Poziotinib

Cat. No.: HY-15730

CAS No.: 1092364-38-9

Molecular Formula: $C_{23}H_{21}Cl_2FN_4O_3$

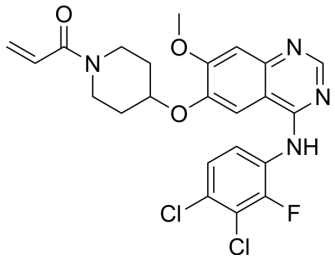
Molecular Weight: 491.34

Target: EGFR; Apoptosis

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (101.76 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0353 mL	10.1763 mL	20.3525 mL
	5 mM	0.4071 mL	2.0353 mL	4.0705 mL
	10 mM	0.2035 mL	1.0176 mL	2.0353 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.87 mg/mL (5.84 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.87 mg/mL (5.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.09 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.25 mg/mL (4.58 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.25 mg/mL (4.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Poziotinib (HM781-36B) is an orally active, irreversible pan-HER inhibitor, which effectively inhibits $EGFR^{wt}$, HER-2 and HER-4 with IC_{50}s of 3.2, 5.3 and 23.5 nM, respectively. Poziotinib (HM781-36B) also shows excellent inhibitory activities against mutated EGFRs, including $EGFR^{T790M}$ and $EGFR^{L858R/T790M}$, with IC_{50}s of 4.2 and 2.2 nM, respectively. Excellent antitumor

	activity[1][2].
IC_{50} & Target	IC50: 3.2 nM ($EGFR^{wt}$), 5.3 nM (HER-2), 23.5 nM (HER-4) 4.2 nM ($EGFR^{T790M}$), 2.2 nM ($EGFR^{L858R/T790M}$)[2]
In Vitro	The IC_{50} levels of Poziotinib (HM781-36B) for N87 and SNU216 were 0.001 and 0.004 μM, respectively, which was 10-1000 fold lower than the IC_{50} levels of other HER family TKIs. HM781-36B more potently inhibited the phosphorylation of HER family and downstream proteins, and induced apoptosis and G1 arrest compared to ZD1839 or GW572016[1]. Poziotinib (HM781-36B) also shows excellent selectivity with other kinases with greater than 100- to 1,000- fold IC_{50} values compared with EGFR family members. Poziotinib (HM781-36B) possesses a functional α,β□unsaturated carbonyl group as Michael acceptor moiety at the C6 position that allows covalent modifications of the EGFR kinase domain active site[2]. The addition of HM781-36B induced potent growth inhibition in both DiFi cells with EGFR overexpression and SNU-175 cells (IC_{50}=0.003 and 0.005 μM, respectively). Furthermore, HM781-36B induced G1 arrest of the cell cycle and apoptosis, and reduced the levels of HER family and downstream signaling molecules, pERK and pAKT, as well as nonreceptor/cytoplasmic tyrosine kinase, BMX[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The growth of tumors in mice treated with HM781-36B alone or in combination with 5-FU was significantly inhibited compared with control mice, and tumor volume in mice receiving coadministraion of HM781-36B and 5-FU was smaller than tumor volume in mice receiving HM781-36B only[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Med Chem. 2022 May 12;65(9):6643-6655.
- Cancers (Basel). 2020 Nov 4;12(11):3249.
- Mol Cancer Res. 2019 Nov;17(11):2233-2243.
- Biochem Biophys Res Commun. 2020 May 21;526(1):158-164.
- Methods Mol Biol. 2018;1711:351-398.

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REFERENCES

[1]. Nam HJ, et al. Antitumor activity of HM781-36B, an irreversible Pan-HER inhibitor, alone or in combination with cytotoxic chemotherapeutic agents in gastric cancer. Cancer Lett. 2011 Mar 28;302(2):155-65.

[2]. Cha MY, et al. Antitumor activity of HM781-36B, a highly effective pan-HER inhibitor in CP-358774-resistant NSCLC and other EGFR-dependent cancer models. Int J Cancer. 2012 May 15;130(10):2445-54.

[3]. Kang MH, et al. Antitumor Activity of HM781-36B, alone or in Combination with Chemotherapeutic Agents, in Colorectal Cancer Cells. Cancer Res Treat. 2015 Mar 5.

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