EXPERIMENTAL SUBSTANCE
MATERIAL SAFETY DATA SHEET
for

Erlotinib hydrochloride

SECTION 1 – CHEMICAL PRODUCT & COMPANY IDENTIFICATION

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Trade Name:	Tarceva
Generic Name:	Erlotinib hydrochloride
Product Code Name:	OSI-774-01
CAS Number:	183319-69-9
Chemical Name:	*N*-(3-Ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine monohydrochloride
Molecular Formula:	$C_{22}H_{24}ClN_3O_4$
Molecular Weight:	429.9 (hydrochloride); 393.4 (free base)
Synonyms:	CP-358,774-01; Ro-508231001; Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor
Appearance:	White to pale yellow powder
Intended Use:	Orally administered drug for the treatment of cancer. Usual human dose is 150 mg/day on a continuous schedule.

SECTION 2 – COMPOSITION/INFORMATION OF INGREDIENTS

Ingredient	Amount (%)	OEL
OSI-774-01	100	Threshold value (air) = 0.025 mg/m3

SECTION 3 – HAZARDS IDENTIFICATION

A) EMERGENCY OVERVIEW:

This substance is a novel compound for the treatment of cancer. The physical, chemical, and toxicological properties have not been thoroughly investigated. Exposure by any route should be minimized. This compound is a severe dust explosion hazard.

B) SUMMARY OF POTENTIAL HEALTH EFFECTS:

Inhalation: Not determined, assumed to be similar to the effects, which may be produced following ingestion.

Ingestion: Effects of a single exposure may include lack of coordination, irregular breathing, diarrhea, nausea, headache, vomiting and fatigue. Repeat oral exposure has a high likelihood of producing skin rash and diarrhea.

Eye: Not expected to be a direct eye irritant based on animal study data.

Skin: This compound may cause skin irritation in humans following skin contact. In animal studies, the compound was not corrosive or poisonous and was considered only a mild sensitizer following dermal contact.

SECTION 4 – FIRST AID MEASURES

Eyes: Flush with water for at least 15 minutes. Seek medical attention immediately if irritation develops.

Skin: Remove contaminated clothing. Flush area with large amounts of water for 15 minutes. Use soap if available. Seek medical attention immediately if skin irritation or rash develops.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult administer oxygen. Seek medical attention immediately.

Ingestion: Seek medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Note to Physician: None

SECTION 5 – FIRE AND EXPLOSION PROPERTIES

General: This compound has a strong dust explosion hazard. Minimum ignition energy indicated a high to very high sensitivity of a dust cloud to ignition. Incompatible with electrostatic discharge in situations, where a dust may be produced.

OSI-774-01 undergoes thermal decomposition. This is an exothermic process. Decomposition reactions that liberate energy may produce flammable or reactive gases, or may generate high pressure in confining vessels or containers (potentially resulting in an explosion).

DSC Results: High thermal hazard of 365J/g around 290 ^{o}C.

ARC Analysis: Onset of decomposition at 205 ^{o}C. High energy decomposition of 751J/g.

Koenen Test: Undertaken to assess the sensitivity to the effect of intense heat under confinement. Result: Negative.

Impact Sensitivity: > 60 J. Friction sensitivity > 360 N.

A) FIRE FIGHTING PROCEDURES:

Instructions: Wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes. Use water spray to keep fire-exposed containers cool.

Hazardous Combustion Products: May include oxides of carbon and nitrogen and HCl gas.

Extinguishing Media: Use appropriate media including water spray jet, dry powder, foam, carbon dioxide

B) DUST EXPLOSION CHARACTERISTICS:

Maximum Explosion Pressure (bar):	9.3 bar
Maximum Pressure Rise Rate (bar/sec):	946 bar/s
Kst:	257 bar.m/sec

Minimum Ignition Energy (mJ):	5-10 mJ
Minimum Ignition Temperature (°C):	460-480 °C
Minimum Oxygen Concentration (% vol):	8.2-9.8% by volume
Minimum Explosive Concentration:	30-40 g/m3
Charge Decay Time:	Ambient 2.2 hours Low: 5.0 hours

SECTION 6 – ACCIDENTAL RELEASE MEASURES

Spill Response Instructions: Use of a filtered vacuum to clean spills of dry solids is not advised, due to the potential for electrostatic discharge and the high dust explosion potential. Report emergency situations immediately. Non-essential personnel should be evacuated from the affected area. Contain the source of the spill if it is safe to do so. Spills should be cleaned up in a manner that minimizes exposure to personnel. Personnel involved in the clean up of spills should wear respiratory protection, gloves, eye protection, and protective coveralls. Wet the material with water and collect solution/slurry for disposal. Clean spill area thoroughly. Collect wash with absorbent material and transfer all waste to a labeled container for disposal.

SECTION 7 – HANDLING AND STORAGE

General Handling: All conductive elements of the system that contact the dry substance should be properly bonded and grounded and equipped with proper explosion relief or suppression systems. This material should not be flowed through non-conductive ducts or pipes because of the potential for electrostatic discharge ignition. Restricting the use of high resistivity materials, such as plastics, should be considered. Use appropriate PPE including respiratory protection when working outside of a closed system.

Storage: OSI-774-01 should be stored at ambient temperature in closed containers away from light, ignition sources including electrostatic charge, heat, sparks, and flame.

SECTION 8 – EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Limit: No occupational exposure limits established by OSHA, ACGIH or NIOSH.

Engineering Controls: General room ventilation and chemical fume hoods.

