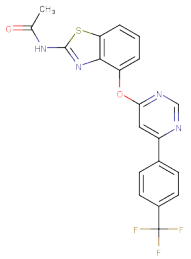
Data Sheet (Cat.No.T6379)

TargetMol
A DRUG SCREENING EXPERT

AMG 517

Chemical Properties



CAS No. : 659730-32-2

Formula: C20H13F3N4O2S

Molecular Weight: 430.4

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	AMG 517 is an effective and specific TRPV1 antagonist, antagonizes proton (IC50: 0.76 nM), capsaicin (IC50: 0.62 nM), and heat activation (IC50: 1.3 nM) of TRPV1.
Targets(IC50)	TRP/TRPV Channel
In vitro	AMG 517 inhibits CAP- (500 nM), acid- (pH 5.0), or heat-(45 °C) induced 45Ca2+ influx into human TRPV1-expressing CHO Cells with IC50 of 0.76 nM, 0.62 nM and 1.3 nM. AMG 517 blocks capsaicin-, proton-, and heat-induced inward currents in TRPV1-expressing cells similarly. AMG 517 inhibits native TRPV1 activation by capsaicin in rat dorsal root ganglion neurons with an IC50 value of 0.68 nM. AMG 517 is a competitive antagonist of both rat and human TRPV1 with dissociation constant (Kb) values of 4.2 and 6.2 nM, respectively. AMG 517 is a highly selective TRPV1 antagonist. The IC50 value for AMG 517 is >20 μM against 2-APB-activated TRPV2 and TRPV3, 4-αPDD-activated TRPV4, allyl isothiocyanate-activated TRPA1, and icilin-activated TRPM8 in cell-based assays that measure agonist-induced increases in intracellular calcium in CHO cells recombinantly expressing the appropriate TRP channel. [1]
In vivo	Oral administration of AMG 517 produces a dose-dependent increase in plasma concentrations, it also produces a dose-dependent decrease in the number of flinches induced by capsaicin treatment. The minimally effective dose (MED), based on a statistically significant difference in number of flinches from the vehicle versus capsaicin-administered group, is 0.3 mg/kg for AMG 517. The corresponding plasma concentrations are 90 to 100 ng/mL for AMG 517. AMG 517 (3 mg/kg) exhibits significant reductions in capsaicin-induced flinch up to 24 h after dosing. AMG 517 blocks thermal hyperalgesia in CFA model of pain.[1] AMG 517 elicits hyperthermia in rodents, dogs and monkeys but not in TRPV1 knockout mice. Interestingly, hyperthermia evoked by TRPV1-selective antagonists is attenuated after repeated dosing of these antagonists to rats, dogs and monkeys, and TRPV1 knockout mice does not exhibit an impairment of thermoregulation.[2]

Solubility Information

Solubility	DMSO: 43 mg/mL (100 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3234 mL	11.6171 mL	23.2342 mL
5 mM	0.4647 mL	2.3234 mL	4.6468 mL
10 mM	0.2323 mL	1.1617 mL	2.3234 mL
50 mM	0.0465 mL	0.2323 mL	0.4647 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Gavva NR, et al. J Pharmacol Exp Ther, 2007, 323(1), 128-137.
Pan X, Li R, Guo H, et al. Dihydropyridine Calcium Channel Blockers Suppress the Transcription of PD-L1 by