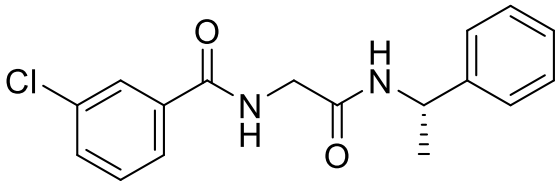
Product data sheet

MedKoo Cat#: 523108 Name: JNJ 63533054 CAS#: 1802326-66-4 Chemical Formula: $C_{17}H_{17}ClN_2O_2$ Exact Mass: 316.09786 Molecular Weight: 316.79	
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:
JNJ 63533054 is a potent and selective GPR139 agonist (EC50 = 16 nM) that is brain and cell penetrant. JNJ 63533054 is selective for GPR139 over a panel of GPCRs, ion channels and transporters, including GPR142 and is orally bioavailable.

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	30.0	94.7

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.16 mL	15.78 mL	31.57 mL
5 mM	0.63 mL	3.16 mL	6.31 mL
10 mM	0.32 mL	1.58 mL	3.16 mL
50 mM	0.06 mL	0.32 mL	0.63 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. Nepomuceno D, Kuei C, Dvorak C, Lovenberg T, Liu C, Bonaventure P. Re-evaluation of Adrenocorticotropic Hormone and Melanocyte Stimulating Hormone Activation of GPR139 in Vitro. Front Pharmacol. 2018 Mar 2;9:157. doi: 10.3389/fphar.2018.00157. PMID: 29599718; PMCID: PMC5863515.

In vivo study

1. Shoblock JR, Welty N, Fraser I, Wyatt R, Lord B, Lovenberg T, Liu C, Bonaventure P. In vivo Characterization of a Selective, Orally Available, and Brain Penetrant Small Molecule GPR139 Agonist. Front Pharmacol. 2019 Mar 21;10:273. doi: 10.3389/fphar.2019.00273. PMID: 30949055; PMCID: PMC6437111.

7. Bioactivity
Biological target:

JNJ 63533054 is a potent and selective GPR139 agonist that specifically activated human GPR139 in the calcium mobilization (EC50 = 16 ± 6 nM) and GTPγS binding (EC50 = 17 ± 4 nM) assays.

In vitro activity

JNJ-63533054 specifically activated human GPR139 in the calcium mobilization (EC50 = 16 ± 6 nM) and GTPγS binding (EC50 = 17 ± 4 nM) assays. JNJ-63533054 also activated the rat and mouse GPR139 receptor with similar potency (rat EC50 = 63 ± 24 nM,

mouse EC50 = 28 ± 7 nM). Addition of a low concentration of NaCl and divalent ions did not shift the affinity of the tracer for GPR139 (data not shown). On membranes from T-Rex CHO cells expressing human GPR139, a high signal-to-noise ratio was observed (total versus nonspecific binding $P < 0.0001$), and no specific binding was detected in membranes from noninduced human GPR139 cells or control membranes from untransfected cells (Fig. 5B). In a saturation study for human GPR139, a single population of high-affinity binding sites for [3H] JNJ-63533054 was observed, and the Kd (10 ± 3 nM) was in agreement with the corresponding EC50 (Fig. 5C). The Bmax value was 26 ± 4 pmol/mg of protein. Saturation studies for the rat GPR139 and mouse GPR139 yielded Kd values within the same range (32 ± 13 nM and 23 ± 4 nM, respectively; Bmax = 8.5 ± 2.5pmol/mg of protein and 6.2 ± 1.6pmol/mg of protein, respectively).

Reference: Mol Pharmacol. 2015 Nov;88(5):911-25. http://molpharm.aspetjournals.org/cgi/pmidlookup?view=long&pmid=26349500

In vivo activity

The aim of this study was to characterize a selective and brain penetrant GPR139 agonist (JNJ-63533054) in relevant in vivo models. JNJ-63533054 was tested for its effect on c-fos activation in the habenula and dorsal striatum. In vivo microdialysis experiments were performed in freely moving rats to measure basal levels of serotonin or dopamine (DA) in prefrontal cortex (mPFC) and nucleus accumbens (NAc). Finally, the compound was profiled in behavioral models of anxiety, despair, and anhedonia. The agonist (10-30 mg/kg, p.o.) did not alter c-fos expression in medial habenula or dorsal striatum nor neurotransmitter levels in mPFC or NAc. JNJ-63533054 (10 mg/kg p.o.) produced an anhedonic-like effect on urine sniffing, but had no significant effect in tail suspension, with no interaction with imipramine, no effect on naloxone place aversion, and no effect on learned helplessness. In the marble burying test, the agonist (10 mg/kg p.o.) produced a small anxiolytic-like effect, with no interaction with fluoxetine, and no effect in elevated plus maze (EPM). Despite GPR139 high expression in medial habenula, an area with connections to limbic and catecholaminergic/serotoninergic areas, the GPR139 agonist had no effect on c-fos in medial habenula. It did not alter catecholamine/serotonin levels and had a mostly silent signal in in vivo models commonly associated with these pathways.

Reference: Front Pharmacol. 2019 Mar 21;10:273. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30949055/

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.