Oxaliplatin Injection

Product Name: Oxaliplatin Injection (Solution for Intravenous Use)

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Names And Addresses	Getwell Pharmaceuticals 474, Udyog Vihar, Phase-V Gurgaon (HR) 122016
Telephone	0124 4014403
Product Name	Oxaliplatin Injection (Solution for Intravenous Use)
Synonyms	*cis*-[(1*R*,2*R*)-1,2-cyclohexanediamine-*N*,*N*'] [oxalato(2-)-*O*,*O*'] platinum.

2. HAZARD INFORMATION / CLASSIFICATION

Emergency Overview Oxaliplatin Injection (Solution for Intravenous Use) contains oxaliplatin, a platinum-containing complex similar to cisplatin. It is used alone or with other agents to treat certain kinds of cancers. It is cytotoxic, neurotoxic, and in the workplace should be considered a potential sensitizer, a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Following an accidental over-exposure, possible target organs may include the gastrointestinal tract, bone marrow, liver, kidneys, lungs, ears (hearing), nervous system, and fetus.

Occupational Exposure Potential There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these materials if workplace exposures are not properly controlled. The actual risk in the workplace is not known.

Signs and Symptoms In the workplace, platinum compounds have been reported to cause allergic skin and respiratory reactions. This material should also be considered irritating to the eyes and respiratory tract. In clinical use, adverse effects have included severe nausea and vomiting, toxic effects on the kidneys and liver, pulmonary toxicity, cardiotoxicity, bone marrow depression, loss of hearing, and neurological effects such as peripheral neuropathies.

Medical Conditions Aggravated by Exposure Pre-existing hypersensitivity to platinum compounds. Pre-existing gastrointestinal, liver, kidney, lung, bone marrow, hearing, cardiovascular, or nervous system ailments, or pregnancy.

Carcinogen Lists: **IARC:** Not listed **NTP:** Not listed **OSHA:** Not listed

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient Name Oxaliplatin

Chemical Formula $C_8H_{14}N_2O_4Pt$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Oxaliplatin	0.5	61825-94-3	TP2275850

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Non-hazardous ingredients include water for injection, USP. Hazardous ingredients present at less than 1% include tartaric acid, NF, and sodium hydroxide, NF

4. FIRST AID MEASURES

Eye Contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Skin Contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Inhalation	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Ingestion	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

5. FIRE FIGHTING MEASURES

Flammability	None anticipated from this product.
Fire & Explosion Hazard	None anticipated for this product.
Extinguishing Media	As with any fire, use extinguishing media appropriate for primary cause of fire.
Special Fire Fighting Procedures	Firefighters should wear self-contained breathing apparatus. Protective equipment and clothing should be worn to minimize contact with the respiratory tract, skin and eyes.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal	Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Absorb liquid with suitable material and clean affected area with soap and water. An undiluted solution of household bleach may be applied to the spill for ten minutes to inactivate oxaliplatin. After inactivation, absorb the liquid with an inert absorbent material (e.g. absorbent pad). Dispose of materials according to the applicable federal, state, or local regulations.

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7. HANDLING AND STORAGE

Handling

Oxaliplatin is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastic agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic agents have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate. Consult your hygienist or safety professional for your site requirements.

Avoid ingestion, inhalation, skin contact, and eye contact. If handling a powder, precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilization of this antineoplastic agent. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is required when working with this material.

Storage

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. For product protection, follow USP controlled room temperature storage recommendations Qnoted on the product case label, the primary container label, or the product insert. Do not freeze and protect from light (keep in original outer carton).

Special Precautions

Persons with known allergies to platinum compounds, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure limits		
Component	**OSHA-PEL**	**ACGIH-TLV**	**Other Limits**
Oxaliplatin	8-hr TWA: 0.002 mg/m3 for platinum, for soluble salts.	8-hr TWA: 0.002 mg/m3 for platinum, for soluble salts.	NA

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
EEL: Employee Exposure Limit.
TWA: 8 hour Time Weighted Average.
STEL: 15-minute Short Term Exposure Limit.

Respiratory Protection

Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (P100 or equivalent) is recommended. For large spills, the use of a self-contained breathing apparatus may be required.

