
Hazardous products of combustion may include carbon monoxide, carbon dioxide and oxides of nitrogen.

Suitable Extinguishing Media
Water spray, carbon dioxide or dry chemical.

Protection of Firefighters
As in any fire, use pressure demand self-contained breathing apparatus (SCBA) and protective clothing to prevent contact with skin and eyes. Use water spray to keep fire-exposed containers cool.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions
Necessary personal protective equipment should be worn when cleaning up a spill (see Section 8)

Small Spills
If a small spill occurs within a ventilated cabinet, wear protective equipment to prevent inhalation or eye/skin contact (see section 8). Wipe up spill with absorbent material and place in an impervious container. Wash the contaminated area with an undiluted household or commercial sodium hypochlorite (bleach) solution. Wash skin thoroughly after handling.

Large Spills
During a large spill, evacuate non-essential personnel from the area. Wear protective equipment to prevent inhalation or eye/skin contact (see section 8). For inactivation of oxaliplatin, apply undiluted household or commercial sodium hypochlorite (bleach) solution to the spill and allow five minutes of contact time. Absorb the liquid with an inert absorbent material (e.g. absorbent pad, clay, vermiculite, etc.). If bleach is not used, soak up spilled liquid with an absorbent material. Avoid excessive physical disturbance of spill during cleanup to minimize aerosol generation. Wash skin thoroughly after handling.

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6. ACCIDENTAL RELEASE MEASURES Continued..

Spill Waste Disposal
Carefully place the waste in a labeled receptacle for safe disposal as a contaminated waste. Use water/dilute solution of surfactant for final clean up of spill area. Remove any contaminated clothing, personal protective equipment and barrier sheeting, and place in a double sealed, labeled waste container marked for disposal. Wash skin thoroughly after handling.

7. HANDLING AND STORAGE

Only authorized and trained personnel should handle oncology compounds.

Handling
To minimize hazards from accidental breakage or spills of containers and to simplify clean-up, store and transport within secondary containers, pans or trays. Use disposable protective coatings and/or barrier sheeting in use areas where possibility of spillage exists to simplify cleanup. Keep this and all drugs out of the reach of children.

Storage
Label all containers with hazard information (see section 15).

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

HEALTHCARE WORKER HANDLING PROCEDURES AND PRACTICES

A workplace risk assessment must be carried out in order to determine the correct engineering control measures, work practices and personal protective equipment.

The Following Guidance Information is excerpted from the NIOSH ALERT:

Elements of a Hazardous Drug Handling Program include:
•Establishment and implementation of written policies and protocols to ensure the safe handling of

MATERIAL SAFETY DATA SHEET

8. EXPOSURE CONTROLS/PERSONAL PROTECTION **Continued..**

oncolytic drugs, including receipt of product
•Training and education of employees on the recognition, evaluation and control of Hazardous Drugs
•Effective planning and design of the workplace
•Use of best practice control measures and specialized equipment such as ventilated cabinets or isolators designed for worker protection
•Wearing recommended personal protective equipment
•An integrated health surveillance program that: includes the assessment and counseling of prospective employees before they commence any work involving oncolytic drugs and related waste.

Engineering Controls: Preparation of this product should be done in an area that is devoted solely to the preparation of hazardous drugs and is restricted to authorized personnel. This product should be prepared within a ventilated cabinet designed to protect workers and adjacent personnel from exposure. Transfers from primary packaging such as vials to dosing equipment should also be performed within a ventilated cabinet.
Use closed-system, drug-transfer devices, glove bags and needle less systems within the ventilated cabinet.
The final prepared product should be sealed in a plastic bag or other sealable container prior to removal from the cabinet. All waste containers in the cabinet should be sealed and wiped prior to removal for disposal.

Personal Protective Clothing: Avoid skin contact by using a disposable gown made of non-linting and non-absorbent fabric. The gown should have a closed front , long sleeves and elastic or knit closed cuffs and should not be reused.

