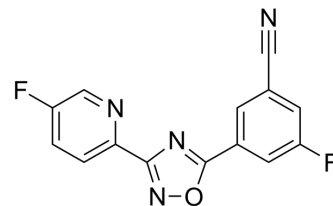


## AZD 9272

Cat. No.:	HY-110254
CAS No.:	327056-26-8
Molecular Formula:	C <sub>14</sub> H <sub>6</sub> F <sub>2</sub> N <sub>4</sub> O
Molecular Weight:	284.22
Target:	mGluR
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 2 mg/mL (7.04 mM; ultrasonic and warming and heat to 60°C)

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		3.5184 mL	17.5920 mL	35.1840 mL
	5 mM		0.7037 mL	3.5184 mL	7.0368 mL
	10 mM		---	---	---

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

### BIOLOGICAL ACTIVITY

Description	AZD 9272 is a brain penetrant mGluR5 antagonist.
IC <sub>50</sub> & Target	mGluR5
In Vitro	<p>AZD 9272 causes a concentration dependent decrease in the magnitude of the intracellular Ca<sup>2+</sup> response to 1.5 μM of the mGluR group I selective agonist DHPG in both the human and the rat mGluR5 expressing cell lines. The maximal inhibition is 100%. The mean IC<sub>50</sub> (±SD) value at the human mGluR5 is 7.6±1.1 nM (n=13) for AZD9272. The mean IC<sub>50</sub> value at the rat mGluR5 is 2.6±0.3 nM (n=3) for AZD9272. In contrast, 10 μM of AZD9272 does not diminish the response to 10 μM ATP in the background GHEK cells. Increasing concentrations of AZD9272 causes a decrease in the potency and the maximal response of DHPG. AZD9272 completely reverses the glutamate-stimulated (EC<sub>80</sub>, 80 μM) phosphatidyl inositol hydrolysis in human mGluR5-GHEK cells in a concentration-dependent manner, with IC<sub>50</sub> of 26±3 nM (n=21)<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>The clearance of AZD 9272 is low following a single intravenous dose at 3 μmol/kg and AZD 9272 is eliminated from plasma with terminal half-lives between 2 and 6 h. The terminal half-lives following oral dosing are similar to the half-lives following intravenous dosing. The volume of distribution at steady state is intermediate for AZD9272<sup>[1]</sup>. AZD9272 causes no cocaine-appropriate responding and causes a non-dose-dependent reduction in response rates at higher doses. AZD9272 at 2.84</p>

mg/kg causes greater than 80% and typically more than 99% MTEP-appropriate responding up to 20 hours after dose, with a decline to approximately 20% at 24 hours after dose, yielding a  $t_{1/2}$  of 21.93 hours, and causes no systematic effects on response rates. The first time point at which AZD9272 causes >90% MTEP-appropriate responding is at 30 minutes after dose [2].

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## PROTOCOL

### Kinase Assay <sup>[1]</sup>

Saturable binding and competition binding studies utilize incubations of 1 hour at 22°C. For saturation studies, membranes from mGluR5-GHEK cells are incubated with increasing concentrations (0.1 to 30 nM) of [<sup>3</sup>H]AZD9272, in the presence or absence of 10 μM MPEP. In a variation of these studies, saturable [<sup>3</sup>H]AZD9272 binding is determined in the presence of low concentrations (10 and 20 nM) of MPEP. Consistency of the  $B_{max}$  in the presence or absence of MPEP supports the interaction of these ligands with a unitary binding site<sup>[1]</sup>.

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### Cell Assay <sup>[1]</sup>

hmGluR5-GHEK cells are seeded onto 96 well plates at 50,000 cells/well in media containing 10 μCi/mL [<sup>3</sup>H]myo-inositol. Cells are incubated overnight (16 h), then washed three times and incubated for 1 hour at 37°C in HEPES buffered saline supplemented with 1 unit/mL glutamate pyruvate transaminase and 2 mM pyruvate. Cells are washed once in HEPES buffered saline and pre-incubated for 10 minutes in HEPES buffered saline containing 10 mM LiCl. Antagonist activity is determined by pre-incubating cells with AZD9272 for 10 minutes, then incubating for 30 minutes at 37°C in the presence of glutamate (EC<sub>80</sub>, 80 μM). AZD9272 is tested at 10 concentrations between 1 nM and 30 μM, in duplicate. The reaction is terminated by the addition of 0.1 mL perchloric acid (5%) on ice, with incubation at 4°C for at least 30 minutes<sup>[1]</sup>.

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### Animal Administration <sup>[1]</sup>

Approximately 48 male Wistar rats weighing 240 to 250 g at the beginning of the experiments are housed in pairs, or group housed up to 8 rats per cage, in a colony room with water accessible at all times and lights on between 6:00 AM and 6:00 PM; by restricting access to food, animals are kept at approximately 80% of free feeding weight. All animals are divided into different groups and trained to discriminate cocaine (3.4 mg/kg i.p., 15 minutes), PCP (1.6 mg/kg i.p., 30 minutes), MTEP (2 mg/kg i.p., 30 minutes), or AZD9272 (1.6 mg/kg p.o., 60 minutes) from no drug<sup>[1]</sup>.

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

## REFERENCES

[1]. Swedberg MD, et al. AZD9272 and AZD2066: selective and highly central nervous system penetrant mGluR5 antagonists characterized by their discriminative effects. J Pharmacol Exp Ther. 2014 Aug;350(2):212-22.

[2]. Raboisson P, et al. Discovery and characterization of AZD9272 and AZD6538-Two novel mGluR5 negative allosteric modulators selected for clinical development. Bioorg Med Chem Lett. 2012 Nov 15;22(22):6974-9.

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

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