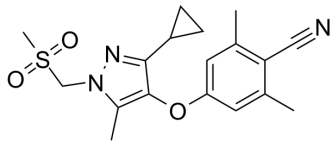
PF-02413873

Cat. No.:	HY-11028
CAS No.:	936345-35-6
Molecular Formula:	$C_{18}H_{21}N_3O_3S$
Molecular Weight:	359.44
Target:	Progesterone Receptor
Pathway:	Others
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 : 100 mg/mL (278.21 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7821 mL	13.9105 mL	27.8211 mL
	5 mM	0.5564 mL	2.7821 mL	5.5642 mL
	10 mM	0.2782 mL	1.3911 mL	2.7821 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (3.48 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (3.48 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (3.48 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-02413873 (PF-2413873) is a potent selective, fully competitive and orally active nonsteroidal progesterone receptor (PR) antagonist, with a K_i of 2.6 nM. PF-02413873 can block progesterone binding and PR nuclear translocation, and inhibit endometrial growth in vivo[1][2].

IC_{50} & Target

Ki: 2.6 nM (progesterone receptor)[1]

In Vitro

PF-02413873 shows potent PR antagonist activity with a derived K_i of 9.7 nM in the T47D native functional assay[1].

PF-02413873 (1 nM-10 μM) induces nuclear translocation only at high concentrations (>3 μM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

PF-02413873 (2.5 and 10 mg/kg; p.o. twice daily for 10 days) induces a statistically significant reduction in endometrial thickness in cynomolgus macaques[1].
PF-02413873 (3 mg/kg; a single p.o.) exhibits $t_{1/2}$ (4.2 h), C_{max} (162 ng/mL) and CL/F (41 mL/min/kg)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Cynomolgus macaques (3.7-5.7 kg; 5-6 years)[1]
Dosage:	2.5, 10 mg/kg
Administration:	P.o. twice daily for 10 days
Result:	Reduced the endometrial thickness of 43 and 56% at the dose of 2.5 and 10 mg/kg, respectively.

Animal Model:	Cynomolgus macaques (3.7-5.7 kg; 5-6 years)[1]
Dosage:	3 mg/kg (Pharmacokinetic Analysis)
Administration:	A single p.o.
Result:	$t_{1/2}$=4.2 h, C_{max}=162 ng/mL, CL/F=41 mL/min/kg.

REFERENCES

[1]. Howe DC, et, al. The translational efficacy of a nonsteroidal progesterone receptor antagonist, 4-[3-cyclopropyl-1-(mesylmethyl)-5-methyl-1H-pyrazol-4-yl]oxy,-2,6-dimethylbenzonitrile (PF-02413873), on endometrial growth in macaque and human. J Pharmacol

[2]. Bungay PJ, et, al. Preclinical and clinical pharmacokinetics of PF-02413873, a nonsteroidal progesterone receptor antagonist. Drug Metab Dispos. 2011 Aug;39(8):1396-405.

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