Gloves: Use two pairs of impervious chemical resistant gloves with the outer one covering the gown cuff at all times, including when unpacking product shipments. Gloves should be changed every 30 minutes or when torn, punctured or contaminated and discarded immediately in the appropriate container. When working in a ventilated cabinet, the outer gloves should be removed and bagged for disposal inside the ventilated cabinet.

Splash Protection: At a minimum, safety glasses with side shields should be worn. Wear a face shield to avoid splash incidents involving the eyes, nose and mouth when adequate engineering controls are not available.

Personal Hygiene: Wash hands with soap and water immediately before using personal protective

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION **Continued..**

clothing (such as disposable gloves and gowns) and after removing personal protective clothing, including gloves. Outer gloves and gowns should be removed and bagged for disposal in the appr opriate container at the site of administration. The waste container should be double-bagged before removal of the inner gloves. Clean and decontaminate work areas before and after each activity and at the end of each shift. See Section 13 for guidance on waste handling.

Workplace Transport: This product should be stored and transported in a closed container that minimizes the risk of breakage.

Spills: For guidance on spill clean up, see Section 6.

Detailed advice can be found in local guidance or in published guidance on the handling of oncolytic and cytotoxic agents. See Section 16.

GENERAL CONTROLS AND PROTECTION FOR LABORATORY AND PRODUCTION

Exposure Controls
A workplace risk assessment must be carried out in order to determine the correct engineering control measures and personal protective equipment.

Occupational Exposure Controls
Use specialized equipment such as ventilated cabinets or other containment devices designed for worker protection when there is risk of airborne exposure above recommended levels in order to prevent eye and skin contact and control airborne exposures. Personal protective equipment can only be used in place of engineering controls as a temporary measure, in emergency situations or when control by other means is not feasible.

Respiratory Protection
Respiratory protective equipment can only be used in place of engineering controls as a temporary measure in emergency situations or when control by other means is not feasible.
Respiratory protection must be selected according to the risk from the work task or situation. In general, positive pressure, supplied air respiratory protective equipment (hood, half suit or full suit), which provides high factors of protection, is used when there is risk of airborne exposure above recommended exposure levels. All respiratory protection should be in compliance with the OSHA Respiratory Protection Standard, 29 CFR 1910.134, or other regulations applicable to the country of

MATERIAL SAFETY DATA SHEET

8. EXPOSURE CONTROLS/PERSONAL PROTECTION Continued..

use.

Hand protection
All vials should be handled wearing impervious chemical resistant gloves, even when emptying boxes for storage before use.

Eye Protection
Avoid eye contact. Use safety goggles for eye protection if there is risk of eye contact.

Skin Protection
If there is a risk of skin contamination, chemically impervious clothing, with long sleeves, a head cover and gloves should be worn to protect exposed skin.

General Hygiene Considerations
Handle with extreme care. Avoid contact with skin, eyes and clothing. Use only with containment or isolation facilities and equipment, personal protective equipment and safe work practices. All personnel should wash thoroughly after handling.

Environmental Exposure Controls
Wastes should be contained to prevent exposure to dusts and labeled indicating contents to ensure safe handling and disposal. Incineration of waste product is recommended. (See Section 13).

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Description of Oxaliplatin injection : clear colorless solution

Unless otherwise stated, data relates to the active drug substance Oxaliplatin:

Basic Physical Properties
Molecular Formula: $C_8H_{14}N_2O_4Pt$
Molecular Weight: 397.3

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9. PHYSICAL AND CHEMICAL PROPERTIES Continued..

pH: 4.0 - 7.0 (in 2 mg/ml aqueous solution)
Vapor Pressure: N/A
Vapor Density (air = 1): 1.0 [for oxaliplatin injection]
Specific Gravity: N/A
Solubility (H2O @ 20 °C) 6 mg/ml
Partition Coefficient (octanol/water) (Kow): 0.02, log Kow = -1.67

10. STABILITY AND REACTIVITY

Stability
Chemically stable when handled and stored per label instructions.

Conditions to Avoid
Freezing due to risk of cracked vials.

