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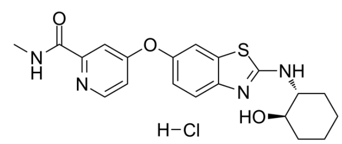
Product Data Sheet

Inhibitors • Screening Libraries • Proteins

Sotuletinib hydrochloride

Cat. No.:	HY-12768A
CAS No.:	2222138-31-8
Molecular Formula:	$C_{20}H_{23}ClN_4O_3S$
Molecular Weight:	434.94
Target:	c-Fms
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (229.92 mM; Need ultrasonic)
DMSO : 100 mg/mL (229.92 mM; Need ultrasonic)

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.2992 mL	11.4958 mL	22.9917 mL
	5 mM	0.4598 mL	2.2992 mL	4.5983 mL
	10 mM	0.2299 mL	1.1496 mL	2.2992 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: ≥ 2.5 mg/mL (5.75 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sotuletinib (BLZ945) hydrochloride is a potent, selective and brain-penetrant CSF-1R (c-Fms) inhibitor with an IC_{50} of 1 nM, showing more than 1,000-fold selectivity against its closest receptor tyrosine kinase homologs[1].

In Vitro

Sotuletinib hydrochloride inhibits CSF-1-dependent proliferation (EC_{50}=67 nM) in bone marrow-derived macrophages (BMDMs), and decreases CSF-1R phosphorylation, similar to CSF-1R antibody blockade. Sotuletinib hydrochloride also reduces viability of CRL-2467 microglia, Ink4a/Arf$^{/}$ BMDMs (PDG genetic background), and NOD/SCID BMDMs. Importantly, Sotuletinib hydrochloride treatment in culture does not affect proliferation of any PDG-derived tumor cell lines (all Csf-1r-negative), or U-87 MG human glioma cells, and PDG cell tumor sphere formation is unaffected. Thus, Sotuletinib

	hydrochloride has no direct effects on glioma cells, and perturbs macrophage survival through CSF-1R inhibition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Mice are treated with Sotuletinib hydrochloride or vehicle, and evaluated for symptom-free survival. Median survival in the vehicle-treated cohort is 5.7 weeks. In striking contrast, Sotuletinib hydrochloride significantly improves long-term survival with 64.3% surviving to the 26-week trial endpoint. This endpoint is chosen because Ink4a/Arf$^{/}$ mice develop spontaneous tumors, including lymphomas and sarcomas, beginning at ~30 weeks. Sotuletinib hydrochloride is well-tolerated over long-term treatment, with no visible side-effects, consistent with histopathological studies. Histological grading revealed high-grade, invasive gliomas in all vehicle-treated mice. By contrast, Sotuletinib hydrochloride-treated animals have significantly less-malignant tumors, and no detectable lesions in 55.6% of asymptomatic mice at the endpoint[1]. Mice receiving Sotuletinib hydrochloride shows reduced CSF1R staining in both cervical tumors and the associated stroma, with a significant decrease in CSF1R^{+} stromal macrophages relative to vehicle-treated mice ($P<0.05$)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Blood. 2019 Nov 28;134(22):1929-1940.
- Bioact Mater. 11 March 2022.
- J Exp Med. 2023 Mar 6;220(3):e20220857.
- J Exp Med. 2020 Nov 2;217(11):e20191820.

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REFERENCES

[1]. Pyonteck SM, et al. CSF-1R inhibition alters macrophage polarization and blocks glioma progression. Nat Med. 2013 Oct;19(10):1264-72.

[2]. Strachan DC, et al. CSF1R inhibition delays cervical and mammary tumor growth in murine models by attenuating the turnover of tumor-associated macrophages and enhancing infiltration by CD8+ T cells. Oncoimmunology. 2013 Dec 1;2(12):e26968.

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

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