Section 1 - Identification

(a) Product Identifier: Oxaliplatin Injection, USP / Oxaliplatin for Injection, USP

(b) Product Code: 25021-233, 25021-211, 25021-212

Common/Trade Name: Eloxatin®, Eloxatine, Dacplat, Oxaliplatin

Chemical Name: cis-[(1 R,2 R)-1,2-cyclohexanediamine-N,N'] [oxalato(2-)-O,O'] platinum

Chemical Family: Antineoplastic

(c) Product Use: To be used only by prescription under the supervision of a medical practitioner.

Used in combination with infusional 5-fluoraouracil / leucovorin, which is indicated for:

- Adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor.
- Treatment of advanced colorectal cancer.

Product Type: Regulated Prescription Drug

Container Information: Vial

(d) Distributor: Sagent Pharmaceuticals, Inc.
1901 N. Roselle Rd, Suite 700
Schaumburg, IL 60195
847-908-1600

(e) Emergency Telephone: 866-625-1618

Section 2 - Hazards Identification

(a) Classification: Mutagenic, cytotoxic, neurotoxic and fetotoxic. The drug substance is a possible carcinogen and a severe eye irritant.

(b) Signal Word, Hazard statement(s), Symbol(s), and/or Precautionary statement(s): 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.

(c) Description of Hazards: 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.

(d) Unknown Acute Toxicity: N/A

Section 3 – Composition/Information on Ingredients

Liquid form:

(a) Chemical Name	(b) Common Name / Synonym	% Composition or other measure	(c) CAS No.	(d) Impurities / Stabilizing Additives
cis-[(1 R,2 R)-1,2-cyclohexanediamine-N,N'] [oxalato(2-)-O,O'] platinum	Oxaliplatin	0.5% by weight	61825-94-3	N/A
Water for Injection	Water	99.5% by weight	7732-18-5	N/A

Lyophylized Powder Form:

(a) Chemical Name	(b) Common Name / Synonym	% Composition or other measure	(c) CAS No.	(d) Impurities / Stabilizing Additives
cis-[(1 R,2 R)-1,2-cyclohexanediamine-N,N'] [oxalato(2)-O,O'] platinum	Oxaliplatin	10% by weight	61825-94-3	N/A
alpha-lactose monohydrate	Lactose Monohydrate		5989-81-1	N/A

Section 4 - First Aid Measures

Eye Exposure: 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 Exposure: 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: Harmful if swallowed. Wash out mouth with water, provided person is conscious and induce vomiting immediately. Seek medical attention.

Injection: Anaphylactic reactions to Oxaliplatin have been reported, and may occur within minutes of Oxaliplatin administration. Epinephrine, corticosteroids, and antihistamines have been employed to alleviate symptoms. Seek medical attention immediately.

Inhalation: The product solution could be inhaled if liquid is aerosolized. If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Seek medical attention.

Notes to Physician: 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.

Section 5 – Fire Fighting Measures

The liquid 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.

(a)	**Extinguishing Media**	Water spray, carbon dioxide or dry chemical.
(b)	**Hazardous Combustion Products:**	Hazardous products of combustion may include carbon monoxide, carbon dioxide and oxides of nitrogen.
(c)	**Special Protective Equipment / Precautions:**	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.

Section 6 - Accidental Release Measures

Spill:

Small Spills

If a small spill occurs within a ventilated cabinet, wear protective equipment to prevent inhalation or eye/skin contact (see section 8). Absorb 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.

Release to Air: If aerosolized, reduce exposures by ventilating area.

Release to Water: Refer to local water authority. Drain disposal is not recommended; refer to local, state, and federal disposal guidelines.

Section 7 - Handling and Storage

General Handling: **Only authorized and trained personnel should handle oncology compounds.**

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 Conditions: Store under normal lighting conditions at 25°C (77°); excursions permitted to 15-30°C (59-86°F).

