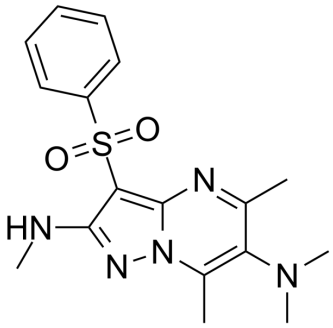
AVN-492

Cat. No.:	HY-101924
CAS No.:	1220646-23-0
Molecular Formula:	$C_{17}H_{21}N_5O_2S$
Molecular Weight:	359.45
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (139.10 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7820 mL	13.9101 mL	27.8203 mL
5 mM	0.5564 mL	2.7820 mL	5.5641 mL
10 mM	0.2782 mL	1.3910 mL	2.7820 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: ≥ 3.75 mg/mL (10.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.75 mg/mL (10.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AVN-492 is a very specific and highly-selective antagonist with picomolar affinity to 5-HT6R (K_i=91 pM).

IC_{50} & Target

5-HT_6 Receptor
91 pM (Ki)

In Vitro

The affinity of AVN-492 to bind to 5-HT6R (K_i=91 pM) is more than three orders of magnitude higher than that to bind to the only other target, 5-HT2BR, (K_i=170 nM). Thus, AVN-492 displays great 5-HT6R selectivity against all other serotonin receptor subtypes, and is extremely specific against any other receptors such as adrenergic, GABAergic, dopaminergic, histaminergic, etc[1].

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

In Vivo	In rats, the plasma, brain, and CSF concentrations of the PO administered AVN-492 are dose-dependent. The drug concentration curves for the plasma and brain are of hyperbolic shape and at all doses the brain-plasma ratio is near 11%. The drug concentration in CSF, however, is nearly linearly dependent on the dose, reaching 50% of the plasma level at 10mg/kg. In mice, the plasma and brain concentrations of AVN-492, given IV at a dose of 2 mg/kg, decreased with time but at both time points, 15 min and 60 min, the brain/plasma ratio (mean±SEM) is nearly the same, at 13.2±0.7% and 9.0±1.5%, respectively. This indicates that the steady-state concentration gradient of AVN-492 is established by at least 15 min after the drug administration[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice and Rats[1] For pharmacokinetic, behavior, and toxicity studies, male Wistar rats (220-242 g), male CD1 mice (24-30 g), male SHK mice (20-25 g), and male Balb/C mice (15-20 g) are used. The pharmacokinetic profiling of AVN-492 is performed on male CD-1 mice and male Wistar rats. Each dose-route group of rodents consist of 3 animals. AVN-492 is administered either intravenously (IV) or orally (PO). At different time points after the drug administration, the animals are quickly euthanized by placing them into CO_2 chamber. Blood samples are drawn through a cardiopuncture. In separate experiments, AVN-492 is orally administered to male Wistar rats at doses of 1 mg/kg, 3 mg/kg, and 10 mg/kg (3 independent groups, 3 animals per group). The animals are anesthetized 60 min later with 5% halothane, positioned in a stereotaxic frame, and samples of cerebrospinal fluid (CSF) are taken through 23G needle from the cisterna magna. CSF samples are checked for the absence of blood contamination. After the CSF samples are taken, the blood samples are drawn through a cardiopuncture and the brains are removed, washed immediately with ice-cold saline, and homogenized in a 1:4 brain tissue/water mixture. AVN-492 is extracted from all the samples with acetonitrile and concentrations are determined. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Ivachtchenko AV, et al. AVN-492, A Novel Highly Selective 5-HT6R Antagonist: Preclinical Evaluation. J Alzheimers Dis. 2017;58(4):1043-1063.

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

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