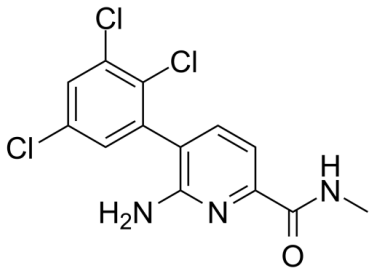
Data Sheet

Product Name:	PF-01247324
Cat. No.:	CS-6331
CAS No.:	875051-72-2
Molecular Formula:	C13H10Cl3N3O
Molecular Weight:	330.60
Target:	Sodium Channel
Pathway:	Membrane Transporter/Ion Channel
Solubility:	DMSO : ≥ 30 mg/mL (90.74 mM)



BIOLOGICAL ACTIVITY:

PF-01247324 is a selective and orally bioavailable **$Na_v1.8$** channel blocker with an **IC_{50}** of 196 nM for recombinant human $Na_v1.8$ channel. IC50 & Target: IC50: 196 nM ($hNa_v1.8$)[1] **In Vitro:** PF-01247324 inhibits native tetrodotoxin-resistant (TTX-R) currents in human dorsal root ganglion (DRG) neurons (IC_{50}=331 nM) and in recombinantly expressed h $Na_v1.8$ channels (IC_{50}=196 nM), with 50-fold selectivity over recombinantly expressed TTX-R hNav1.5 channels (IC_{50}=10 μM) and 65-100-fold selectivity over TTX-sensitive (TTX-S) channels (IC_{50}=10-18 μM). 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]. **In Vivo:** Experiments n rodents demonstrates 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 μM respectively[1]. Mice that received PF-01247324 shows significant improvements in motor coordination and cerebellar-like symptoms compared to control[2].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [1][2]Rat: 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].

Mouse: 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.

CAIndexNames:

2-Pyridinecarboxamide, 6-amino-N-methyl-5-(2,3,5-trichlorophenyl)-

SMILES:

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

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

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