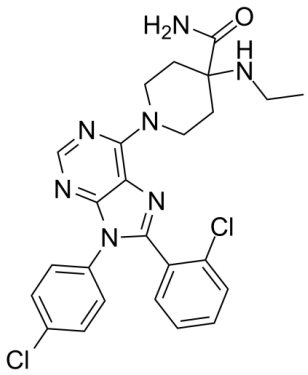
Data Sheet

Product Name:	Otenabant
Cat. No.:	CS-1279
CAS No.:	686344-29-6
Molecular Formula:	C25H25Cl2N7O
Molecular Weight:	510.42
Target:	Cannabinoid Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : 100 mg/mL (195.92 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Otenabant is a potent and selective **cannabinoid receptor CB1** antagonist with **K_i** of 0.7 nM, exhibits 10,000-fold greater selectivity against human CB2 receptor. IC50 & Target: Ki: 0.7 nM (CB1) **In Vitro:** Otenabant HCl has low affinity with K_i of 7.6 μM for human CB2 receptors[1]. Otenabant HCl inhibits CB1 receptor with moderate unbound microsomal clearance, low hERG affinity, and adequate CNS penetration[2]. **In Vivo:** Otenabant acutely stimulates energy expenditure in rats and decreases the respiratory quotient indicating a metabolic switch to increased fat oxidation. Otenabant (10 mg/kg, p.o.) promotes a 9%, vehicle adjusted weight loss in a 10 day weight loss study in diet-induced obese mice[1]. Otenabant HCl reverses four cannabinoid agonistmediated behaviors (locomotor activity, hypothermia, analgesia, and catalepsy) following administration of the synthetic CB1 receptor agonist CP-55940. Otenabant HCl exhibits dose-dependent anorectic activity in a model of acute food intake in rodents and increased energy expenditure and fat oxidation[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [2]Membranes are prepared from CHOK1 cells stably transfected with the human CB-1 receptor cDNA. GTPγ [^{35}S] binding assays are performed in a 96-well FlashPlate format in duplicate using 100 pM GTPγ [^{35}S] and 10μg membrane per well in assay buffer composed of 50 mM Tris HCl, pH 7.4, 3 mM $MgCl_2$, pH 7.4, 10 mM $MgCl_2$, 20 mM EGTA, 100 mM NaCl, 30 μM GDP, 0.1% bovine serum albumin, and the following protease inhibitors: 100 μg/mL bacitracin, 100 μg/mL benzamidine, 5 μg/mL aprotinin, 5 μg/mL leupeptin. The assay mix is then incubated with increasing concentrations of antagonist (10^{-10} M to 10^{-5} M) for 10 min and challenged with the cannabinoid agonist CP-55,940 (10 μM). Assays are performed at 30°C for 1 h. The FlashPlates are then centrifuged at 2000 g for 10 min. Stimulation of GTPγ [^{35}S] binding is then quantified using a Wallac Microbeta. EC_{50} calculations are done using Prism by GraphPad. Inverse agonism is measured in the absence of agonist. **Animal Administration:** Otenabant is suspended in 0.5% methyl cellulose.[1]Male, 14 week old C57/Bl6/6J mice which has been maintained on a high fat diet (45% kcal from fat) for 6 weeks are selected for the DIO weight loss study. The animals body weights range at least five standard deviations from age-matched chow-fed control animals mean body weight. Mice are singly housed. The mean starting weight of all animals is 38.9±0.5 g. On day 0, mice are randomLy assigned to treatment groups (n=10 per group). Mice are dosed daily with vehicle or 10 mg/kg (p.o.) CP-945,598 over 10 days, starting approximately at 30 min before the start of the 12 h dark cycle. BW and food intake are recorded daily. Analysis of variance and comparison of means are calculated for daily and cumulative FI and cumulative BW measurements. $P < 0.05$ is considered statistically significant.

References:

[1]. John R. Hadcock, et al. In vitro and in vivo pharmacology of CP-945,598, a potent and selective cannabinoid CB1 receptor antagonist for the

management of obesity. Biochemical and Biophysical Research Communications, 2010; 394;366-371.

[2]. Griffith DA, et al. Discovery of 1-[9-(4-chlorophenyl) -8-(2-chlorophenyl)- 9H-purin-6-yl] -4-ethylaminopiperidine-4-carboxylic acid amide hydrochloride (CP-945,598), a novel, potent, and selective cannabinoid type 1 receptor antagonist. JMedChem. 2009 ;5

CAIndexNames:

4-Piperidinecarboxamide, 1-[8-(2-chlorophenyl)-9-(4-chlorophenyl)-9H-purin-6-yl]-4-(ethylamino)-

SMILES:

ClC1=CC=CC=C1C2=NC3=C(N4CCC(NCC)(C(N)=O)CC4)N=CN=C3N2C5=CC=C(Cl)C=C5

Caution: Product has not been fully validated for medical applications. For research use only.

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