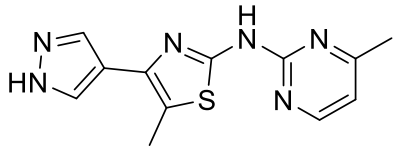
Product data sheet

MedKoo Cat#: 526673 Name: ADX88178 CAS#: 1235318-89-4 Chemical Formula: $C_{12}H_{12}N_6S$ Exact Mass: 272.0844 Molecular Weight: 272.33	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

ADX-88178 is a novel potent, selective, and brain-penetrant positive allosteric modulator of the mGlu4 receptor in rodent models of anxiety, obsessive compulsive disorder (OCD), fear, depression, and psychosis. ADX88178 dose-dependently reduced the number of buried marbles in the marble burying test and increased open-arm exploration in the elevated plus maze (EPM) test, indicative of anxiolytic-like efficacy.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	16.67	61.21

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.67 mL	18.36 mL	36.72 mL
5 mM	0.73 mL	3.67 mL	7.34 mL
10 mM	0.37 mL	1.84 mL	3.67 mL
50 mM	0.07 mL	0.37 mL	0.73 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Abulwerdi G, Stoica BA, Loane DJ, Faden AI. Putative mGluR4 positive allosteric modulators activate Gi-independent anti-inflammatory mechanisms in microglia. Neurochem Int. 2020 Sep;138:104770. doi: 10.1016/j.neuint.2020.104770. Epub 2020 May 23. PMID: 32454165; PMCID: PMC7392812.

2. Volpi C, Mondanelli G, Pallotta MT, Vacca C, Iacono A, Gargaro M, Albini E, Bianchi R, Belladonna ML, Celanire S, Mordant C, Heroux M, Royer-Urios I, Schneider M, Vitte PA, Cacquevel M, Galibert L, Poli SM, Solari A, Bicciato S, Calvitti M, Antognelli C, Puccetti P, Orabona C, Fallarino F, Grohmann U. Allosteric modulation of metabotropic glutamate receptor 4 activates IDO1-dependent, immunoregulatory signaling in dendritic cells. Neuropharmacology. 2016 Mar;102:59-71. doi: 10.1016/j.neuropharm.2015.10.036. Epub 2015 Oct 30. PMID: 26522434; PMCID: PMC4720030.

In vivo study

1. Ponnazhagan R, Harms AS, Thome AD, Jurkuvenaite A, Gogliotti R, Niswender CM, Conn PJ, Standaert DG. The Metabotropic Glutamate Receptor 4 Positive Allosteric Modulator ADX88178 Inhibits Inflammatory Responses in Primary Microglia. J Neuroimmune Pharmacol. 2016 Jun;11(2):231-7. doi: 10.1007/s11481-016-9655-z. Epub 2016 Feb 12. PMID: 26872456; PMCID: PMC4848139.

2. Kalinichev M, Le Poul E, Boléa C, Girard F, Campo B, Fonsi M, Royer-Urios I, Browne SE, Uslaner JM, Davis MJ, Raber J, Duvoisin R, Bate ST, Reynolds IJ, Poli S, Celanire S. Characterization of the novel positive allosteric modulator of the metabotropic glutamate receptor 4 ADX88178 in rodent models of neuropsychiatric disorders. J Pharmacol Exp Ther. 2014 Sep;350(3):495-505. doi: 10.1124/jpet.114.214437. Epub 2014 Jun 19. PMID: 24947466; PMCID: PMC4152882.

7. Bioactivity

Biological target:

ADX88178 is a metabotropic glutamate receptor 4 positive allosteric modulator (mGluR4 PAM) with an EC50 of 4 nM for human mGluR4.

In vitro activity

Pretreatment with ADX88178 caused a concentration-dependent reduction of nitrite levels, with 20 μM causing the most significant attenuation in NO levels (LPS vs. LPS+ADX88178 20 μM; $P < 0.0001$; Fig. 3A). There was a robust increase in TNF-α (control vs. LPS, $P < 0.0001$; Fig. 3B) and IL-1β (control vs. LPS, $P < 0.001$; Fig. 3C) protein levels after LPS stimulation, which were significantly reduced by ADX88178 (TNF-α: LPS vs. LPS+ADX88178, $P < 0.0001$; Fig. 3B, IL-1β: LPS vs. LPS+ADX88178, $P < 0.05$; Fig. 3C). The mRNA expression of pro-inflammatory cytokines (TNF-α and IL-1β), inflammatory microRNA (miR-155), as well as anti-inflammatory Arginase-1 were also evaluated. LPS stimulation significantly increased expression of TNF-α (control vs. LPS, $P < 0.001$; Fig. 3D), IL-1β (control vs. LPS, $P < 0.01$; Fig. 3E), and miR-155 (control vs. LPS, $P < 0.0001$; Fig. 3F). Similar to data obtained from BV2 microglia, ADX88178 reduced LPS-stimulated levels of the following inflammatory mediators in primary microglia: TNF-α (LPS vs. LPS+ADX88178, $P < 0.01$; Fig. 3D), IL-1β (LPS vs. LPS+ADX88178, $P < 0.05$; Fig. 3E), and miR-155 (LPS vs. LPS+ADX88178, $P < 0.001$; Fig. 3F).

Reference: Neurochem Int. 2020 Sep;138:104770. https://pubmed.ncbi.nlm.nih.gov/32454165/

In vivo activity

To determine if activation of mGlu4 on microglial cells also leads to alterations in MHCII expression, microglia from WT and mGlu4 KO mice were pretreated for 45 min with ADX88178 and then stimulated with LPS for 24 h. Based on the potency of the ADX88178 compound in the TNF assay, this experiment was performed with 1 nM, 10 nM, and 100 nM ADX88178. The cells were then fixed and stained for immunocytochemical detection. MHCII expression was determined using confocal microscopy and quantified with ImageJ software. As shown in Fig. 2A, we found that LPS led to a marked enhancement of MHCII staining in WT microglia. There was a significant decrease ($p < 0.001$, one-way ANOVA with a Tukey's post hoc test) in MHCII expression when microglia from WT mice were pretreated with ADX88178 prior to LPS stimulation. Similar pretreatment of microglia from mGlu4 KO mice showed that ADX88178 treatment did not alter MHCII expression in the KO cells (Fig. 2B), confirming the specificity of attenuation by ADX88178 through mGlu4.

Reference: J Neuroimmune Pharmacol. 2016 Jun; 11(2): 231–237. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4848139/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.