# Product data sheet

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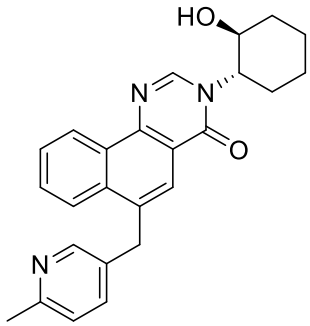
|---|---|
| MedKoo Cat#: 522634<br>Name: MK-7622<br>CAS#: 1227923-29-6<br>Chemical Formula: $C_{25}H_{25}N_3O_2$<br>Exact Mass: 399.1947<br>Molecular Weight: 399.494 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**

MK-7622 is a cholinesterase inhibitor under evaluation for the treatment of Alzheimer's disease. No studies have been published on this compound in the peer-reviewed literature or other publicly available documents. In October 2013, Merck began a Phase 2 trial in the United States to evaluate the compound's tolerability and efficacy as a symptomatic adjunct to donepezil therapy in patients with probable AD as diagnosed by two conventional diagnostic criteria, the NINCDS-ADRDA and DSM-IV.

**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 | 100.0 | 250.33 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.50 | 12.52 | 25.03 |
| 5 mM | 0.50 | 2.50 | 5.01 |
| 10 mM | 0.25 | 1.25 | 2.50 |
| 50 mM | 0.05 | 0.25 | 0.50 |

**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. Uslaner JM, Kuduk SD, Wittmann M, Lange HS, Fox SV, Min C, Pajkovic N, Harris D, Cilissen C, Mahon C, Mostoller K, Warrington S, Beshore DC. Preclinical to Human Translational Pharmacology of the Novel M1 Positive Allosteric Modulator MK-7622. J Pharmacol Exp Ther. 2018 Jun;365(3):556-566. doi: 10.1124/jpet.117.245894. Epub 2018 Mar 21. PMID: 29563325.
2. Moran SP, Dickerson JW, Cho HP, Xiang Z, Maksymetz J, Remke DH, Lv X, Doyle CA, Rajan DH, Niswender CM, Engers DW, Lindsley CW, Rook JM, Conn PJ. M1-positive allosteric modulators lacking agonist activity provide the optimal profile for enhancing cognition. Neuropsychopharmacology. 2018 Jul;43(8):1763-1771. doi: 10.1038/s41386-018-0033-9. Epub 2018 Mar 14. PMID: 29581537; PMCID: PMC6006294.

In vivo study

1.. Uslaner JM, Kuduk SD, Wittmann M, Lange HS, Fox SV, Min C, Pajkovic N, Harris D, Cilissen C, Mahon C, Mostoller K, Warrington S, Beshore DC. Preclinical to Human Translational Pharmacology of the Novel M1 Positive Allosteric Modulator MK-7622. J Pharmacol Exp Ther. 2018 Jun;365(3):556-566. doi: 10.1124/jpet.117.245894. Epub 2018 Mar 21. PMID: 29563325.
2. Moran SP, Dickerson JW, Cho HP, Xiang Z, Maksymetz J, Remke DH, Lv X, Doyle CA, Rajan DH, Niswender CM, Engers DW, Lindsley CW, Rook JM, Conn PJ. M1-positive allosteric modulators lacking agonist activity provide the optimal profile for enhancing cognition. Neuropsychopharmacology. 2018 Jul;43(8):1763-1771. doi: 10.1038/s41386-018-0033-9. Epub 2018 Mar 14. PMID: 29581537; PMCID: PMC6006294.

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**7. Bioactivity**

Biological target:

MK-7622 (M1 receptor modulator) is a muscarinic M1 receptor positive allosteric modulator.

In vitro activity

To assess the in vitro activity of the M1 PAMs used in this study, compounds were tested using CHO cells stably expressing the M1 receptor. The previously published M1 PAM PF-06764427 [10, 16] (Fig. 1a, left) and Merck's MK-7622 [27] (Fig.(Fig.1a,1a, right) were evaluated for their ability to mobilize intracellular calcium (Ca2+) in the M1-CHO cells. The raw calcium traces (Fig. 1b) indicate that both PF-06764427 and MK-7622 induce robust increases in Ca2+ mobilization in the absence of an orthosteric mAChR agonist. Interestingly, there is a similar degree of intracellular Ca2+ mobilization with MK-7622 alone (Ago EC50 2930 nM ± 95, Fig. 1d). Both PF-06764427 (PAM EC50 30 nM ± 3, Fig. 1e) and MK-7622 (PAM EC50 16 nM ± 4, Fig. 1f) act as potent and selective [10] (Supplemental Fig. 1) M1 PAMs in the presence of the orthosteric agonist ACh. Therefore, in addition to their PAM activity, both PF-06764427 and MK-7622 have significant intrinsic agonist activity in this cell-based Ca2+ mobilization assay.

Neuropsychopharmacology. 2018 Jul; 43(8): 1763–1771. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6006294/

In vivo activity

In light of the finding that both PF-06764427 and MK-7622 have robust allosteric agonist activity in both cell line and native tissue assays, it was hypothesized that MK-7622 would induce behavioral convulsions in a manner similar to those observed with PF-06764427. Therefore, a dose-escalation study in mice was performed to assess seizure liability of the M1 ago-PAM MK-7622. Consistent with the previous study with PF-06764427, 30 and 100 mg/kg MK-7622 induces robust convulsions that reached stage 5 on the modified Racine scale [16, 26, 32] in wild-type but not M1 KO mice (Fig. 5a). Interestingly, MK-7622 (1, 3, and 10 mg/kg) did not significantly improve performance in the novel object recognition task ($p = 0.9110$, one-way ANOVA) (Fig. 5c).Collectively, these findings suggest that M1 ago-PAMs, such as MK-7622 and PF-06764427, induce behavioral convulsions that are not observed with PAMs lacking agonist activity such as VU0453595.

Neuropsychopharmacology. 2018 Jul; 43(8): 1763–1771. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6006294/