Section 8 - Exposure Controls / Personal Protection

(a) Exposure Limits

Compound	Issuer	Type	Exposure Limit
Oxaliplatin	OSHA	PEL	8-hr TWA: 0.002 mg/m^3
	ACGIH	TLV	8-hr TWA: 0.002 mg/m^3

TWA: 8 hour time weighted average

(b) 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 needleless 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.

(c) Individual Protection Measures

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 by 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 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.
Other Protective Equipment:	All vials should be handled wearing impervious chemical resistant gloves, even when emptying boxes for storage before use.
Additional Exposure Precautions:	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.

Section 9 - Physical and Chemical Properties

(a)	**Appearance**	Liquid or lyophilized white powder
(b)	**Odor**	Odorless
(c)	**Odor Threshold**	NE
(d)	**pH**	4.0 - 7.0
(e)	**Melting Point:**	NE
(f)	**Initial Boiling Point:**	***Liquid form:*** 100°C
(g)	**Flash Point**	Non-flammable
(h)	**Evaporation Rate:**	NE

(i)	**Flammability**	Non-flammable
(j)	**Upper Lower Flammability or Explosion Limits**	NE
(k)	**Vapor Pressure**	NE
(l)	**Vapor Density**	***Liquid form:*** 1.0
(m)	**Relative Density**	N/A
(n)	**Solubility**	***Liquid form:*** (H_2O @ 20°C) 6 mg/ml; practically insoluble in dehydrated alcohol; very slightly soluble in methyl alcohol ***Powder form:*** Freely miscible in water
(o)	**Partition Coefficient: n-octanol/water**	0.02, log Kow = -1.67
(p)	**Auto-ignition Temperature**	NE
(q)	**Decomposition Temperature**	NE
(r)	**Viscosity**	NE

Section 10 - Stability and Reactivity

(a)	**Reactivity**	Not determined
(b)	**Chemical Stability**	Stable under recommended storage conditions and rate
(c)	**Possibility of Hazardous Reactions**	Not determined
(d)	**Conditions to Avoid**	Not determined
(e)	**Incompatible Materials**	Platinum therapeutic agents are reported to be incompatible with oxidizing agents of aluminum and aluminum-containing materials, sodium bicarbonate, sodium bisulfate, and sodium metabisulfite. Avoid chloride salts. Keep from contact with oxidizing materials, highly oxygenated or halogenated solvents and organic compounds containing reducible functional groups.
(f)	**Hazardous Decomposition Products**	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx) and nitrogen oxides (NOx).

Section 11 - Toxicological Information

(a) Likely Routes of Exposure

Ingestion, Inhalation, Intravenous, Skin, Eye

(b) Symptoms related to the physical, chemical and toxicological characteristics

In humans:

Anticipated effects of acute exposure, based on clinical trials with Oxaliplatin drug product, 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 and very rare anaphylactic – (severe, possibly life-threatening allergic reactions) have been observed.

Sensitization Potential:

In the workplace, platinum compounds have been reported to cause allergic skin and respiratory reactions. Hypersensitivity reactions, sometimes severe or life-threatening, have been reported during clinical use of this product.

(c) Delayed and immediate effects and also chronic effects from short and long term exposure

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 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 lifethreatening allergic reaction).

(d) Acute Toxicity

Component	Type	Route	Species	Dosage
Drug	LD_{10}	Intravenous	Mouse	16.5 - 20.0 mg/kg
	LD_{10}	Intraperitoneal	Mouse	17.5 mg/kg
	LD_{10}	Intraperitoneal	Rat	14.0 mg/kg
	LD_{50}	Oral	Rat	>100 mg/kg

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.

A. Developmental Toxicity

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

B. Reproductive Toxicity

Reproductive toxicity studies in rats demonstrated adverse effects on fertility and embryo-fetal development at maternal doses that were below the recommended human dose based on body surface area.

Testicular damage, characterized by degeneration, hypoplasia, and atrophy, was observed in dogs administered oxaliplatin at a dosage of 0.75 mg/kg/day x 5 days every 28 days for three cycles. A no effect level was not identified. This daily dose is approximately one-sixth of the recommended human dose on a body surface area basis.

