

Product Data Sheet

Product Name: Otenabant

Cat. No.: GC10843

Chemical Properties

Cas. No. 686344-29-6

Chemical Name 1-[8-(2-chlorophenyl)-9-(4-chlorophenyl)purin-6-yl]-4-(ethylamino)piperidine-4-carboxamide

SMILES CCNC1(CCN(CC1)C2=NC=NC3=C2N=C(N3C4=CC=C(C=C4)Cl)C5=CC=CC=C5Cl)C(=O)N

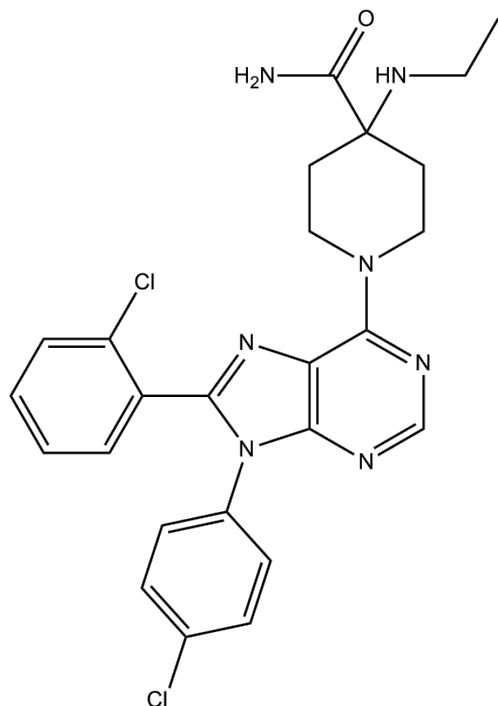
Formula $C_{25}H_{25}Cl_2N_7O$ M.Wt 510.42

Solubility DMSO : 100 mg/mL (195.92 mM; Need ultrasonic) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



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

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Protocol

Kinase experiment:

Membranes are prepared from CHOK1 cells stably transfected with the human CB-1 receptor cDNA. GTP γ [35S] binding assays are performed in a 96-well FlashPlate format in duplicate using 100 pM GTP γ [35S] and 10 μ g membrane per well in assay buffer composed of 50 mM Tris HCl, pH 7.4, 3 mM MgCl₂, pH 7.4, 10 mM MgCl₂, 20 mM EGTA, 100 mM NaCl, 30 μ M GDP, 0.1% bovine serum albumin, and the following protease inhibitors: 100 μ g/mL bacitracin, 100 μ g/mL benzamidine, 5 μ g/mL aprotinin, 5 μ g/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 μ M). Assays are performed at 30°C for 1 h. The FlashPlates are then centrifuged at 2000 g for 10 min. Stimulation of GTP γ [35S] binding is then quantified using a Wallac Microbeta. EC₅₀ calculations are done using Prism by GraphPad. Inverse agonism is measured in the absence of agonist.

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**Animal
experiment:**

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

Background

IC 50 value: 0.7nM(Ki for binding)/0.2 nM (Ki for function) Otenabant (CP-945,598) is a recently discovered selective, high affinity, competitive CB1 receptor antagonist that inhibits both basal and cannabinoid agonist-mediated CB1 receptor signaling. Cannabinoid CB1 receptor antagonists exhibit pharmacologic properties favorable for the treatment of metabolic disease. in vitro, ex vivo, and in vivo data indicate that Otenabant (CP-945,598) is a novel CB(1) receptor competitive antagonist that may further our understanding of the endocannabinoid system[1]. in vitro : Otenabant (CP-945,598) exhibits sub-nanomolar potency at human CB1 receptors in both binding ($K_i = 0.7$ nM) and functional assays ($K_i = 0.2$ nM). The compound has low affinity ($K_i = 7600$ nM) for human CB2 receptors[1]. in vivo: Otenabant (CP-945,598) reverses four cannabinoid agonist-mediated CNS-driven responses (hypo-locomotion, hypothermia, analgesia, and catalepsy) to a synthetic cannabinoid receptor

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agonist. Otenabant (CP-945,598) exhibits dose and concentration-dependent anorectic activity in two models of acute food intake in rodents, fast-induced re-feeding and spontaneous, nocturnal feeding. Otenabant (CP-945,598) also acutely stimulates energy expenditure in rats and decreases the respiratory quotient indicating a metabolic switch to increased fat oxidation. CP-945,598 at 10 mg/kg promoted a 9%, vehicle adjusted weight loss in a 10 day weight loss study in diet-induced obese mice[1]. After oral administration of a single dose of [(14)C]CP-945,598. Total mean recoveries of the radioactive dose were 97.7, 97.8, and 99.3% from mice, rats, and dogs respectively[2]. Clinical trial: A phase 1 study of the roles of endocannabinoids in insulin secretion and action is recruiting.

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