Brepocitinib P-Tosylate

Cat. No.: HY-112708A

CAS No.: 2140301-96-6

Molecular Formula: $C_{25}H_{29}F_2N_7O_4S$

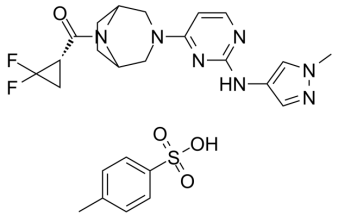
Molecular Weight: 561.6

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt

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

DMSO : 50 mg/mL (89.03 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7806 mL	8.9031 mL	17.8063 mL
	5 mM	0.3561 mL	1.7806 mL	3.5613 mL
	10 mM	0.1781 mL	0.8903 mL	1.7806 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 (3.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.70 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Brepocitinib (PF-06700841) P-Tosylate is a potent dual Janus kinase 1 (JAK1) and TYK2 inhibitor with IC_{50}s of 17 nM and 23 nM, respectively. Brepocitinib P-Tosylate also inhibits JAK2 and JAK3 with IC_{50}s of 77 nM and 6.49 μM, respectively[1].

IC_{50} & Target

JAK1	JAK2	JAK3
17 nM (IC_{50})	77 nM (IC_{50})	6.9 μM (IC_{50})

In Vitro

Brepocitinib (Compound 23) potently inhibits TYK2/JAK2 mediated IL-12/pSTAT4 and IL-23/pSTAT3 (human whole blood (HWB) IC_{50}s of 65 and 120 nM, respectively). Brepocitinib has good potency against IL6/pStat1 in the $CD3^+$ cellular subset (IC_{50} of 81 nM), but lower inhibition of IL6/pSTAT3, again in the $CD3^+$ cellular subset (IC_{50} of 641 nM). Brepocitinib also inhibits

	the JAK1/JAK3 driven γ-common chain cytokines, represented by IL-15/pStat5 and IL-21/pSTAT3 with reasonable potency (HWB IC_{50}s of 238 and 204 nM, respectively). Brepocitinib inhibits EPO/pSTAT5 (JAK2 homodimer) in HWB spiked with $CD34^+$ progenitor cells (IC_{50} of 577 nM). IL10/pSTAT3 (TYK2/JAK1) and IL27/pSTAT3 (JAK1/JAK2/TYK2) are also inhibited by Brepocitinib with IC_{50}s of 305 nM and 86 nM, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Brepocitinib (Compound 23; 3-30 mg/kg; oral administration; for 7 consecutive days; female Lewis rats) treatment significantly reduces paw volume increase in a dose-dependent manner. The plasma concentrations in animals dosed with Brepocitinib at peak (30 min) and trough (24 h) time intervals post final dose respectively are as follows: 3 mg/kg, 3.54 μM, 0.0221 μM; 10 mg/kg, 10.95 μM, 0.06 μM; and 30 mg/kg, 23.89 μM, 0.06 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Lewis rats with induced arthritis[1]
Dosage:	3 mg/kg, 10 mg/kg, or 30 mg/kg
Administration:	Oral administration; for 7 consecutive days
Result:	Increased in paw volume was significantly lower and dose-dependent.

CUSTOMER VALIDATION

- Inflamm Bowel Dis. 2020 Dec 9;izaa318.
- Heliyon. 2023 Jan 13.

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REFERENCES

[1]. Fensome A, et al. Dual Inhibition of TYK2 and JAK1 for the Treatment of Autoimmune Diseases: Discovery of ((S)-2,2-Difluorocyclopropyl)((1 R,5 S)-3-(2-((1-methyl-1 H-pyrazol-4-yl)amino)pyrimidin-4-yl)-3,8-diazabicyclo[3.2.1]octan-8-yl)methanone (PF-06700

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