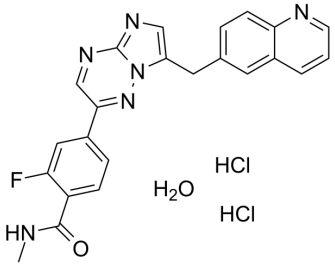
Capmatinib dihydrochloride hydrate

Cat. No.:	HY-13404C
CAS No.:	1865733-40-9
Molecular Formula:	$C_{23}H_{21}Cl_2FN_6O_2$
Molecular Weight:	503.36
Target:	c-Met/HGFR; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20.83 mg/mL (41.38 mM; ultrasonic and warming and heat to 60°C)

H_2O : 3.33 mg/mL (6.62 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9866 mL	9.9332 mL	19.8665 mL
	5 mM	0.3973 mL	1.9866 mL	3.9733 mL
	10 mM	0.1987 mL	0.9933 mL	1.9866 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Capmatinib (INC280; INCB28060) dihydrochloride hydrate is a potent, orally active, selective, and ATP competitive c-Met kinase inhibitor (IC_{50}=0.13 nM). Capmatinib dihydrochloride hydrate can inhibit phosphorylation of c-MET as well as c-MET pathway downstream effectors such as ERK1/2, AKT, FAK, GAB1, and STAT3/5. Capmatinib dihydrochloride hydrate potently inhibits c-MET-dependent tumor cell proliferation and migration and effectively induces apoptosis. Antitumor activity. Capmatinib dihydrochloride hydrate is largely metabolized by CYP3A4 and aldehyde oxidase[1][2][3].

In Vitro

Capmatinib (INCB28060) inhibits c-MET phosphorylation with an IC_{50} value of approximately 1 nM and a concentration of approximately 4 nM inhibits c-MET more than 90%, which is reversible and the effect is significantly reduced in several hours after the compound is removed and completely disappeared by 48 hours[1].

Capmatinib (INCB28060) (0-10000 nM; 72 h) inhibits the proliferation of SNU-5, S114, H441 and U-87MG[1].

Capmatinib (INCB28060) (0.06-62.25 nM; 2h) effectively inhibits phosphorylation of c-MET as well as c-MET pathway downstream effectors such as ERK1/2, AKT, FAK, GAB1, and STAT3/5[1].

Capmatinib (INCB28060) (0.24-63 nM; over night) prevents HGF-stimulated H441 cell migration[1].
Capmatinib (INCB28060) (0.5-50 nM; 20 min) suppresses phosphorylation of both EGFR and HER-3 rapidly[1].
Capmatinib (INCB28060) (0-333 nM; 24 h) induces apoptosis in SNU-5 cells[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	SNU-5, S114, H441 and U-87MG
Concentration:	0-10000 nM
Incubation Time:	72 h
Result:	Inhibited the cell viability of SNU-5 and S114, as well as the colony formation of H441 and U-87MG, with IC_{50} values of 1.2 nM, 12.4 nM, ~0.5 nM and 2 nM, respectively.

Cell Migration Assay [1]

Cell Line:	H441 (stimulated with 50 ng/mL recombinant human HGF for 24h)
Concentration:	0.24, 1, 4, 16 and 63 nM
Incubation Time:	Over night
Result:	Prevented HGF-stimulated H441 cell migration, with IC_{50} of approximately 2 nM, and less cell migration at 16 nM.

Western Blot Analysis[1]

Cell Line:	SNU-5
Concentration:	0.06, 0.24, 0.98, 3.91, 15.63 and 62.25 nM
Incubation Time:	2 h
Result:	Effectively inhibited phosphorylation of c-MET as well as c-MET pathway downstream effectors such as ERK1/2, AKT, FAK, GAB1, and STAT3/5.

Western Blot Analysis[1]

Cell Line:	H1993 cells
Concentration:	0.5, 5 and 50 nM
Incubation Time:	20 min
Result:	Suppressed phosphorylation of both EGFR and HER-3 rapidly and as effectively as the compound inhibited c-MET phosphorylation in H1993 cells.

Apoptosis Analysis[1]

Cell Line:	SNU-5 cells
Concentration:	0.017, 0.15, 1.37, 12.33, 111 and 333 nM
Incubation Time:	24 h
Result:	Effectively induced DNA fragmentation.

In Vivo

Capmatinib (INCB28060) (1-30 mg/kg; PO, twice daily, for 2 weeks) exhibits dose-dependent inhibition of tumor growth, and

shows well tolerance at all doses during the treatment periods, with no evidence of overt toxicity or weight loss in U-87MG tumor mice model[1].

Capmatinib (INCB28060) (0.03-10 mg/kg; PO, single dosage) causes inhibition of c-MET phosphorylation in S114 tumor mice model[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Balb/c nu/nu mice (inoculated subcutaneously with 5×10^6 U-87MG glioblastoma cells)[1]
Dosage:	1, 3, 10 and 30 mg/kg
Administration:	PO, twice daily, for 2 weeks
Result:	Exhibited dose-dependent inhibition of tumor growth with 35% and 76% at 1 and 3 mg/kg once daily; resulted in partial regressions in 6 of 10 U-87MG tumor-bearing mice at 10 mg/kg once daily; and showed well tolerance at all doses during the treatment periods, with no evidence of overt toxicity or weight loss.

Animal Model:	Female Balb/c nu/nu mice (inoculated subcutaneously with 4×10^6 S114 tumor cells)[1]
Dosage:	0.03, 0.1, 0.3, 1, 3 and 10 mg/kg
Administration:	PO, single dosage
Result:	Caused approximately 50% and 90% inhibition of c-MET phosphorylation at 0.03 and 0.3 mg/kg after administration of 30 min, and inhibition of phospho-c-MET exceeded 90% after 7 hours.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Exp Clin Cancer Res. 2022 Sep 16;41(1):275.
- Commun Biol. 2022 Nov 26;5(1):1295.
- Cancer Res Treat. 2020 Jul;52(3):973-986.
- Separations. 2023 Apr 10, 10(4), 247.

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REFERENCES

[1]. Liu X, et al. A novel kinase inhibitor, INCB28060, blocks c-MET-dependent signaling, neoplastic activities, and cross-talk with EGFR and HER-3. Clin Cancer Res. 2011 Nov 15;17(22):7127-38.

[2]. Baltschukat S, et al. Capmatinib (INC280) Is Active Against Models of Non-Small Cell Lung Cancer and Other Cancer Types with Defined Mechanisms of MET Activation. Clin Cancer Res. 2019 May 15;25(10):3164-3175.

[3]. Dhillon S. Capmatinib: First Approval. Drugs. 2020 Jul;80(11):1125-1131.

Caution: Product has not been fully validated for medical applications. For research use only.

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