

AbbVie	ABT-288
Mechanism of Action	Histamine receptor 3 (H3) antagonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?familyId=33&objectId=264 http://www.ncbi.nlm.nih.gov/gene/11255
Overview	ABT-288 is a potent and selective antagonist of human H3 receptors (Ki = 1.9 nM). After systemic injections in rats ABT-288 enhances the in vivo release of several neurotransmitters (histamine, ACh, DA) in the cortex and exhibits pro-cognitive effects in several animal models. ABT-288 induces pro-wake actions in rats (mechanistic based). ABT-288 exhibits drug-like properties with excellent oral bioavailability. ABT-288 demonstrated activity in a number of preclinical models of cognition and was studied for cognitive impairment associated with Alzheimer’s disease and schizophrenia. ABT-288 also induces analgesia in rat models of osteoarthritis and neuropathic pain.
Safety/Tolerability	ABT-288 exhibits a wide cardiovascular and CNS safety margins in preclinical models. In healthy volunteers and healthy elderly, ABT-288 was safe and well tolerated up to doses of 3 mg QD. Dose-limiting effects at greater doses included insomnia, night sweats, nausea, and anxiety. In stable subjects with schizophrenia, daily doses of up to 45 mg/day were safe and well tolerated. Doses of 1 and 3 mg daily for 12 weeks, and 10 and 25 mg daily were safety administered to subjects with Alzheimer’s disease and schizophrenia, respectively. No significant effects on QTc or liver function tests have been noted.
Additional Information	The pharmacokinetic profile in humans supports once daily dosing, with an elimination half-life of approximately 45 hours and low-moderate variability in exposures (CV~30-40%).
Suitable for and Exclusions	Women of child bearing potential should use a double-barrier or chemical contraception as effects on the fetus have not been studied. Subjects taking ABT-288 should avoid the use of antihistamines such as diphenhydramine. No disease indication exclusions.
Clinical Trials	http://clinicaltrials.gov/ct2/results?term=ABT-288
Publications	http://www.ncbi.nlm.nih.gov/pubmed?term=A-960656