

PF-8380 (hydrochloride)

Catalog No: tcsc3147



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg



Specifications

Formula:

$C_{22}H_{22}Cl_3N_3O_5$

Pathway:

Metabolic Enzyme/Protease

Target:

Phosphodiesterase (PDE)

Purity / Grade:

>98%

Solubility:

DMSO : ≥ 5.2 mg/mL (10.10 mM); H₂O :

Observed Molecular Weight:

514.79

Product Description

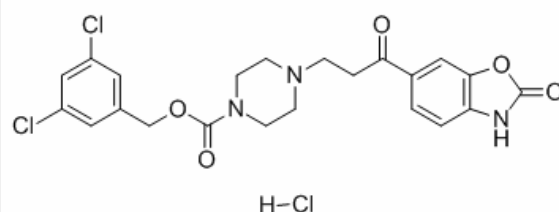
PF-8380 hydrochloride is a potent **autotaxin** inhibitor with an **IC₅₀** of 2.8 nM in isolated enzyme assay and 101 nM in human whole blood.

IC₅₀ & Target: IC₅₀: 2.8 nM (Autotaxin)^[1]

In Vitro:

PF-8380 also inhibits rat autotaxin with an IC_{50} of 1.16 nM with FS-3 substrate. Potency of PF-8380 is maintained when using enzyme produced from fetal fibroblasts used in combination with lysophosphatidyl choline (LPC) as a substrate. In human whole blood incubated with PF-8380 for 2 h, autotaxin is inhibited with an IC_{50} of 101 nM^[1]. Autotaxin (ATX), an enzyme with lysophospholipase D (lysoPLD) activity, catalyzes the production of lysophosphatidic acid (LPA) from lysophosphatidylcholine (LPC). Pre-treatment of GL261 and U87-MG cells with 1 μ M PF-8380 followed by 4 Gy irradiation results in decreased clonogenic survival, decreases migration (33% in GL261; $P=0.002$ and 17.9% in U87-MG; $P=0.012$), decreases invasion (35.6% in GL261; $P=0.0037$ and 31.8% in U87-MG; $P=0.002$), and attenuates radiation-induced Akt phosphorylation^[2].

In Vivo: The pharmacokinetic profile of PF-8380 is evaluated at an intravenous dose of 1 mg/kg and oral doses of 1 to 100 mg/kg out to 24 h. PF-8380 has mean clearance of 31 mL/min/kg, volume of distribution at steady state of 3.2 L/kg, and effective $t_{1/2}$ of 1.2 h. Oral bioavailability is moderate, ranging from 43 to 83%. Plasma concentrations increased with single oral escalating doses, but C_{max} increased at a rate that is approximately proportional to dose from 1 to 10 mg/kg and less than proportional to dose from 10 to 100 mg/kg. PF-8380 exposures estimated by area under the curve are approximately proportional to dose and linear up to 100 mg/kg. Plasma C16:0, C18:0, and C20:0 LPA levels are measured immediately after collection. Maximal reduction of LPA levels is observed by the 3 mg/kg dose at 0.5 h with all LPA returning at or above baseline at 24 h^[1]. Treatment with 10 mg/kg PF-8380 increases tumor-associated vascularity modestly by 20% ($P=0.497$). When compared to control, treatment of PF-8380 45 min before 4 Gy irradiation decreases vascularity by nearly 48% when compared to control ($P=0.031$) and by 65% when compared to mice that received radiation alone ($P=0.011$)^[2].



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!