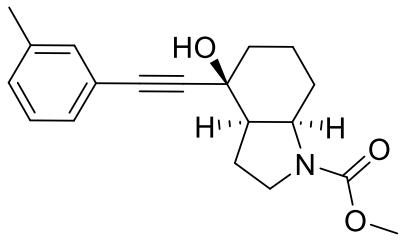
Product data sheet

MedKoo Cat#: 319677 Name: Mavoglurant CAS#: 543906-09-8 Chemical Formula: $C_{19}H_{23}NO_3$ Exact Mass: 313.1678 Molecular Weight: 313.397	
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:
Mavoglurant, aslo known as AFQ056, is an experimental drug candidate for the treatment of fragile X syndrome. Mavoglurant exerts its effect as an antagonist of the metabotropic glutamate receptor 5 (mGLU5). Novartis discontinued development of mavoglurant for fragile X syndrome in April 2014 following disappointing trial results. Currently Novartis is conducting a clinical trial with this drug on obsessive compulsive disorder.

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	120.0	382.91

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	3.19 mL	15.95 mL	31.91 mL
5 mM	0.64 mL	3.19 mL	6.38 mL
10 mM	0.32 mL	1.60 mL	3.19 mL
50 mM	0.06 mL	0.32 mL	0.64 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. Tabolacci E, Pirozzi F, Gomez-Mancilla B, Gasparini F, Neri G. The mGluR5 antagonist AFQ056 does not affect methylation and transcription of the mutant FMR1 gene in vitro. BMC Med Genet. 2012 Mar 7;13:13. doi: 10.1186/1471-2350-13-13. PMID: 22397687; PMCID: PMC3320553.
2. Vranesic I, Ofner S, Flor PJ, Bilbe G, Bouhelal R, Enz A, Desrayaud S, McAllister K, Kuhn R, Gasparini F. AFQ056/mavoglurant, a novel clinically effective mGluR5 antagonist: identification, SAR and pharmacological characterization. Bioorg Med Chem. 2014 Nov 1;22(21):5790-803. doi: 10.1016/j.bmc.2014.09.033. Epub 2014 Sep 20. PMID: 25316499.

In vivo study

1. Zerbi V, Markicevic M, Gasparini F, Schroeter A, Rudin M, Wenderoth N. Inhibiting mGluR5 activity by AFQ056/Mavoglurant rescues circuit-specific functional connectivity in Fmr1 knockout mice. Neuroimage. 2019 May 1;191:392-402. doi: 10.1016/j.neuroimage.2019.02.051. Epub 2019 Feb 23. PMID: 30807820.
2. Vranesic I, Ofner S, Flor PJ, Bilbe G, Bouhelal R, Enz A, Desrayaud S, McAllister K, Kuhn R, Gasparini F. AFQ056/mavoglurant, a novel clinically effective mGluR5 antagonist: identification, SAR and pharmacological characterization. Bioorg Med Chem. 2014 Nov 1;22(21):5790-803. doi: 10.1016/j.bmc.2014.09.033. Epub 2014 Sep 20. PMID: 25316499.

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7. Bioactivity

Biological target:

Mavoglurant (AFQ056) is a potent, selective, non-competitive and orally active mGluR5 antagonist, with an IC50 of 30 nM.

In vitro activity

To determine whether AFQ056 may have secondary effects on the methylation and transcription of FMR1, three FXS lymphoblastoid cell lines and one normal control male line were treated. A quantitative RT-PCR was performed to assess transcriptional reactivation of the FMR1 gene. No FMR1-mRNA increase was observed after treatment with AFQ056 in any of the four cell lines, with respect to the untreated controls. The partial decrease in FMR1 transcription observed in WT at 1 mM AFQ056 after 3 and 8 days of treatment (panel A) was due at least in part to cell mortality. AFQ056 treatment had no effect on methylation, leaving the promoter as methylated as in the untreated controls both WT and FXS (Figure 22). These results demonstrate that the AFQ056 effect on fully methylated FXS patients is not due to a secondary effect on DNA methylation and consequent transcriptional activation of FMR1.

Reference: BMC Med Genet. 2012; 13: 13. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3320553/

In vivo activity

In this study, the activity of the metabotropic glutamate receptor-5 (mGluR5) was inhibited using AFQ056/Mavoglurant, a drug that is assumed to normalize excitatory/inhibitory neural signaling imbalances in FXS. Resting-state-fMRI (rs-fMRI) and diffusion-weighted imaging (DWI) were employed to test whether Mavoglurant re-established brain connectivity - at least partly - within some of the affected circuits in Fmr1-/y mice that are related to social behavior deficits. In line with previous findings, it was observed that Fmr1-/y mice exhibited impaired social interaction, reduced connectivity in three main functional networks and altered network topology. At the group level, Mavoglurant did neither rescue abnormal social behavioral nor white matter abnormalities; however, for some, but not all of these circuits Mavoglurant had a genotype-specific effect of restoring functional connectivity. Analyses of network connectivity strength showed that chronic treatment with AFQ056/Mavoglurant was sufficient to restore the connectivity profile towards Fmr1+/y levels in temporal associative and somatosensory networks (Genotype × Treatment interaction, p-value = 0.009 and 0.001, respectively), but not in anterior-posterior cingulate network (p-value = 0.136).These results show that rs-fMRI connectivity is sufficiently sensitive to pick up system-level changes after the pharmacological inhibition of mGluR5 activity. Overall, the effects of Mavoglurant are confined to specific networks suggesting that behavioral benefits might be restricted to narrow functional domains.

Reference: Neuroimage. 2019 May 1;191:392-402. https://pubmed.ncbi.nlm.nih.gov/30807820/

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.