PF-3893787 hydrochloride

Cat. No.: HY-19705B

CAS No.: 2096455-90-0

Molecular Formula: $C_{13}H_{25}Cl_3N_6$

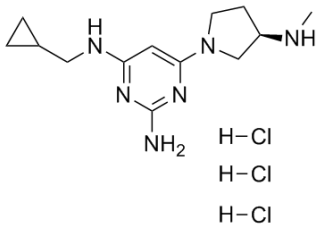
Molecular Weight: 371.74

Target: Histamine Receptor

Pathway: GPCR/G Protein; Immunology/Inflammation

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



Solvent & Solubility

In Vitro

DMSO : ≥ 83.33 mg/mL (224.16 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6901 mL	13.4503 mL	26.9005 mL
	5 mM	0.5380 mL	2.6901 mL	5.3801 mL
	10 mM	0.2690 mL	1.3450 mL	2.6901 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

PF-3893787 hydrochloride is a novel **histamine H4 receptor** antagonist binding affinity (K_i=2.4 nM) and is also a functional (K_i=1.56 nM) antagonist.

IC_{50} & Target

Ki: 2.4 nM (H4R bind), 1.56 nM (H4R func)[1]

In Vitro

PF-3893787 is tested and observed binding K_i=2.4 nM and functional K_i=1.56 nM for H4R. Data from functional assays produce convergent projections of the free plasma efficacious concentration and PF-3893787 (Compound 13) is fast on/fast off on rhH4R. The in vitro IC_{50} on human native isolated eosinophils assessing actin polymerisation is 1.16 nM and assuming need 10 times the IC_{50} for >90% receptor occupancy (and therefore near complete inhibition of the response) suggested a concentration of 12 nM. The data in the whole blood GAFS assay demonstrates that the imetit induced shape change is completely blocked at a total blood concentration of 30 nM (which correcting for PPB and blood partitioning equates to approximately 10 nM free). For the purpose of dose projection and safety margin calculation, a Ceff/Cmin concentration of 10-15 nM is used[1].

REFERENCES

[1]. Mowbray CE, et al. Challenges of drug discovery in novel target space. The discovery and evaluation of PF-3893787: a novel histamine H4 receptor antagonist. Bioorg Med Chem Lett. 2011 Nov 1;21(21):6596-602.

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