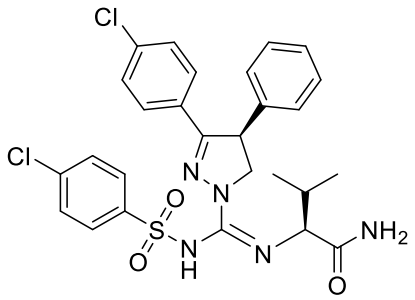
Product data sheet

MedKoo Cat#: 530481 Name: JD5037 CAS#: 1392116-14-1 Chemical Formula: $C_{27}H_{27}Cl_2N_5O_3S$ Exact Mass: 571.1212 Molecular Weight: 572.505	
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:
JD5037 is a peripherally restricted (PR) cannabinoid-1 receptor blocker (CB1R antagonist). JD5037 is an antiobesity drug candidate which acts as a peripherally-restricted cannabinoid inverse agonist at CB1 receptors. It is very selective for the CB1 subtype, with a Ki of 0.35nM, >700-fold higher affinity than it has for CB2 receptors. In animal studies, JD5037 does not readily cross the blood brain barrier and thus is not expected to produce the psychiatric side effects in humans which led to the withdrawal of rimonabant from the market. Its antiobesity effects are believed to be mediated by blockade of peripheral CB1 receptors, resulting in decreased leptin expression and secretion and increased leptin clearance by the kidneys.

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	174.67
Ethanol	2	3.49

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.75 mL	8.73 mL	17.47 mL
5 mM	0.35 mL	1.75 mL	3.49 mL
10 mM	0.17 mL	0.87 mL	1.75 mL
50 mM	0.03 mL	0.17 mL	0.35 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. Tan S, Liu H, Ke B, Jiang J, Wu B. The peripheral CB1 receptor antagonist JD5037 attenuates liver fibrosis via a CB1 receptor/β-arrestin1/Akt pathway. Br J Pharmacol. 2020 Jun;177(12):2830-2847. doi: 10.1111/bph.15010. Epub 2020 Mar 3. PMID: 32017042; PMCID: PMC7236068.

In vivo study

1. Kale VP, Gibbs S, Taylor JA, Zmarowski A, Novak J, Patton K, Sparrow B, Gorospe J, Anand S, Cinar R, Kunos G, Chorvat RJ, Terse PS. Preclinical toxicity evaluation of JD5037, a peripherally restricted CB1 receptor inverse agonist, in rats and dogs for treatment of nonalcoholic steatohepatitis. Regul Toxicol Pharmacol. 2019 Dec;109:104483. doi: 10.1016/j.yrtph.2019.104483. Epub 2019 Sep 30. PMID: 31580887; PMCID: PMC7017916.

7. Bioactivity
Biological target:

Product data sheet

JD-5037 is a potent CB1R antagonist with an IC50 of 1.5 nM.

In vitro activity

Liver samples from both humans and mouse models were investigated. The peripheral CB1 receptor antagonist JD5037, β-arr1 wild type (β-arr1-WT) and β-arr1 knockout (β-arr1-KO) littermate models, and primary hepatic stellate cells (HSCs) were also used. The mechanisms underlying CB1 receptor-regulated HSCs activation in fibrosis and the therapeutic potential of JD5037 were further analysed. CB1 receptors were induced in samples from patients with liver fibrosis and from mouse models. These receptors promoted activation of HSCs in liver fibrosis via recruiting β-arrestin1 and Akt signalling, while blockage of CB1 receptors with JD5037 attenuated CB1 receptor-regulated HSCs activation and liver fibrosis by suppressing β-arrestin1/Akt signalling.

Reference: Br J Pharmacol. 2020 Jun;177(12):2830-2847. https://doi.org/10.1111/bph.15010

In vivo activity

JD5037 was administered by oral gavage at 10, 40, and 150 mg/kg/day dose levels for up to 34 days to Sprague Dawley rats, and at 5, 20, and 75 mg/kg/day dose levels for 28 consecutive days to Beagle dogs. In rats, higher incidences of stereotypic behaviors were observed in 10 mg/kg females and 40 mg/kg males, and slower responses for reflex and sensory tests were observed only in males at 10 and 40 mg/kg during neurobehavioral testing. Sporadic minimal incidences of decreased activity (males) and seizures (both sexes) were observed in rats during daily clinical observations, without any clear dose-relationship. Male dogs at 75 mg/kg during treatment period, but not recovery period, had an increased incidence of gut associated lymphoid tissue hyperplasia and inflammation in the intestine. In both species, highest dose resulted in lower AUCs indicative of non-linear kinetics. Free access to food increased the plasma AUC_{∞} by ~4.5-fold at 20 mg/kg in dogs, suggesting presence of food may help in systemic absorption of JD5037 in dogs. Based on the study results, 150 mg/kg/day in rats, and 20 and 75 mg/kg/day doses in male and female dogs, respectively, were determined to be the no-observed-adverse-effect-levels (NOAELs).

Reference: Regul Toxicol Pharmacol. 2019 Dec;109:104483. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/31580887/