

Product Data Sheet

Product Name: PF-01247324

Cat. No.: GC19281

Chemical Properties

Cas. No. 875051-72-2

SMILES O=C(C1=NC(N)=C(C2=CC(Cl)=CC(Cl)=C2Cl)C=C1)NC

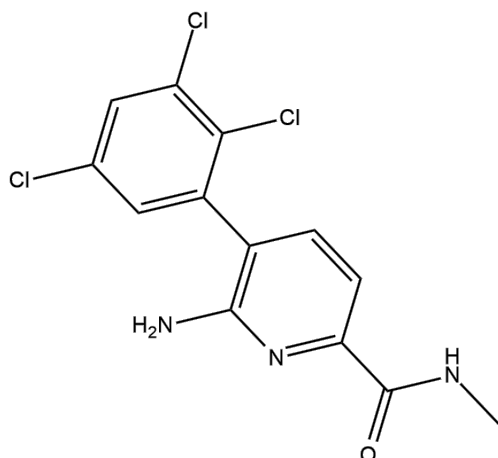
Formula $C_{13}H_{10}Cl_3N_3O$ M.Wt 330.6

Solubility DMSO : ≥ 30 mg/mL (90.74 mM) 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

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

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Animal experiment: Rats: For male Sprague Dawley rats (170-300 g), PF-01247324 is formulated as solutions of 0, 10, 30, 100 mg/kg in 0.5%MC/0.1%Tween 80 vehicle and dosed via oral gavage prior to behavioural testing. Test animals are placed in a box separated by walls with a wire mesh floor allowing access to the plantar surface of the paw. Tactile testing is conducted[1]. Mice: PF-01247324 is suspended in 0.5% methylcellulose, 0.1% Tween 80 and administered by oral gavage at a dose of 1000 mg/kg in a volume of 10 mL/kg one hour before behavioral testing. Control groups are administered an equal volume of vehicle[2].

References:

- [1]. Payne CE, et al. A novel selective and orally bioavailable Nav 1.8 channel blocker, PF-01247324, attenuates nociception and sensory neuron excitability. Br J Pharmacol. 2015 May;172(10):2654-70.
[2]. Shields SD, et al. Oral administration of PF-01247324, a subtype-selective Nav1.8 blocker, reverses cerebellar deficits in a mouse model of multiple sclerosis. PLoS One. 2015 Mar 6;10(3):e0119067.

Background

PF-01247324 is a selective and orally bioavailable Nav1.8 channel blocker with an IC₅₀ of 196 nM for recombinant human Nav1.8 channel.

PF-01247324 inhibits native tetrodotoxin-resistant (TTX-R) currents in human dorsal root ganglion (DRG) neurons (IC₅₀=331 nM) and in recombinantly expressed h Nav1.8 channels (IC₅₀=196 nM), with 50-fold selectivity over recombinantly expressed TTX-R hNav1.5 channels (IC₅₀=10 uM) and 65-100-fold selectivity over TTX-sensitive (TTX-S) channels (IC₅₀=10-18 uM). In vitro current clamp shows that PF-01247324 reduces excitability in both rat and human DRG neurons and also alters the waveform of the action potential[1].

Experiments in rodents demonstrate efficacy in both inflammatory and neuropathic pain models. PF-01247324 reduces phase 2 flinching by 37% at 100 mg/kg. There is a significant effect of 30 mg/kg of PF-01247324 in the rat model carrageenan-induced thermal hyperalgesia and in CFA-induced mechanical hyperalgesia at exposures of 0.218 and 0.126 uM respectively[1]. Mice that received PF-

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01247324 shows significant improvements in motor coordination and cerebellar-like symptoms compared to control[2].

References:

[1]. Payne CE, et al. A novel selective and orally bioavailable Nav 1.8 channel blocker, PF-01247324, attenuates nociception and sensory neuron excitability. Br J Pharmacol. 2015 May;172(10):2654-70.

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