In a fertility study, male rats were given oxaliplatin at dosages of 0, 0.5, 1, or 2 mg/kg/day for five days every 21 days for a

total of three cycles prior to mating with females that received two cycles of oxaliplatin on the same schedule. A dosage of 2 mg/kg/day did not affect pregnancy rate, but caused developmental mortality (increased early resorptions, decreased live fetuses, decreased live births) and delayed growth (decreased fetal weight).

Pregnant rats were given oxaliplatin at a dosage of 1 mg/kg/day during gestation days 1-5 (pre-implantation), 6-10, or 11-16 (during organogenesis). Oxaliplatin caused developmental mortality (increased early resorptions) when administered on days 6-10 and 11-16 and adversely affected fetal growth (decreased fetal weight, delayed ossification) when administered on days 6-10.

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

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

(e) Hazardous Chemical Listings

NTP: Not listed IARC: Not listed OSHA: Not listed

Section 12 - Ecological Information

(a) Ecotoxicity N/A

(b) Persistence and degradability

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

Hydrolysis ($t_{1/2}$ at 25C): pH = 9: 1.09 days; pH = 7: 27.4 days; pH = 5: 49.19 days

(c) Bioaccumulative 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

(d)	**Mobility in soil**	dissociate in the environmental pH range. Water Solubility, Kow and Henry's Law Constant data indicate that Oxaliplatin will migrate to the water compartment of the environment.
(e)	**Other Adverse Effects**	N/A

Section 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.

Section 14 - Transport Information

(a)	**UN Number**	N/A
(b)	**UN Proper Shipping Name**	N/A
(c)	**Transport Hazard Class(es)**	N/A
(d)	**Packing Group**	N/A
(e)	**Environmental Hazards**	N/A
(f)	**Transport in bulk (according to Annex II of MARPOL 73/78 and the IBC Code)**	N/A
(g)	**Special Precautions**	N/A

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Sagent usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

U.S. Regulations:

TSCA: Not on this list
CERCLA: Not on this list
SARA 302: Not on this list
SARA 313: Not on this list

Section 16 - Other Information

As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:
Sagent Pharmaceuticals, Inc.
1901 N. Roselle Rd, Suite 700
Schaumburg, IL 60195
847-908-1600

Glossary: This glossary contains definitions of general terms used in SDSs. Not all of these Glossary Terms will apply to this SDS.

ACGIH	American Conference of Governmental Industrial Hygienists
AIHA	American Industrial Hygiene Association
CAS Number	Chemical Abstract Service Registry Number
CERCLA	Comprehensive Environmental Response Compensation and Liability Act (of 1980)
CHAN	Chemical Hazard Alert Notice
CHEMTREC	Chemical Transportation Emergency Center
DOT	Department of Transportation
EPA	Environmental Protection Agency
HEPA	High Efficiency Particulate Air (Filter)
IARC	International Agency for Research on Cancer
ICAO/IATA	International Civil Aviation Organization/International Air Transport Association
IMO	International Maritime Organization
KOW	Octanol/Water Partition Coefficient
LEL	Lower Explosive Limit
MSDS	Material Safety Data Sheet
MSHA	Mine Safety and Health Administration
NA	Not Applicable, except in Section 14 where NA = North America
NE	Not Established
NADA	New Animal Drug Application
NAIF	No Applicable Information Found
NCI	National Cancer Institute
NIOSH	National Institute for Occupational Safety and Health
NOS	Not Otherwise Specified
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
OEL	Occupational Exposure Limit
PEL	Permissible Exposure Limit (OSHA)
RCRA	Resource Conservation and Recovery Act
RQ	Reportable Quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SDS	Safety Data Sheet
STEL	Short Term Exposure Limit
TLV	Threshold Limit Value (ACGIH)
TPQ	Threshold Planning Quantity
TSCA	Toxic Substances Control Act
TWA	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	Upper Explosive Limit
UN	United Nations
USP	United States Pharmacopeia
WEEL	Workplace Environmental Exposure Level (AIHA)