Incompatible Materials
Incompatibility of this material has not been thoroughly investigated. Avoid aluminum and aluminum-containing materials and chloride salts. Keep from contact with oxidizing materials, highly oxygenated or halogenated solvents and organic compounds containing reducible functional groups.

Hazardous Decomposition Products
Hazardous products of combustion may include carbon monoxide, carbon dioxide and oxides of nitrogen.

Possibility of Hazardous Reactions
Will not occur.

11. TOXICOLOGICAL INFORMATION

Unless otherwise stated, data relates to the active drug substance Oxaliplatin:

A. Effects of Acute Exposure:

In Humans
Anticipated effects of acute exposure, based on clinical trials with Oxaliplatin drug product, include

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11. TOXICOLOGICAL INFORMATION **Continued..**

nausea, vomiting, diarrhea, peripheral neurotoxicity with cold sensitivity and rare laryngeal dysesthesias (sensation of difficulty with breathing or swallowing), and possible myelosuppression (low blood counts). Mucositis (sore mouth, or soreness of other mucous membranes) and transient elevation of liver enzymes have been observed. As with other platinum compounds, allergic and very rare anaphylactic – (severe, possibly life-threatening allergic reactions) have been observed.

Sensitization Potential: As with other platinum compounds, oxaliplatin may produce allergic reactions that have, on very rare occasions, been severe or life threatening.

Animal Studies
Vomiting and diarrhea have been observed following single parenteral doses of oxaliplatin. Cardiotoxicity was seen only in dogs and associated with deaths in dogs at doses at ≥ 7.5 mg/kg (which is equivalent to > 150 mg/m2).

LD10: 16.5 - 20.0 mg/kg Mouse IV
17.5 mg/kg Mouse IP
14.0 mg/kg Rat IP

There was one LD10 mouse IV study for Oxaliplatin injection Solution. The LD10 mouse IV = 17.0 mg/kg, showing no difference in the intravenous LD10 for the lyophilized and aqueous formulation of oxaliplatin.

LD50: >100 mg/kg Rat PO

Eye irritant based on data from in vivo tests.

Non-irritating to the skin based on an in vivo tests.

B. Effects of Chronic (Repeated) Exposure : Data obtained from studies (pre-clinical and clinical) conducted with parenteral administration only.

In Humans
In clinical trials with oxaliplatin drug product, the following was observed: nausea, vomiting, diarrhea, and myelosuppression, including anemia (low red blood cell count), leucopenia, neutropenia (low white blood cell count, with possible increased risk of infection), and thrombocytopenia (low platelet count, with possible increased risk of bleeding), acute and dose-related chronic, reversible

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11. TOXICOLOGICAL INFORMATION Continued..

neurotoxicity with cold sensitivity and rare laryngeal dysesthesias (sensation of difficulty with breathing or swallowing). Mucositis (sore mouth, or soreness of other mucous membranes) and transient elevation of liver enzymes have been reported. As with other platinum compounds allergic reaction and very rare anaphylactoid (severe, possibly life-threatening allergic reaction).

Animal Studies
Oxaliplatin has produced bone marrow, gastrointestinal (vomiting, and diarrhea), neural toxicity and kidney toxicity at high doses in rats. Cardiotoxicity has been associated with fatal doses only in dogs.

C. Developmental Toxicity: Oxaliplatin produced evidence of fetal toxicity in the rat but it was not teratogenic to the rat or rabbit.

D. Reproductive Toxicity: There was no impairment of fertility of treated rats. However, testicular hypoplasia has been detected in dogs following repeated doses of oxaliplatin.

E. Genotoxicity: Positive genotoxic agent in both in vitro and in vivo tests. Oxaliplatin interacts with DNA, blocking DNA replication and transcription.

F. Carcinogenicity: May be carcinogenic based on cytotoxic and genotoxic data.

12. ECOLOGICAL INFORMATION

Unless otherwise stated, data relates to the active drug substance Oxaliplatin:

Mobility
Water Solubility, Kow and Henry's Law Constant data indicate that Oxaliplatin will migrate to the water compartment of the environment.

