PF-06372865

Cat. No.: HY-120874

CAS No.: 1614245-70-3

Molecular Formula: $C_{22}H_{21}FN_4O_3S$

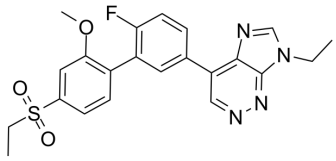
Molecular Weight: 440.49

Target: GABA Receptor

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (113.51 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2702 mL	11.3510 mL	22.7020 mL
	5 mM	0.4540 mL	2.2702 mL	4.5404 mL
	10 mM	0.2270 mL	1.1351 mL	2.2702 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: ≥ 2.5 mg/mL (5.68 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.68 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-06372865 is an orally active, α2/α3/α5 subtype-selective $GABA_A$ positive allosteric modulator (PAM). PF-06372865 is a high affinity ligand at $GABA_A$ receptors containing α1/α2/α3/α5 subunits (K_is of 2.9 nM, 21 nM, 134 nM for α2, α1 PAM, α2 PAM, respectively), with low affinity for α4/α6 subunits. PF-06372865 can across the blood-brain barrier (BBB). PF-06372865 has anxiolytic activity and has the potential for epilepsy[1].

IC_{50} & Target

Ki: 2.9 nM (α2), 21 nM (α1 PAM) and 134 nM (α2 PAM)[1]

In Vitro

PF-06372865 (compound 34) has K_i values of 0.18 nM, 2.9 nM, 1.1 nM, 18 nM for human $GABA_A$ α1β3γ2, α2β2γ2, α3β3γ2, α5β2γ2 and 0.34 nM, 4.58 nM for rat $GABA_A$ α1β3γ2, α2β2γ2[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

PF-06372865 (compound 34; 3, 10 mg/kg; orally; single dose) significantly increases the paw withdrawal threshold (PWT) in chronic constriction injury (CCI) animals[1].

PF-06372865 (0.3, 3, 10 mg/kg for mouse and 1, 3, 10 mg/kg for rat; orally) exhibits efficacy in two models of epilepsy, PTZ induced seizures (mouse), and amygdala kindling (rat)[1].

PF-06372865 (0.1, 0.32, 1, 3.2 and 10 mg/kg; orally) has anxiolytic activity at 3.2 and 10 mg/kg in elevated plus maze (male C57Bl/6 mice)[1].

PF-06372865 has a $T_{1/2}$ of 1.1 hours, a Cl_p of 22 mL/min/kg, and a V_{ss} of 2.1 L/kg for rats[1].

PF-06372865 has a $T_{1/2}$ of 0.9 hours, a Cl_p of 29 mL/min/kg, and a V_{ss} of 3.4 L/kg for dogs[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Chronic constriction injury (CCI) model (male Wistar rats)[1]
Dosage:	3, 10 mg/kg
Administration:	Orally
Result:	Significantly increased paw withdrawal latency.

REFERENCES

[1]. Owen RM, et al. Design and Identification of a Novel, Functionally Subtype Selective GABAA Positive Allosteric Modulator (PF-06372865). J Med Chem. 2019 Jun 27;62(12):5773-5796.

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