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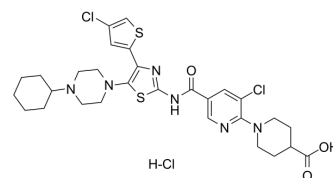
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Avatrombopag hydrochloride

Cat. No.:	HY-13463B
CAS No.:	570403-17-7
Molecular Formula:	C ₂₉ H ₃₅ Cl ₃ N ₆ O ₃ S ₂
Molecular Weight:	686.12
Target:	Thrombopoietin Receptor
Pathway:	Immunology/Inflammation
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 : 8.33 mg/mL (12.14 mM); ultrasonic and warming and heat to 60°C					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg		
				5 mg		
				10 mg		
				10 mg		
			1 mM	1.4575 mL	7.2874 mL	14.5747 mL
			5 mM	0.2915 mL	1.4575 mL	2.9149 mL
			10 mM	0.1457 mL	0.7287 mL	1.4575 mL
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 0.83 mg/mL (1.21 mM); Clear solution					

BIOLOGICAL ACTIVITY

Description	Avatrombopag (AKR-501) hydrochloride is an orally active, nonpeptide thrombopoietin (TPO) receptor agonist (EC ₅₀ =3.3 nM). Avatrombopag hydrochloride mimics the biological activities of TPO. Avatrombopag hydrochloride increases platelet production by activating the intracellular signaling system, and promotes production of platelets and megakaryocytes from hemopoietic precursor cells. Avatrombopag hydrochloride is a substrate of cytochrome P450 (CYP) 2C9 and CYP3A ^{[1][2][3]} .
In Vitro	Avatrombopag (E5501; AKR-501) hydrochloride specifically targets the TPO receptor and stimulated megakaryocytopoiesis throughout the development and maturation of megakaryocytes just as recombinant human TPO (rhTPO) did. Avatrombopag hydrochloride is showed to have effect in humans and chimpanzees only ^[1] . Avatrombopag hydrochloride (0-100 nM) supports the proliferation of TPO receptor expressing Ba/F3 cell in a concentration-dependent fashion. Avatrombopag hydrochloride (0-3 μM) induces tyrosine phosphorylation of STAT3 and STAT5, and threonine phosphorylation of ERK in the cells, as did rhTPO ^[1] . Avatrombopag hydrochloride promotes megakaryocyte colony formation from human CB CD34 ⁺ cells in a concentration-dependent fashion. The EC ₅₀ is 25 nM for Avatrombopag hydrochloride and the maximum activity of Avatrombopag hydrochloride is similar to that of rhTPO ^[1] .

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

In Vivo

Avatrombopag hydrochloride (0.3-3 mg/kg; p.o.; daily for 14 days) increases the number of human platelets in NOD/SCID mice transplanted with human FL CD34⁺ cells^[1].

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

Animal Model:	NOD/SCID mice (transplanted with human FL CD34 ⁺ cells) ^[1]
Dosage:	0.3, 1, and 3 mg/kg
Administration:	P.o.; daily for 14 days
Result:	Dose-dependently increased the number of human platelets, resulting in approximately a 2.7-fold increase at 1 mg/kg/d and a 3.0-fold increase at 3 mg/kg/d on day 14 after the start of administration.

CUSTOMER VALIDATION

- J Clin Invest. 2022 Jan 27;e149856.
- J Thromb Haemost. 2022 May 27.

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REFERENCES

- [1]. Fukushima-Shintani M, et al. AKR-501 (YM477) a novel orally-active thrombopoietin receptor agonist. Eur J Haematol. 2009;82(4):247-254.
- [2]. Xu H, et al. Avatrombopag for the treatment of thrombocytopenia in patients with chronic liver disease. Expert Rev Clin Pharmacol. 2019 Sep;12(9):859-865.
- [3]. Nomoto M, et al. Pharmacokinetic/pharmacodynamic drug-drug interactions of avatrombopag when coadministered with dual or selective CYP2C9 and CYP3A interacting drugs. Br J Clin Pharmacol. 2018;84(5):952-960.

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

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