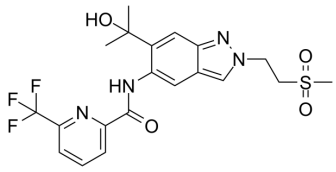
Zabedosertib

Cat. No.:	HY-139374
CAS No.:	1931994-81-8
Molecular Formula:	$C_{20}H_{21}F_3N_4O_4S$
Molecular Weight:	470.47
Target:	IRAK
Pathway:	Immunology/Inflammation
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 : 125 mg/mL (265.69 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1255 mL	10.6277 mL	21.2553 mL
	5 mM	0.4251 mL	2.1255 mL	4.2511 mL
	10 mM	0.2126 mL	1.0628 mL	2.1255 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 (4.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zabedosertib (BAY 1834845) is a selective, orally active IRAK4 inhibitor with immunomodulatory potential, IC_{50} is 3.55 nM. IRAK4 is a protein kinase involved in signaling innate immune responses from Toll-like receptors[1]. Zabedosertib exhibits anti-inflammatory property against IL-β, LPS (HY-D1056) and Imiquimod (HY-B1080) induced inflammation[2].

IC_{50} & Target

IRAK4
3.55 nM (IC_{50})

In Vitro

Zabedosertib decreases inflammatory cytokines secretion (500 nM), such as IL-1, IFN-γ, TNF-α, and IL-17[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Zabedosertib (150 mg/kg, p.o., twice) prevents lung injury and reduces inflammation in LPS induced ARDS in BALB/c mice[2].
Zabedosertib inhibits IL-β(p.o., 40-80 mg/kg, once), LPS (p.o., 10-40 mg/kg, once) and Imiquimod (p.o., 15-150 mg/kg, twice

daily for 7 days) induced inflammation[3].
Zabedosertib has a Pharmacokinetic profile in rats[3]:
Pharmacokinetic Analysis of Zabedosertib in rats[1]

species	$Dose_{iv}$ (mg/kg)	$AUC_{norm,iv}$ (kg·h/L)	CL_{blood} (L/h/kg)	V_{ss} (L/kg)	$T_{1/2,iv}$ (h)	$Dose_{po}$ (mg/kg)	$AUC_{norm,po}$ (kg·h/L))	$C_{max,norm}$ (kg/L)	T_{max} (h)	F (%)
rat	0.5	5.6	0.24	0.92	4.2	2.0	5.3	0.55	4.0	94
dog	0.5	15	0.088	1.6	17	1.0	15	0.57	2.0	104

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

Animal Model:	LPS induced ARDS in BLAB/c mice[2]
Dosage:	150 mg/kg
Administration:	p.o., twice (30 min before and 6 h after LPS-injection or 4 h and 12 h after LPS-injection)
Result:	Decreased inflammatory cells infiltration. Combination of Zabedosertib and DEX (HY-14648) decreased T-cells, monocytes and macrophages.

Animal Model:	BALB/c mice[3]
Dosage:	IL-β:40-80 mg/kg, LPS: 10-40 mg/kg, Imiquimod: 15-150 mg/kg
Administration:	oral gavage, IL-β: once, LPS: once, Imiquimod: twice daily for 7 days
Result:	Inhibited IL-β, LPS induced inflammation in a dose-dependent manner. Inhibited Imiquimod induced inflammation.

CUSTOMER VALIDATION

- Emerg Microbes Infect. 2021 Jul 20;104867.

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REFERENCES

[1]. Li Q, et al., Oral IRAK4 inhibitor BAY-1834845 prevents acute respiratory distress syndrome. Biomed Pharmacother. 2022 Sep;153:113459.

[2]. Bothe U, et al., Discovery of IRAK4 Inhibitors BAY1834845 (Zabedosertib) and BAY1830839. J Med Chem. 2024 Jan 25;67(2):1225-1242.

[3]. Bothe, Ulrich; Siebenreicher, Holger; Schmidt, Nicole; Nubbemeyer, Reinhard; Boemer, Ulf; Guenther, Judith; Steuber, Holger; Lange, Martin; Stegmann, Christian; Sutter, Andreas; et al.New substituted indazoles, methods for the production thereof, pharmaceutical preparations that contain said new substituted indazoles, and use of said new substituted indazoles to produce drugs.WO2016083433A1

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

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