

Pfizer Inc.	CP-945598 (otenabant)
Mechanism of Action	Cannabinoid receptor 1 (CB1) antagonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=56 http://www.ncbi.nlm.nih.gov/gene/1268
Overview	CP-945598 is a high affinity (K _i = 0.75 nM), selective (~10,000 x over CB-2), competitive antagonist of the human and rat CB-1 receptor. It inhibits both basal and cannabinoid agonist-mediated CB-1 receptor signaling. CP-945598 reduces acute food intake in rodents, decreases food intake and body weight in obese Beagle dogs, and acutely stimulates energy expenditure in rats.
Safety/Tolerability	<p>The overall clinical experience with CP-945598 has been positive through Phase 2 into Phase 3. The primary side effects are nausea, vomiting, diarrhea, loose stools, dizziness, headache, hiccups, abdominal pain, fatigue, insomnia, somnolence, pruritus and decreased appetite.</p> <p>Suicidal thoughts and behavior (suicidality) have been reported for another CB-1 antagonist (rimonabant). Psychiatric adverse events, including depression, depressed mood, anxiety and suicidal ideation have been reported with CP-945598.</p> <p>Most of the observed side effects were mild to moderate in severity and resolved quickly.</p> <p>CP-945598 is neither embryo-lethal nor teratogenic in rats and rabbits at maternally toxic doses.</p>
Additional Information	CP-945598 significantly reduced food intake and body weight in overweight to obese subjects with hypertension or dyslipidemia over 6 weeks to 6 months administration.
Suitable for and Exclusions	Benefit/risk is most plausible in acute, sub-acute and/or high morbidity indications given the potential for psychiatric adverse effects.
Clinical Trials	http://www.clinicaltrials.gov/search?term=%22CP-945,598%22
Publications	http://www.ncbi.nlm.nih.gov/pubmed?term=CP-945%2C598 http://dmd.aspetjournals.org/content/39/12/2191.full.pdf+html http://pubs.acs.org/doi/pdfplus/10.1021/jm8012932