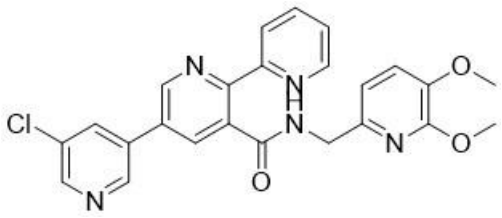
Product data sheet

MedKoo Cat#: 530433 Name: MK-1064 CAS#: 1207253-08-4 Chemical Formula: $C_{24}H_{20}ClN_5O_3$ Exact Mass: 461.1255 Molecular Weight: 461.906	
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-1064 is a potent, selective and orally active Orexin OX2 Receptor Antagonist for potential treatment of insomnia. Preclinically, MK-1064 promotes sleep and increases both rapid eye movement (REM) and non-REM (NREM) sleep in rats at OX2R occupancies higher than the range observed for dual orexin receptor antagonists. Similar to dual antagonists, MK-1064 increases NREM and REM sleep in dogs without inducing cataplexy.

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	60.00	129.90

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.16	10.82	21.65
5 mM	0.43	2.16	4.33
10 mM	0.22	1.08	2.16
50 mM	0.04	0.22	0.43

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

TBD

In vivo study

1. Amodeo LR, Wills DN, Sanchez-Alavez M, Ehlers CL. Effects of an Orexin-2 Receptor Antagonist on Sleep and Event-Related Oscillations in Female Rats Exposed to Chronic Intermittent Ethanol During Adolescence. Alcohol Clin Exp Res. 2020 Jul;44(7):1378-1388. doi: 10.1111/acer.14361. Epub 2020 Jun 12. PMID: 32424852; PMCID: PMC7720846.
2. Grafe LA, Eacret D, Luz S, Gotter AL, Renger JJ, Winrow CJ, Bhatnagar S. Orexin 2 receptor regulation of the hypothalamic-pituitary-adrenal (HPA) response to acute and repeated stress. Neuroscience. 2017 Apr 21;348:313-323. doi: 10.1016/j.neuroscience.2017.02.038. Epub 2017 Feb 28. PMID: 28257896; PMCID: PMC6322837.

7. Bioactivity

Biological target:

MK-1064 is a selective orexin 2 receptor antagonist which targets 2-SORA.

In vitro activity

TBD

Product data sheet

In vivo activity

The contribution of orexin receptor signaling in both struggle behavior and body weight change in response to restraint stress was determined through use of a selective OX2R antagonist, MK-1064. Specifically, after DREADDs' expression, rats underwent five consecutive days of 30-min restraint, with either vehicle or CNO to stimulate DREADDs prior to each restraint, and with either vehicle or MK-1064 to antagonize the orexin 2 receptor (paradigm depicted in Fig. 3A). Struggle behavior indicates the number of attempts to escape during restraint, which is an important component of the stress response and habituates with repeated restraint (Grissom et al., 2008). As demonstrated in Fig. 3B, the CNO/vehicle group spent significantly more time struggling than the other three treatment groups. Essentially, stimulating orexins with CNO increases struggle behavior, and blocking OX2R with MK-1064 reverses this effect. Coincident with changes observed in struggle behavior, body weight decreased from the first to the last day of restraint in levels of high orexin, but this was eliminated with MK-1064 pretreatment (Fig. 3C). Thus, while all rats lost weight over the 5 days of restraint stress, further stimulating orexins prior to each 30-min restraint exacerbated this effect and these results appear mediated through OX2R. Pretreatment with MK-1064, however, significantly attenuated the ACTH response in combination with either vehicle (Fig. 4B), or CNO pre-treatment (Fig. 4C), indicating that OX2R is responsible for mediating at least part of the ACTH response to acute restraint. Importantly, the ACTH response was similarly attenuated by MK-1064 in either the presence or absence of CNO (Fig. 4D), indicating that activation of orexin signaling through mechanisms not involving OX2R contributes little to the ACTH response on this first day of restraint stress. The results from this study improve the understanding of the role of orexin receptors in regulating the HPA response to both acute and repeated stress. The involvement of OX2R in acute stress has been confirmed.

Reference: Neuroscience. 2017 Apr 21; 348: 313–323. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6322837/