Personal Protective Equipment: Eye protection, compatible chemicals-resistant gloves, and coveralls should be worn. In addition, dust tight respiratory protection should be used when working with this substance outside of the hood, ventilated enclosure, or closed system. Effective engineering controls are considered to be the primary means to control worker exposure. Respiratory protection should not substitute for feasible engineering controls.

SECTION 9 – PHYSICAL AND CHEMICAL PROPERTIES

Physical Form: Crystalline powder

Color: White to pale yellow

Melting Point: 231 – 232 °C

Molecular Weight: 429.907

Molecular Formula: $C_{22}H_{23}N_3O_4$ **.** HC1

Solubility:

Water	810mg/L
Buffer, pH2.1	414mg/L
Buffer, pH6.9	1.8mg/L
Buffer, pH9.6	1.2mg/L
Acetonitrile	<10mg/L
Acetone	<10mg/L
Hexane	<10mg/L

Partition Coefficient: Log $P_{o/w}$ = 3.37 (n-octanol/water 20 °C)
(EC Directive 92/69/EEC, A.8 (1992))

Dissociation Constant: 5.6 (Protonation of secondary amine at acidic pH)

SECTION 10 – STABILITY AND REACTIVITY

Reactivity: Stable under normal conditions.

Incompatibility: Not fully determined. As a precautionary measure, keep away from sources of ignition and heat, and strong oxidizers.

SECTION 11 – TOXICOLOGY INFORMATION

Acute Exposure:

Species, Route	Minimum Lethal Dose (Free Base)
Mouse, Oral:	2000 mg/kg
Rat, Oral	1000 mg/kg
Mouse, Intravenous:	75 mg/kg
Rat, Intravenous:	50 mg/kg
Dog, Oral	>200 mg/kg
Dog, Intravenous	>20 mg/kg

No effects were observed in mice following an oral dose of 1000 mg/kg, or in rats at doses less than 500 mg/kg. Effects above these doses, excluding death, include a transient decrease in activity and irregular respiration (2000 mg/kg) and a decrease body weight gain (500,1000,2000 mg/kg.) Effects observed in dogs following oral administration included: emesis, decreased activity, pale gums, cold skin, tremors, salivation, and/or ataxia (200 mg/kg.)Intravenous administration produced convulsions at single doses of 25 mg/kg or greater in mice, or 35 mg/kg or greater in rats. No effects were observed in rats or mice following a single intravenous dose of 15 mg/kg. Intravenous administration to dogs caused transient ataxia, pale gums, pupil dilation, tremors, elevated heart rate, and depressed blood pressure.

Repeated Exposure: Repeat oral toxicity studies up to 6 months and 1 year have been conducted in rats and dogs respectively. Effects produced in rats included decreased food consumption and body weight gain, increases in total bilirubin, and marginal increases in alanine aminotransferase (ALT), ovarian atrophy, renal papillary necrosis with tubular dilatation, multifocal necrosis, angectasis of the adrenal gland, and follicular degeneration/inflammation of the skin.

Effects in dogs at 50 mg/kg included emesis, loose stool, body weight loss, a decrease in RBC indices, corneal atrophy, and increases in alkaline phosphatase (ALP) and bilirubin, renal papillary necrosis and gastrointestinal inflammation and glandular dilatation

Eye Effects:	Classified as non-irritating, based on an eye irritation study in rabbits.
Skin Effects:	No deaths or clinical signs of toxicity were produced in rabbits following the application of a dose of 2000 mg/kg to skin.
Reproductive Effects:	No impairment of fertility in either male or female rats treated with up to 10 mg/kg/day
Developmental Effects:	No teratogenic effects in the fetuses of either rats or rabbits treated with maternally toxic doses (10 mg/kg/day rats; 50 mg/kg/day rabbits). No adverse effects on physical or behavioral development of first or second generation offspring of rats treated with up to 12 mg/kg/day.
Genotoxicity:	Not positive for mutagenicity or clastogenicity in the standard battery of genotoxicity tests
Sensitization Potential:	Based on data from studies in guinea pigs, this compound is characterized as a mild sensitizer.
Carcinogenicity:	Not determined
Additional Data:	**N/A**

SECTION 12 – ECOLOGICAL INFORMATION

Ecological Info:

Surrogate Species	**(EC/LC- 50)**
Daphnia magna IQ (mg/1)	>1.0

NPDES	**Permit Species (LC-50)**
Mysid Shrimp (mg/L):	>5.0
Sheepshead Minnow (mg/L):	>5.0
Red Algae (mg/L):	>5.0

W WTP Inhibition

POLYTOX @ WWTP (MIC) (mg/L)	5
POLYTOX @ WWTP (IC-50) (mg/L)	>5.0

SECTION 13 – DISPOSAL INFORMATION

Disposal Procedure: Must dispose of in accordance with all local, state, and federal regulations.

SECTION 14 – TRANSPORTATION INFORMATION

Transportation Info: Proper shipping name: Not regulated.

SECTION 15 – REGULATORY INFORMATION

EU Risk and Safety Phrases:
Caution: material not yet fully tested
S22: Avoid breathing dust
Xn: Harmful
R22: Harmful if swallowed
R2: Risk of explosion by shock, friction, fire or other sources of ignition.
R51: Toxic to aquatic organisms

TSCA Status: FDA Exemption – not in inventory

Reporting Requirements: The United States Environmental Protection Agency (USEPA) has not established a Reportable Quantity for releases of this material.
In New Jersey, report all releases which are likely to endanger the public health, harm the environment or cause a complaint to the NJDEPE Hotline (1-609-292-5560) and to local officials.
State and local regulations very and may impose additional reporting requirements.

SECTION 16 – OTHER INFORMATION

Disclaimer: **OSI Pharmaceuticals 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.**