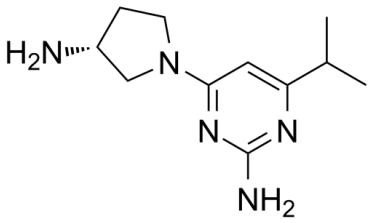
Data Sheet

Product Name:	JNJ-39758979
Cat. No.:	CS-0020957
CAS No.:	1046447-90-8
Molecular Formula:	C11H19N5
Molecular Weight:	221.30
Target:	Histamine Receptor
Pathway:	GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling
Solubility:	DMSO : 33.33 mg/mL (150.61 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

JNJ-39758979 is a selective, high-affinity **histamine H_4 receptor** antagonist with a **K_i** of 12.5 nM. IC50 & Target: Ki: 12.5 nM (histamine H_4 receptor)[1] **In Vitro:** JNJ-39758979 is a selective, high-affinity histamine H_4 receptor antagonist with a K_i of 12.5 nM. The affinity of JNJ-39758979 for the rat (K_i=188 nM) and guinea pig H_4R (K_i=306 nM) is moderate, and JNJ-39758979 has little if any affinity for the dog H_4R (K_i≥10 μM). JNJ-39758979 is metabolically stable ($t_{1/2}$ >120 min) when incubated in vitro with human, rat, dog, or monkey liver microsomes[1]. **In Vivo:** JNJ-39758979 shows dose-proportional pharmacokinetic (PK) in rat in the range of 2 to 500 mpK. JNJ-39758979 rapidly reaches the kidneys and liver (mean t_{max}=2.0 h). The elimination of JNJ-39758979 is slow from the brain, liver, and kidneys, with mean $t_{1/2}$ values of 42.5, 22.3, and 20.5 h, respectively. The highest exposure (based on C_{max} and $AUC_{0\text{-}inf}$ values) is observed in the liver followed by the kidney and brain. Tissue-to-plasma ratios for liver and kidney range from 23.2 to 95.8; the tissue-to-plasma ratios in brain increases with time from 0.256 to 22.7 up to 48 h after dosing. JNJ-39758979 is able to inhibit histamine-induced itch at doses of 5 and 20 mg/kg in mice. JNJ-39758979 exhibits dose-dependent inhibition of the clinical score in a mouse collagen-induced arthritis model[1].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [1]The model of histamine-induced scratching in C57/bl6 mice (n=6 to 8 per group) is used to judge the antipruritic effects of JNJ-39758979. JNJ-39758979 is given p.o. in 20% hydroxypropyl-β-cyclodextran 30 min before an intradermal injection of histamine (100 μg). Bouts of scratching are calculated using an automated system. Immediately after histamine injection, mice are placed in containers above a solenoid, and magnets previously placed on the mouse ear generate scratch-specific signals that are counted over a 20 min time span[1].

References:

[1]. Savall BM, et al. Discovery and SAR of 6-alkyl-2,4-diaminopyrimidines as histamine H? receptor antagonists. J Med Chem. 2014 Mar 27;57(6):2429-39.

CAIndexNames:

2-Pyrimidinamine, 4-[(3R)-3-amino-1-pyrrolidinyl]-6-(1-methylethyl)-

SMILES:

NC1=NC(C(C)C)=CC(N2C[C@H](N)CC2)=N1

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

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