Material Safety Data Sheet

Revision Date: May 1, 2014

1. Identification of substance

Product Name:	Erlotinib HCl (OSI-744)
Cat. Number:	S1023
Manufacturer/Supplier:	Selleck Chemicals 9330 Kirby drive, STE 200, Houston, TX 77054 USA Toll Free：(877) 796-6397 (US and Canada only) Tel：+1-832-582-8158 Fax：+1-832-582-8590

2. Composition/data on components

Chemical Name:	N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine hydrochloride
Synonyms:	Tarceva
Hazardous Ingredient:	Erlotinib HCl (OSI-744)
CAS Registry Number:	183319-69-9
Molecular Weight:	429.90
Molecular Formula:	$C_{22}H_{23}N_3O_4.HCl$

3. Hazard identification

Hazard Description:	Toxic. Contains a pharmaceutically active ingredient. Handling should only be performed by personnel trained and familiar with handling of potent active pharmaceutical ingredients. Moderate to severe irritant to the skin and eyes.

4. First aid measures

After Inhalation:	if inhaled, remove to fresh air; if breathing is difficult, give oxygen; if breathing stops, give artificial respiration
After skin contact:	flush with copious amounts of water; remove contaminated clothing and shoes; call a physician

After eye contact:	check for and remove contact lenses and flush with copious amounts of water; assure adequate flushing by separating the eyelids with fingers; call a physician
After swallowing:	if swallowed, wash out mouth with copious amounts of water; call a physician

5. Fire fighting measures

Suitable extinguishing agents:	water spray, carbon dioxide, dry chemical powder or foam
Protective equipment:	wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes.
Unusual fire hazard:	emits toxic fumes such as carbon monoxide, etc.

6. Accidental release measures

After Inhalation:	cordon off area of spill; wear self-contained breathing apparatus, protective clothing and heavy rubber gloves
Measures for cleaning/collecting	absorb solutions with finely- powdered liquid-binding material (diatomite, universal binders); decontaminate surfaces and equipment by scrubbing with alcohol; dispose of contaminated material according to Section 13

7. Handling

Information for safe handling	avoid inhalation and contact with skin, eyes and clothing; material may be an irritant

8. Exposure controls and personal protection

Personal protective equipment as follows:	
Breathing equipment:	NIOSH/MSHA-approved respirator
Protection of hands:	chemical-resistant rubber gloves
Eye protection:	chemical safety goggles

9. Stability and reactivity

Stability:	stable if stored as directed; avoid strong oxidizing agents
Thermal decomposition /	protect from light and heat

conditions to be avoided:	
Dangerous products of decomposition:	thermal ecomposition may produce toxic gases such as carbon monoxide, carbon dioxide, and nitrogen oxides

10. Toxicological information

RTECS#:	
Acute toxicity:	none known
Primary irritant effect:	not known
On the skin:	none known
On the eye:	not known; may be an irritant

11. Ecological information

General notes:	no data available

12. Disposal consideration

Dispose of in accordance with prevailing country, federal, state and local regulations

13. Transport information

DOT:	
Proper shipping name:	none
Non-Hazardous for transport:	this substance is considered to be non-hazardous for transport
IATA class:	
IATA class:	none
Non-Hazardous for transport:	this substance is considered to be non-hazardous for transport

Technical Data

Molecular Weight (MW)	429.90
Formula	$C_{22}H_{23}N_3O_4$.HCl
CAS No.	183319-69-9
Synonyms	Tarceva
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble	DMSO 3 mg/mL
	Water <1 mg/mL
	Ethanol <1 mg/mL
Storage	3 years -20℃Powder
	6 months-80℃in DMSO
Chemical Name	N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine hydrochloride

Preparing Stock Solutions

	1 mg	5 mg	10 mg
1 mM	2.3261 mL	11.6306 mL	23.2612 mL
5 mM	0.4652 mL	2.3261 mL	4.6522 mL
10 mM	-	-	-
50 mM	-	-	-

