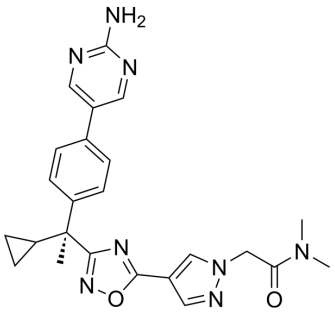
(S)-BI 665915

Cat. No.:	HY-12995A
CAS No.:	1360550-05-5
Molecular Formula:	$C_{24}H_{26}N_8O_2$
Molecular Weight:	458.52
Target:	FLAP
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	(S)-BI 665915 is an orally active oxadiazole-containing 5-lipoxygenase-activating protein (FLAP) inhibitor with an IC_{50} of 1.7 nM for FLAP binding. (S)-BI 665915 inhibits FLAP functional in human whole blood with an IC_{50} of 45 nM. (S)-BI 665915 demonstrates an excellent cross-species agent metabolism and pharmacokinetics (DMPK) profile and a dose-dependent inhibition of LTB_4 production[1].
IC_{50} & Target	IC50: 1.7 nM (FLAP) and 45 nM (FLAP functional in human whole blood)[1]
In Vitro	(S)-BI 665915 shows significantly weaker activity in mouse whole blood (mWB) assay than in human whole blood (mWB IC_{50} =4800 nM; hWB IC_{50}=45 nM)[1]. (S)-BI 665915 shows a modest human hepatocyte clearance (41% percent of hepatic blood flow) and relatively high plasma protein binding (unbound fraction of 4.7%)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	(S)-BI 665915 (oral; 1-100 mg/kg) demonstrates dose-dependent LTB4 production inhibition in mouse whole blood, 2 h after single oral dose[1]. (S)-BI 665915 (iv of 1 mg/kg or po of 10 mg/kg) shows low iv plasma clearance in all three species, with clearance values of 7 % Qh in rat, 2.8 % Qh in dog, and 3.6 % Qh in cynomolgus monkey, respectively. The volume of distribution (V_{ss}) across species tested is in a range of 0.5 to 1.2 L/kg, and the bioavailability was good (45 to 63 %) in all species tested[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 mice[1]
Dosage:	1, 3, 10, 30, 100 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral
Result:	Demonstrated dose-dependent LTB4 production inhibition in mouse whole blood, 2 h after single oral dose.

Animal Model:	Rat; dog; cynomolgus monkey[1]
Dosage:	1 mg/kg (iv) or 10 mg/kg (po)

Administration:	Iv or po
Result:	Showed low iv plasma clearance in all three species, with clearance values of 7 % Qh in rat, 2.8 % Qh in dog, and 3.6 % Qh in cynomolgus monkey, respectively.

REFERENCES

[1]. Takahashi H, et al. Synthesis, SAR, and series evolution of novel oxadiazole-containing 5-lipoxygenase activating protein inhibitors: discovery of 2-[4-(3-{(r)-1-[4-(2-amino-pyrimidin-5-yl)-phenyl]-1-cyclopropyl-ethyl}-[1,2,4]oxadiazol-5-yl)-pyrazol-1-yl]-N,N-dimethyl-acetamide (BI 665915). J Med Chem. 2015 Feb 26;58(4):1669-90.

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