

Pfizer Inc.	CP-601927
<b>Mechanism of Action</b>	Nicotinic acetylcholine receptor $\alpha 4\beta 2$ ( $\alpha 4\beta 2$ nAChR) partial agonist <a href="http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=465&amp;familyId=76">http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=465&amp;familyId=76</a> <a href="http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=472&amp;familyId=76">http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=472&amp;familyId=76</a> <a href="http://www.ncbi.nlm.nih.gov/gene/1137">http://www.ncbi.nlm.nih.gov/gene/1137</a> ; <a href="http://www.ncbi.nlm.nih.gov/gene/1141">http://www.ncbi.nlm.nih.gov/gene/1141</a>
<b>Overview</b>	CP-601927 is a CNS-penetrant, high affinity, selective (> 39-fold affinity relative to other nAChRs and no biologically-significant secondary pharmacodynamic interactions, as assessed in a broad <i>in vitro</i> binding screen), partial agonist at the $\alpha 4\beta 2$ nAChR.
<b>Safety/Tolerability</b>	CP-601927 was generally safe and well tolerated in doses up to 2 mg BID in nonsmokers. Based on the pharmacologic properties of CP-601927, the toxicologic findings, and previous human experience, the primary potential risks to humans are nausea, vomiting, dizziness, insomnia, somnolence, abdominal pain, headache, vertigo, irritability, dyspepsia, and liver enzyme elevation.  Nonclinical toxicology data support clinical studies up to 6 weeks in duration.
<b>Additional Information</b>	In a SPECT study in recreational smokers, CP-601927 displaces [ <sup>123</sup> I]5-I-A-85380, a ligand of brain $\alpha 4\beta 2$ nAChRs following a 1 or 3 mg dose of CP-601927. The displacing effect of CP-601927 appears to be comparable to that of nicotine dosed as a 7 mg/day patch.  CP-601,927 did not demonstrate efficacy in a 4 week study in attention deficit hyperactivity disorder (ADHD) or in a smoking cessation study.
<b>Suitable for and Exclusions</b>	Clinical trials of up to 6 weeks duration with careful monitoring of hepatic function and for evidence of suicidality.
<b>Clinical Trials</b>	<a href="http://www.clinicaltrials.gov/search?term=%22CP-601,927%22">http://www.clinicaltrials.gov/search?term=%22CP-601,927%22</a>
<b>Publications</b>	<a href="http://onlinelibrary.wiley.com/doi/10.1002/bdrb.20298/full">http://onlinelibrary.wiley.com/doi/10.1002/bdrb.20298/full</a> <a href="http://dx.doi.org/10.1016/S0016-5085(09)62444-6">http://dx.doi.org/10.1016/S0016-5085(09)62444-6</a> <a href="http://www.ncbi.nlm.nih.gov/pubmed?term=CP-601%2C927">http://www.ncbi.nlm.nih.gov/pubmed?term=CP-601%2C927</a>