Biological Activity

Description	Erlotinib HCl (OSI-744) is an **EGFR** inhibitor with **IC50** of 2 nM, >1000-fold more sensitive for EGFR than human c-Src or v-Abl.
Targets	HER1/EGFR
IC50	2 nM [1]
In vitro	Erlotinib HCl potently inhibits EGFR activation in intact cells including HNS human head and neck tumor cells (IC50 20nM), DiFi humancolon cancer cells andMDA MB-468 human breast cancer cells. Erlotinib HCl (1 μM) induces apoptosis in DiFi humancolon cancer cells. [1] Erlotinib inhibits growth of a panel of NSCLC cell lines including A549, H322, H3255, H358 H661, H1650, H1975, H1299, H596 with IC50 ranging from 29 nM to >20 μM. [2]Erlotinib HCl(2 μM) significantly inhibits growth of AsPC-1 and BxPC-3 pancreatic cells. [3] The effects of Erlotinib HCl in combination with gemcitabine are considered additive in KRAS-mutated pancreatic cancer cells. Ten micromolar of Erlotinib HCl inhibits EGFR phospho-rylation at the Y845 (Src-dependent phosphorylation) and Y1068 (auto-phosphorylation) sites. [4] Combination with Erlotinib HCl could down-modulate rapamycin-stimulated Akt activity and produces a synergistic effect on cell growth inhibition. [5]
In vivo	At doses of 100 mg/kg, Erlotinib HCl completely prevents EGF-induced autophosphorylation of EGFR in human HN5 tumors growing as xenografts in athymic mice and of the hepatic

	EGFR of the treated mice. [1] Erlotinib HCl (100 mg/Kg) inhibits H460a and A549 tumor models with 71 and 93% inhibition rate. [5]
Features	

Protocol (Only for Reference)

Kinase Assay: [1]

Kinase assays	96-well plates are coated by incubation overnight at 37 °C with 100 μL per well of 0.25 mg/mL PGT in PBS. Excess PGT is removed by aspiration, and the plate is washed 3 times with washing buffer (0.1% Tween 20 in PBS). The kinase reaction is performed in 50 μL of 50 mM HEPES (pH 7.3), containing 125 mM sodium chloride, 24 mM magnesium chloride, 0.1 mM sodium orthovanadate, 20 μM ATP, 1.6 μg/mL EGF, and 15 ng of EGFR, affinity purified from A431 cell membranes. Erlotinib HCl in DMSO is added to give a final DMSO concentration of 2.5%. Phosphorylation is initiated by addition of ATP and proceeded for 8 minutes at room temperature, with constant shaking. The kinase reaction is terminated by aspiration of the reaction mixture and is washed 4 times with washing buffer. Phosphorylated PGT is measured by 25 minutes of incubation with 50 μL per well HRP-conjugated PY54 antiphosphotyrosine antibody, diluted to 0.2 μg/mL in blocking buffer (3% BSA and 0.05% Tween 20 in PBS). Antibody is removed by aspiration, and the plate is washed 4 times with washing buffer. The colonmetric signal is developed by addition of TMB Microwell Peroxidase Substrate, 50μL per well, and stopped by the addition of 0.09 M sulfuric acid, 50 μL per well. Phosphotyrosine is estimated by measurement of absorbance at 450 nm. The signal for controls is typically 0.6-1.2 absorbance units, with essentially no back ground in wells without AlP, EGFR, or PGT and is proportional to the time of incubation for 10 minutes.

Cell Assay: [2]

Cell lines	A549, H322, H3255, H358 H661, H1650, H1975, H1299, H596 cells
Concentrations	30 nM-20 μM
Incubation Time	72 hours
Method	Exponentially growing cells are seeded in 96-well plastic plates and exposed to serial dilutions of erlotinib, pemetrexed, or the combination at a constant concentration ratio of 4:1 in triplicates for 72 h. Cell viability is assayed by cell count and the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay. Growth inhibition is expressed as the percentage of surviving cells in drug-treated versus PBS-treated control cells (which is considered as 100% viability). The IC50 value is the concentration resulting in 50% cell growth inhibition by a 72-h exposure to drug(s) compared with untreated control cells and is calculated by the CalcuSyn software.