Skin Protection

When handling this product, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability

	to chemotherapy agents. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.
Eye Protection	As a minimum, the use of chemical safety goggles is recommended when handling thismaterial.
Engineering Controls	When handling this product, local exhaust ventilation is recommended to minimize employee exposure if the generation of aerosols is likely. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	A sterile, preservative-free aqueous solution in a vial
Odor	Odorless
Odor Threshold:	NA
pH:	4.0 to 7.0 for a 0.2% aqueous solution
Melting point/Freezing point:	NA
Initial Boiling Point/Boiling Point Range	NA
Evaporation Rate:	NA
Flash Point:	NA
Flammability (solid, gas):	NA
Upper/Lower Flammability or Explosive Limits:	NA
Vapor Pressure	NA
Vapor Density (Air =1)	NA
Evaporation Rate	NA
Specific Gravity	NA
Solubility	Oxaliplatin is slightly soluble in water (about 6 mg/ml at 20^{o}C); practically insoluble in dehydrated alcohol; very slightly soluble in methyl alcohol.
Partition coefficient: n-octanol/water:	NA
Auto-ignition temperature	NA
Decomposition temperature	NA

10. STABILITY AND REACTIVITY

Chemical Stability	Stable under recommended storage conditions and use.
Incompatibilities	Platinum therapeutic agents are reported to be incompatible with oxidizing agents of aluminum, sodium bicarbonate, sodium bisulfate, and sodium metabisulfite. Avoid contact with chloride salts.

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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).

Hazardous Polymerization Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity

Not determined for the product mixture. Information for the active ingredient, oxaliplatin, is as follows:

Ingredient(s)	Percent	Route	Test Type	Value	Units	Species
Oxaliplatin	100	Oral	LD50	> 100	mg/kg	Rat
Oxaliplatin	100	Intraperitoneal	LD50	14.3	mg/kg	Rat
Oxaliplatin	100	Intraperitoneal	LD50	19.8	mg/kg	Mouse

LD50 is the dosage producing 50% mortality.

Aspiration Hazard None anticipated from normal handling of this product.

Dermal Irritation/Corrosion None anticipated from normal use of this product. Based on a study in animals,inadvertent skin contact with this product is not anticipated to produce irritation.

Ocular Irritation/Corrosion None anticipated from normal use of this product. Based on a study in animals, inadvertent eye contact with this product may produce irritation, redness and discomfort.

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

Reproductive Effects 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

effected fetal growth (decreased fetal weight, delayed ossification) when administered on days 6-10.

Mutagenicity Oxaliplatin was not mutagenic in the Ames test, but was mutagenic in mammalian cells in vitro (L5178Y mouse lymphoma assay). Oxaliplatin was clastogenic both in vitro (chromosome aberration in human lymphocytes) and in vivo (mouse bone marrow micronucleus assay).

Carcinogenicity Long-term animal studies have not been performed to evaluate the carcinogenic potential of oxaliplatin.

Target Organ Effects This product should be considered irritating to the eyes and respiratory tract. Following an accidental over-exposure, possible target organs may include the gastrointestinal tract, bone marrow, liver, kidneys, lungs, ears (hearing), nervous system, and fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity Not determined for product.

***Biodegradation** Not determined for product. Hydrolysis studies suggest that oxaliplatin will not readily hydrolyze in the environment. The $T_{1/2}$ for hydrolysis was 27.4 days at pH 7.0 and 25^{o}C. In microbial inhibition studies in bacteria, minimum inhibitory concentrations of oxaliplatin were generally greater than 20 mg/L.

***Bioaccumulation** Not determined for product. Based on a log octanol/water partition coefficient of about -1.7, oxaliplatin is considered unlikely to bioaccumulate in aquatic organisms.

Mobility in Soil Not determined for product.

13. DISPOSAL CONSIDERATIONS

Waste Disposal All waste materials must be properly characterized. Disposal should be performed in accordance with the federal, state or local regulatory requirements.

