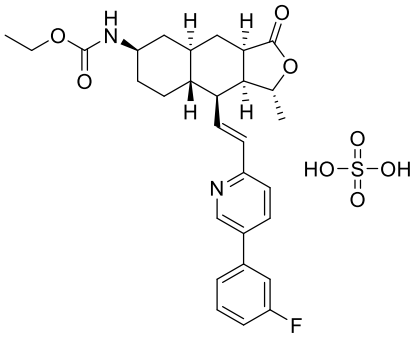
Product data sheet

MedKoo Cat#: 314207 Name: Vorapaxar sulfate CAS#: 705260-08-8 (sulfate) Chemical Formula: $C_{29}H_{35}FN_2O_8S$ Molecular Weight: 590.6634	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Vorapaxar, also known as SCH 530348, is a thrombin receptor (protease-activated receptor, PAR-1) antagonist based on the natural product himbacine. Vorapaxar was approved in 2014. Vorapaxar is a new anti-platelet drug that is part of the PAR-1 antagonist family, a new class of anti-platelet drug. It functions by inhibiting thrombin-related platelet aggregation. This mechanism works by a different pathway than other anti-platelet medications such as aspirin and P2Y12 inhibitors. Unlike many other medication, vorapaxar does not affect ADP-mediated platelet aggregation, coagulation parameters, or bleeding time.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	125.0	211.63

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.69 mL	8.47 mL	16.93 mL
5 mM	0.34 mL	1.69 mL	3.39 mL
10 mM	0.17 mL	0.85 mL	1.69 mL
50 mM	0.03 mL	0.17 mL	0.34 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Chackalamannil S, Wang Y, Greenlee WJ, Hu Z, Xia Y, Ahn HS, Boykow G, Hsieh Y, Palamanda J, Agans-Fantuzzi J, Kurowski S, Graziano M, Chintala M. Discovery of a novel, orally active himbacine-based thrombin receptor antagonist (SCH 530348) with potent antiplatelet activity. J Med Chem. 2008 Jun 12;51(11):3061-4. doi: 10.1021/jm800180e. Epub 2008 May 1. PMID: 18447380.
2. Hawes BE, Zhai Y, Hesk D, Wirth M, Wei H, Chintala M, Seiffert D. In vitro pharmacological characterization of vorapaxar, a novel platelet thrombin receptor antagonist. Eur J Pharmacol. 2015 Sep 5;762:221-8. doi: 10.1016/j.ejphar.2015.05.046. Epub 2015 May 27. PMID: 26022529.

In vivo study

1. Chackalamannil S, Wang Y, Greenlee WJ, Hu Z, Xia Y, Ahn HS, Boykow G, Hsieh Y, Palamanda J, Agans-Fantuzzi J, Kurowski S, Graziano M, Chintala M. Discovery of a novel, orally active himbacine-based thrombin receptor antagonist (SCH 530348) with potent antiplatelet activity. J Med Chem. 2008 Jun 12;51(11):3061-4. doi: 10.1021/jm800180e. Epub 2008 May 1. PMID: 18447380.
2. Waasdorp M, Duitman J, Florquin S, Spek CA. Vorapaxar treatment reduces mesangial expansion in streptozotocin-induced diabetic nephropathy in mice. Oncotarget. 2018 Apr 24;9(31):21655-21662. doi: 10.18632/oncotarget.25069. PMID: 29774092; PMCID: PMC5955164.

Product data sheet

7. Bioactivity

Biological target:

Vorapaxar sulfate (SCH 530348 sulfate) shows potent inhibition of thrombin-induced platelet aggregation with an IC50 of 47 nM and haTRAP-induced platelet aggregation with an IC50 of 25 nM.

In vitro activity

SCH 530348 is a synthetic tricyclic 3-phenylpyridine and an orally active himbacine-based thrombin-receptor antagonist. SCH 530348 shows potent inhibition of thrombin-induced platelet aggregation with an IC50 of 47 nM and haTRAP-induced platelet aggregation with an IC50 of 25 nM, whereas it shows no inhibition of platelet aggregation induced by other agonists such as ADP, collagen and a PAR-4 agonist peptide. SCH 530348 also has no affect on the prothrombin time (PT), partial thromboplastin time (PTT), or activated partial thromboplastin time (aPTT). Moreover, SCH 530348 causes no increase in the bleeding time or in surgical bleeding compared with inactive control. SCH530348 is found to be selective for PAR-1 when tested over a number of ion channels and receptors, including PAR-4 receptor.

Reference: J Med Chem. 2008 Jun 12;51(11):3061-4. https://pubmed.ncbi.nlm.nih.gov/18447380/

In vivo activity

SCH 530348 is well absorbed in rat (68%; 10 mg/kg) and in monkey (82%; 1 mg/kg) models. Tmax is observed at about 3 h in rats and 1 h in monkeys. The elimination half-life is 5.1 h in rats and 13 h in monkeys. The oral bioavailability is 33% in rats and 86% in monkeys. In preclinical studies in cynomolgus monkey platelets, oral administration of SCH 530348 at a dose greater than 0.1 mg/kg resulted in 100% inhibition of thrombin-receptor agonist peptide (TRAP)-induced platelet aggregation for 24 h with partial recovery occurring at 48 h.

Reference: J Med Chem. 2008 Jun 12;51(11):3061-4. https://pubmed.ncbi.nlm.nih.gov/18447380/