Animal Study: [6]

Animal Models	Male 5-week-old BALB-nu/nu with HPAC cells
Formulation	6% Captisol
Dosages	50 mg/kg
Administration	Oral administration

Conversion of different model animals based on BSA (Value based on data from FDA Draft Guidelines)

Species	Baboon	Dog	Monkey	Rabbit	Guinea pig	Rat	Hamster	Mouse
Weight (kg)	12	10	3	1.8	0.4	0.15	0.08	0.02
Body Surface Area (m^2)	0.6	0.5	0.24	0.15	0.05	0.025	0.02	0.007
K_m factor	20	20	12	12	8	6	5	3

Animal A (mg/kg) = Animal B (mg/kg) multiplied by $\frac{\textbf{Animal B } K_m}{\textbf{Animal A } K_m}$

For example, to modify the dose of resveratrol used for a mouse (22.4 mg/kg) to a dose based on the BSA for a rat, multiply 22.4 mg/kg by the K_m factor for a mouse and then divide by the K_m factor for a rat. This calculation results in a rat equivalent dose for resveratrol of 11.2 mg/kg.

$$\text{Rat dose (mg/kg)} = \text{mouse dose (22.4 mg/kg)} \times \frac{\text{mouse } K_m(3)}{\text{rat } K_m(6)} = 11.2 \text{ mg/kg}$$

1

References

[1] Moyer JD, et al. Cancer Res. 1997, 57(21), 4838-4848.

[2] Li T, et al. Clin Cancer Res, 2007, 13(11), 3413-3422.

[3] Ali S, et al. Mol Cancer Ther, 2008, 7(6), 1708-1719.

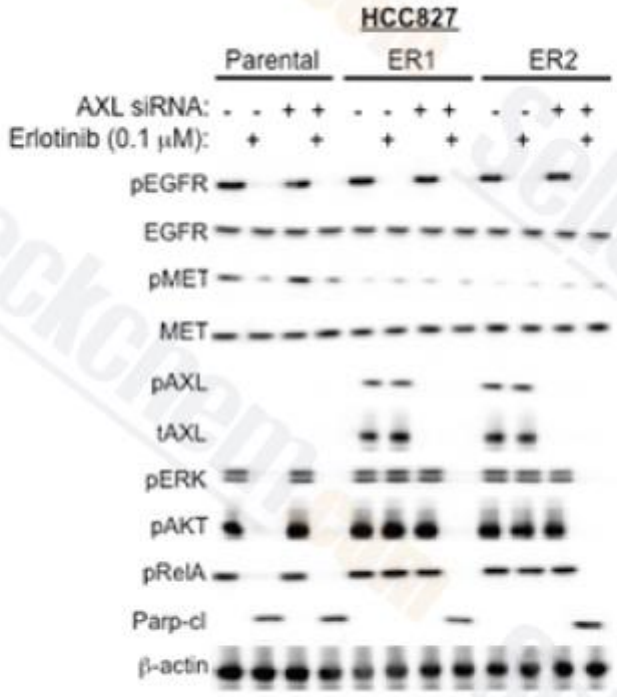
[4] Buck E, et al. Mol Cancer Ther. 2006, 5(11), 2676-2784.

[5] Higgins B, et al. Anticancer Drugs. 2004, (5), 503-512.

[6] Furugaki K,et al. Oncol Lett. 2010, 1(2), 231-235.

