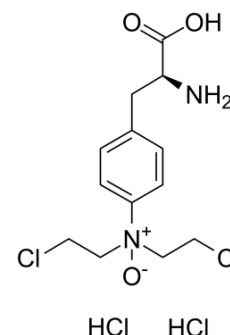


PX-478

Cat. No.:	HY-10231
CAS No.:	685898-44-6
Molecular Formula:	C ₁₃ H ₂₀ Cl ₄ N ₂ O ₃
Molecular Weight:	394.12
Target:	HIF/HIF Prolyl-Hydroxylase; Autophagy
Pathway:	Metabolic Enzyme/Protease; Autophagy
Storage:	-20°C, stored under nitrogen, away from moisture * The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (253.73 mM; Need ultrasonic)
 H₂O : ≥ 35 mg/mL (88.81 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.5373 mL	12.6865 mL	25.3730 mL
	5 mM	0.5075 mL	2.5373 mL	5.0746 mL
	10 mM	0.2537 mL	1.2686 mL	2.5373 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 5 mg/mL (12.69 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 5 mg/mL (12.69 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 5 mg/mL (12.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PX-478 is an orally active HIF-1α inhibitor with potent antitumor activities. PX-478 can cross the blood-brain barrier^{[1][2]}.

IC₅₀ & Target

HIF-1α^[1]

In Vitro

PC3 and DU 145 cells express HIF-1α protein are treated with PX-478 for 20 hr under normoxia. PC3 cells are more sensitive to PX-478 as compared with DU 145 cells. Densitometric analysis shows that the IC₅₀ for HIF-1α inhibition for PC3 cells under normoxic condition is 20-25 μM, whereas the IC₅₀ for HIF-1α inhibition for the DU 145 cells is 40-50 μM. PC3 and DU 145 cells

are treated with different concentrations of PX-478 (10, 20, 30, 40, 50, and 60 μM) for 18-20 hr under normoxia or hypoxia. Under normoxia, PC3 cells are more sensitive to PX-478 than DU 145 cells. IC_{50} for clonogenic survival (n=3) is 17 μM for PC3 cells and 35 μM for DU 145 cells. When cells are treated with the drug under hypoxic condition for 18 hr, the IC_{50} is 16 μM for PC3 cells and 22 μM for DU 145 cells. Thus DU 145 cells are more sensitive to PX-478 under hypoxic condition^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

PX-478 is administered to mice with congenital HO (Nfatc1-Cre/caACVR1^{fl/fl}) every other day starting from birth for 2 wk. Treated mice have significantly less ectopic bone at the ankle joints compared with mutant mice treated with vehicle (6.8 mm^3 vs. 2.2 mm^3 , $P < 0.01$)^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay^[1]

To determine the effect of PX-478 in combination with radiation, cells are treated with PX-478 for 24 hr under normoxic condition, irradiated and plated after 1 hr. Colonies are stained with crystal violet after 12 days and the colonies of >50 cells are counted. For combination treatments, net survival is calculated by correcting the toxicity of PX-478 alone. Enhancement factor (EF) is calculated by dividing the dose of radiation required to reduce plating efficiency to 10% when cells are treated with radiation alone by the dose of radiation required to reduce plating efficiency to 10% when cells are treated with PX-478 and radiation^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration^[2]

Mice^[2]
Caution: Product has not been fully validated for medical applications. For research use only.
PX-478 is dissolved in PBS solution via intraperitoneal injection. Mice receive injections every other day for the duration of the study. Nfatc1-Cre/caACVR1^{fl/wt} mice are administered PX-478 (100 mg/kg) every other day for a total of 2 wk. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Circulation. 2020 Jul 28;142(4):384-400.
- Sci Transl Med. 2020 Apr 8;12(538):eaay1620.
- Mol Nutr Food Res. 2018 Aug;62(16):e1800164.
- Front Immunol. 2018 Jul 23;9:1667.
- J Biol Chem. 2017 Jun 30;292(26):11009-11020.

See more customer validations on www.MedChemExpress.com

REFERENCES

- [1]. Palayoor ST, et al. PX-478, an inhibitor of hypoxia-inducible factor-1alpha, enhances radiosensitivity of prostate carcinoma cells. Int J Cancer. 2008 Nov 15;123(10):2430-2437.
- [2]. Agarwal S, et al. Inhibition of Hif1 α prevents both trauma-induced and genetic heterotopic ossification. Proc Natl Acad Sci U S A. 2016 Jan 19;113(3):E338-47.

India Contact:

Life Technologies (India) Pvt. Ltd.

306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444
Email: customerservice@lifetechindia.com Website: www.lifetechindia.com