Persistence and degradability
Hydrolysis test data indicate that Oxaliplatin will not readily hydrolyze in the environment.

Hydrolysis (t1/2 at 25°C): pH = 9: 1.09 days pH = 7: 27.4 days pH = 5: 49.19 days

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12. ECOLOGICAL INFORMATION Continued..

Microbial Inhibition (minimum inhibitory concentration, mg/L):

Aspergillus, Penicillium and Chaetomium:	>1,000
Pseudomonas and Anabaena:	800
Bacillus:	400
Azobacter:	20

Bioaccumulation Potential

The octanol/water partition coefficient (Kow) value of 0.02 indicates that Oxaliplatin is not likely to bioaccumulate. Dissociation constant (pKa) data indicate that oxaliplatin will not dissociate in the environmental pH range.

13. DISPOSAL CONSIDERATIONS

Dispose of in accordance with local, state and federal regulations. Wastes should be double contained (e.g.double sealed bags) and labeled indicating contents to ensure safe handling and disposal. Incineration of waste product is recommended.

14. TRANSPORT INFORMATION

IATA and DOT (USA) Shipping Name and Classification: Not classified as dangerous goods or hazardous materials for transport.

US DOT Reportable Quantity: Not Assigned.

15. REGULATORY INFORMATION

U.S. Federal Regulatory Information:

This product does not contain any ingredients which are regulated on the U.S. EPA List of Toxic Chemicals (40 CFR 372), and is therefore not subject to release reporting under section 313 of EPCRA.

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15. REGULATORY INFORMATION Continued..

OSHA chemical hazards according to 29 CFR 1910.1200: Mutagen, possible carcinogen, cytotoxic, fetotoxic, cardiotoxic, neurotoxic, and possible irritant.

EC Regulatory Information for the pure drug substance Oxaliplatin:

Symbol: T: Toxic

Risk phrases:

R60: May impair fertility

R61: May cause harm to the unborn child

R64: May cause harm to breastfed babies.

R68: Possible risk of irreversible effects.

R40: Limited evidence of a carcinogenic effect.

R48/23/24/25 Toxic: Danger of serious damage to health by prolonged exposure through inhalation and if swallowed.

R42/43: May cause sensitization by inhalation and skin contact.

Safety Phrases: S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

S53: Avoid exposure --- obtain special instructions before use.

16. OTHER INFORMATION

Published guidance on the handling and transport of cytotoxic drugs:

NIOSH Alert - Preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings
http://www.cdc.gov/niosh/docs/2004-165/

National Study Commission on Cytotoxic Exposure: Recommendations for handling Cytotoxic

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16. OTHER INFORMATION **Continued..**

Agents :
http://www.nih.gov/od/ors/ds/pubs/cyto/index.htm

UK MARC (Management and Awareness of the Risks of Cytotoxics) Guidelines:
http://www.marcguidelines.com/

ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs
http://www.ashp.org/bestpractices/drugdistribution/Prep_TAB_Cytotoxic.pdf

Australian Workcover Authority - Handling Cytotoxic Drugs In The Workplace
http://www.workcover.vic.gov.au/dir090/vwa/publica.nsf/0/107b078308331fe2ca256cd7001af348/$FILE/handling_cytotoxic.pdf

Royal College of Nursing
Clinical practice Guidelines: the administration of cytotoxic chemotherapy (recommendations and technical report)

The Cytotoxics Handbook – Chapter 3 Health and Safety Aspects of Cytotoxic Services
Edited by Michael Allwood, Andrew Stanley and Patricia Wright, Radcliffe Medical Press Ltd., ISBN # 185775 504 9

To the best of our knowledge, the information contained herein is accurate. However, **Sun Pharmaceutical Industries Ltd.**does not assume any liability whatsoever for the accuracy or completeness of the information contained herein except for the product's administration/use as intended. Final determination of the suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we can not guarantee that these are the only hazards, which exist.

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