[7] Bago-Horvath Z, et al. 2012, DOI: 10.1159/000337257

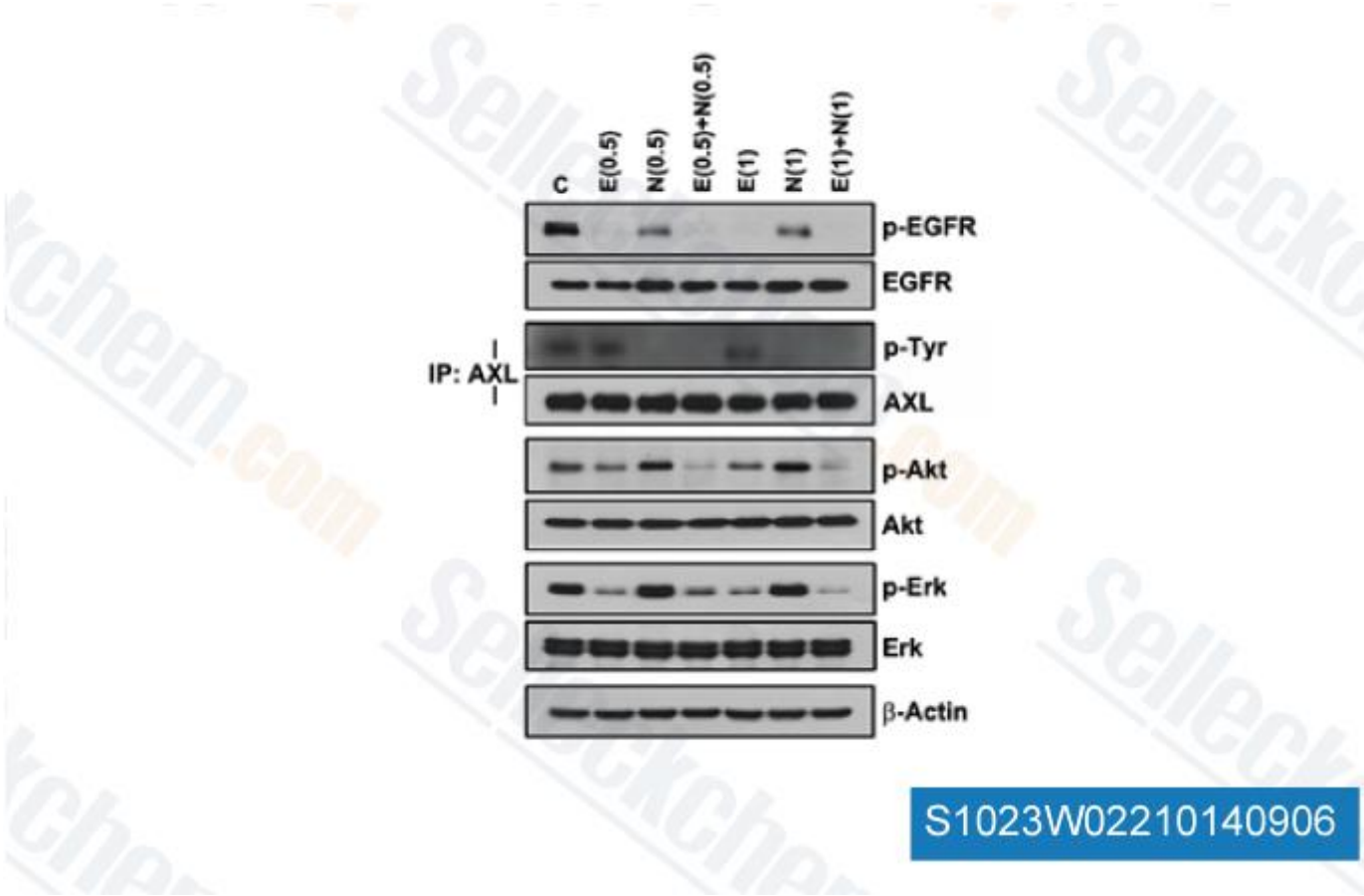
Customer Reviews



Data from [**Nat Genet**, 2012, 44(8):852-60]

Erlotinib HCl (OSI-744) purchased from **Selleck**

Erlotinib IC50 in HCC827 cell lines measured 48h after treatment with vehicle (control) or with erlotinib. Erlotinib IC50 is shown in parentheses. Data are representative of 3 independent experiments. Effects of treatment for 48h with a vehicle or the indicated doses of MP-470 in parental or ER1 and ER2 cell lines in the absence and presence of erlotinib on the indicated biomarkers.



Data from [**Cancer Res**, 2014, 4(1):253-62]

Erlotinib HCl (OSI-744) purchased from **Selleck**

Effects of combined treatment with erlotinib and NPS-1034 in HCC827/ER cells with AXL activation. Lysates were immunoprecipitated with an anti-AXL antibody and immunoblotted with antibodies for phosphotyrosine (p-Tyr) and AXL. HCC827/ER cells were treated with erlotinib. E, erlotinib; N, NPS-1034. **, $P < 0.001$ for the combination of erlotinib plus NPS-1034 versus either the control or drug alone.

Erlotinib HCl (OSI-744) has been referenced in 49 publications.