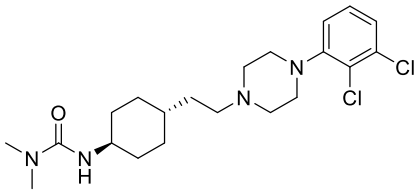
Product data sheet

MedKoo Cat#: 330051 Name: Cariprazine free base CAS#: 839712-12-8 (free base) Chemical Formula: $C_{21}H_{32}Cl_2N_4O$ Exact Mass: 426.1953 Molecular Weight: 427.414	
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:
Cariprazine, also known as RGH-188 and MP-214, is an antipsychotic drug received FDA approval on September 17, 2015. Cariprazine acts as a D2 and D3 receptor partial agonist, with high selectivity towards the D3 receptor. Action on the dopaminergic systems makes it also potentially useful as an add-on therapy in major depressive disorder. Cariprazine is approved for schizophrenia and bipolar disorder. It has also been investigated as a potential adjunct in treatment-resistant major depressive 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	6.67	14.38

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.16 mL	10.78 mL	21.56 mL
5 mM	0.43 mL	2.16 mL	4.31 mL
10 mM	0.22 mL	1.08 mL	2.16 mL
50 mM	0.04 mL	0.22 mL	0.43 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. Kiss B, Horváth A, Némethy Z, Schmidt E, Laszlovszky I, Bugovics G, Fazekas K, Hornok K, Orosz S, Gyertyán I, Agai-Csongor E, Domány G, Tihanyi K, Adham N, Szombathelyi Z. Cariprazine (RGH-188), a dopamine D(3) receptor-preferring, D(3)/D(2) dopamine receptor antagonist-partial agonist antipsychotic candidate: in vitro and neurochemical profile. J Pharmacol Exp Ther. 2010 Apr;333(1):328-40. doi: 10.1124/jpet.109.160432. Epub 2010 Jan 21. PMID: 20093397.

2. Gao Y, Peterson S, Masri B, Hougland MT, Adham N, Gyertyán I, Kiss B, Caron MG, El-Mallakh RS. Cariprazine exerts antimanic properties and interferes with dopamine D2 receptor β-arrestin interactions. Pharmacol Res Perspect. 2015 Feb;3(1):e00073. doi: 10.1002/prp2.73. Epub 2014 Dec 2. PMID: 25692006; PMCID: PMC4317219.

In vivo study

1. Gao Y, Peterson S, Masri B, Hougland MT, Adham N, Gyertyán I, Kiss B, Caron MG, El-Mallakh RS. Cariprazine exerts antimanic properties and interferes with dopamine D2 receptor β-arrestin interactions. Pharmacol Res Perspect. 2015 Feb;3(1):e00073. doi: 10.1002/prp2.73. Epub 2014 Dec 2. PMID: 25692006; PMCID: PMC4317219.

2. Zimnisky R, Chang G, Gyertyán I, Kiss B, Adham N, Schmauss C. Cariprazine, a dopamine D(3)-receptor-preferring partial agonist, blocks phencyclidine-induced impairments of working memory, attention set-shifting, and recognition memory in the mouse. Psychopharmacology (Berl). 2013 Mar;226(1):91-100. doi: 10.1007/s00213-012-2896-5. Epub 2012 Oct 19. PMID: 23079899; PMCID: PMC3572273.

7. Bioactivity

Biological target:

Cariprazine is a novel antipsychotic drug candidate that exhibits high affinity for the D3 (Ki=0.085 nM) and D2 (Ki=0.49 nM) receptors, and moderate affinity for the 5-HT1A receptor (Ki=2.6 nM).

In vitro activity

Cariprazine had lower affinity at human and rat hippocampal 5-HT(1A) receptors (pK(i) 8.59 and 8.34, respectively) and demonstrated low intrinsic efficacy. Cariprazine displayed low affinity at human 5-HT(2A) receptors (pK(i) 7.73). Moderate or low affinity for histamine H(1) and 5-HT(2C) receptors (pK(i) 7.63 and 6.87, respectively) suggest cariprazine's reduced propensity for adverse events related to these receptors. Cariprazine demonstrated different functional profiles at dopamine receptors depending on the assay system. It displayed D(2) and D(3) antagonism in [(35)S]GTPgammaS binding assays, but stimulated inositol phosphate (IP) production (pEC(50) 8.50, E(max) 30%) and antagonized (+/-)-quinpirole-induced IP accumulation (pK(b) 9.22) in murine cells expressing human D(2L) receptors. It had partial agonist activity (pEC(50) 8.58, E(max) 71%) by inhibiting cAMP accumulation in Chinese hamster ovary cells expressing human D(3) receptors and potently antagonized R(+)-2-dipropylamino-7-hydroxy-1,2,3,4-tetrahydronaphtalene HBr (7-OH-DPAT)-induced suppression of cAMP formation (pK(b) 9.57). In these functional assays, cariprazine showed similar (D(2)) or higher (D(3)) antagonist-partial agonist affinity and greater (3- to 10-fold) D(3) versus D(2) selectivity compared with aripiprazole.

Reference: J Pharmacol Exp Ther. 2010 Apr;333(1):328-40.
https://jpet.aspetjournals.org/cgi/pmidlookup?view=long&pmid=20093397

In vivo activity

Cariprazine was tested in vivo for antimanic-like activity, using the ouabain-induced hyperactivity model in rats. Cariprazine was more potent than aripiprazole in inhibiting isoproterenol-induced cAMP although both compounds showed similar maximum efficacy. In assays of D2R/β-arrestin 2-dependent interactions, cariprazine showed very weak partial agonist activity, unless the levels of receptor kinase were increased; as an antagonist it showed similar potency to haloperidol and ~fivefold greater potency than aripiprazole. In an animal model of mania, cariprazine showed similar efficacy as lithium in attenuating the effects of ouabain-induced hyperactivity. In summary, the differential effects of cariprazine on D2R G protein and β-arrestin 2 mediators of signal transduction pathways could contribute to its potent antimanic-like activity.

Reference: Pharmacol Res Perspect. 2015 Feb;3(1):e00073. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/25692006/

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.