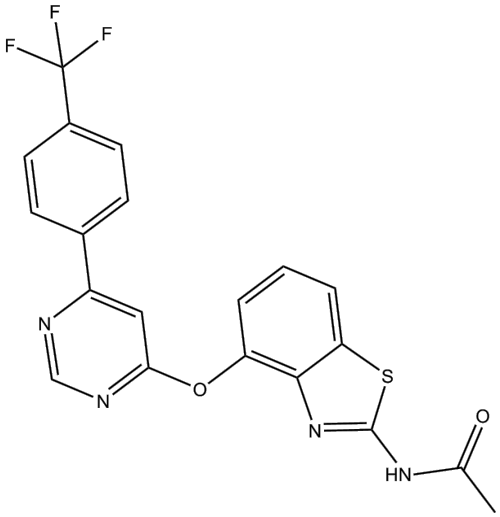
Product Data Sheet

Product Name: AMG-517
Cat. No.: GC13003

Chemical Properties

Cas. No.	659730-32-2		
Chemical Name	N-[4-[6-[4-(trifluoromethyl)phenyl]pyrimidin-4-yl]oxy-1,3-benzothiazol-2-yl]acetamide		
SMILES	CC(=O)NC1=NC2=C(C=CC=C2S1)OC3=NC=NC(=C3)C4=CC=C(C=C4)C(F)(F)F		
Formula	$C_{20}H_{13}F_3N_4O_2S$	M.Wt	430.4
Solubility	≥ 21.5mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment[1]:

Cell lines CHO cells

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Preparation method	The solubility of this compound in DMSO is > 21.5mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting condition	1-2 nM
Applications	AMG 517 is a selective antagonist of both rat and human TRPV1 with dissociation constant values of 4.2 and 6.2 nM, respectively. AMG 517 effectively and completely inhibited capsaicin, proton, and heat activation of TRPV1 in vitro. AMG 517 potently inhibited capsaicin-, acid-, and heat-induced Ca2+ uptake into CHO cells expressing TRPV1 with IC50 values of 1 to 2 nM.

Clinical experiment [2]:

Clinical samples	Healthy adults
Dosage form	Oral administration, 2, 5 and 10 mg
Application	AMG 517 blocked TRPV1 and elicited a generally plasma concentration-dependent hyperthermia in healthy humans. AMG 517 caused hyperthermia by increasing thermogenesis and inducing tail skin vasoconstriction, indicating that TRPV1 regulates metabolic heat production and vasomotor tone in humans.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Gavva N R, Bannon A W, Hovland D N, et al. Repeated administration of vanilloid receptor TRPV1 antagonists attenuates hyperthermia elicited by TRPV1 blockade[J]. Journal of Pharmacology and Experimental Therapeutics, 2007, 323(1): 128-137.

[2]. Gavva N R, Treanor J J S, Garami A, et al. Pharmacological blockade of the vanilloid receptor TRPV1 elicits marked hyperthermia in humans[J]. Pain, 2008, 136(1): 202-210.

Background

AMG-517 is an antagonist of TRPV1 channel with IC50 value of 1-2 nM [1].
TRP1, transient receptor potential cation channel subfamily V member 1, is a subfamily of the transient receptor potential protein group and plays an important role in detecting and regulating body temperature or sensing pain. TRPV1 can be activated by diverse stimuli, including several ingredients of the inflammatory soup which leads to a painful, burning sensation. It is reported that TRPV1 channel may play a pivotal role in many diseases like SIRS [1] [2].
AMG-517 is a TRPV1 antagonist. When tested with stable CHO cell lines expressing TRPV1, treated with AMG-517 inhibited the activation of TRPV1 [1].
In C57BL/6 mice with SIRS induced by LPS, pretreatment with AMG-517 (210 µg/kg) markedly decreased the survival rate and increased the risk of mortality [2]. When tested with Trpv1-/- mice, intraperitoneally treated with AMG-517 (256 nmol/kg) inhibited TRPV1 with inducing hyperthermia in a dose-dependent manner [3]. In capsaicin-induced flinch male Sprague-Dawley rats, oral administration of AMG-517 markedly decreased the number of flinches in a dose-dependent manner [1].

References:

[1].Gavva, N.R., et al., Repeated administration of vanilloid receptor TRPV1 antagonists attenuates hyperthermia elicited by TRPV1 blockade. J Pharmacol Exp Ther, 2007. 323(1): p. 128-37.
[2].Wanner, S.P., et al., Aging reverses the role of the transient receptor potential vanilloid-1 channel in systemic inflammation from anti-inflammatory to proinflammatory. Cell Cycle, 2012. 11(2): p. 343-9.
[3].Garami, A., et al., Contributions of different modes of TRPV1 activation to TRPV1 antagonist-induced hyperthermia. J Neurosci, 2010. 30(4): p. 1435-40.

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