Container Handling and Disposal Dispose of containers and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

DOT STATUS: Not Regulated
Proper Shipping Name: NA
Hazard Class: NA
UN Number: NA
Packing Group: NA
Reportable Quantity: NA

ICAO/IATA STATUS Not Regulated

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Proper Shipping Name:	NA
Hazard Class:	NA
UN Number:	NA
Packing Group:	NA
Reportable Quantity:	NA

IMDG STATUS	Not Regulated

Proper Shipping Name:	NA
Hazard Class:	NA
UN Number:	NA
Packing Group:	NA
Reportable Quantity:	NA

Notes: DOT – US Department of Transportation Regulations

15. REGULATORY INFORMATION

TSCA Status	Exempt
CERCLA Status	Not listed
SARA 302 Status	Not listed
SARA 313 Status	Not listed
RCRA Status	Not listed
PROP 65 (Calif.)	Not listed

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

U.S. OSHA Classification

Irritant
Possible Sensitizer
Reproductive Toxin
Possible Carcinogen
Target Organ Toxin

GHS Classification

Hazard Class	Acute Oral Toxicity	Eye Irritation	Skin Sensitization	Respiratory Sensitization	Reproductive Toxicity	Mutagenicity	Carcinogenicity	Target Organ Toxicity
Hazard Category	4	2B	1	1	2	2	2	2
Symbol								
Signal Word	Warning	Warning	Warning	Danger	Warning	Warning	Warning	Warning
Hazard Statement	Harmful if swallowed	Causes Eye irritation	May cause an allergic skin reaction	May cause allergic or asthmatic symptoms or breathing difficulties if inhaled.	Suspected of damaging fertility or the unborn child	Suspected of causing genetic defects if ingested.	Suspected of causing cancer if ingested.	May cause damage to the gastrointestinal tract, bone marrow, liver, kidneys, lungs, ears (hearing), and nervous system through prolonged or

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GHS Precautionary Statements:

Prevention: Obtain special instructions before use.
Do not handle until all safety precautions have been read and understood. Use personal protective equipment as required.
Avoid breathing aerosols or vapors.
In case of inadequate ventilation wear respiratory protection. Wear protective gloves.
Contaminated work clothing should not be allowed out of the workplace. Do not eat, drink or smoke when using this product.
Wash hands thoroughly after handling.

Response: IF SWALLOWED: Immediately call a POISON CENTER or doctor. Rinse mouth.
IF INHALED: If breathing is difficult, remove to fresh air and keep at rest in a position comfortable for breathing. If experiencing respiratory symptoms call a POISON CENTER or a doctor.
IF ON SKIN: Wash with plenty of soap and water. If skin irritation or

rash occurs, seek medical attention. Take off contaminated clothing and wash before reuse.
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention. IF exposed or concerned, get medical attention.

EU Classification

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance oxaliplatin.

Classification(s):	Harmful	Irritant Skin Sensitizer	Respiratory Sensitizer	Carcinogen Category 2	Mutagen Category 2	Reproductive Toxin Category 2
Symbol:						
Indication of Danger:	Xn	Xi/Xn	Xn	T	T	T

Risk Phrases:

R22 - Harmful if swallowed
R36/37- Irritating to eyes and respiratory system
R42 - May cause sensitization by inhalation;
R43 - May cause sensitization by skin contact
R45 - May cause cancer
R46 - May cause heritable genetic damage
R48/20/22 - Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed
R60 - May impair fertility
R61 - May cause harm to the unborn child
R64 - May cause harm to breastfed babies

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Safety Phrases: S23: Do not breathe vapor or spray
S24: Avoid contact with the skin
S36/37/39 Wear suitable protective clothing, gloves and eye/face protection.

16. OTHER INFORMATION

Notes:

ACGIH TLV	American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS	Chemical Abstracts Service Number
CERCLA	US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT	US Department of Transportation Regulations
EEL	Employee Exposure Limit
IATA	International Air Transport Association
LD_{50}	Dosage producing 50% mortality
NA	Not applicable/Not available
NE	Not established
NIOSH	National Institute for Occupational Safety and Health
OSHA PEL	US Occupational Safety and Health Administration – Permissible Exposure Limit
Prop 65	California Proposition 65
RCRA	US EPA, Resource Conservation and Recovery Act
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
STEL	15-minute Short Term Exposure Limit
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

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