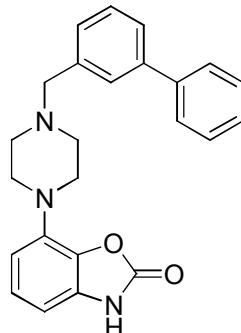


Partial dopamine D₂ agonist; 5-HT_{1A} agonist

7-[4-([1,1'-Biphenyl]-3-ylmethyl)-1-piperazinyl]-2(3H)-benzoxazolone (Bifeprunox)



Chemical Formula: C₂₄H₂₃N₃O₂

Molecular Weight: 385.46

OTAVA Catalogue Number: **7070707030**

CAS Registry Number: 350992-10-8

Purity: 97%+

Ref. 1: Feenstra et al. **New 1-aryl-4-(biaryl)methylene)piperazines as potential atypical antipsychotics sharing dopamine D₂-receptor and serotonin 5-HT_{1A}-receptor affinities.** *Bioorganic & Medicinal Chemistry Letters* (2001), 11, 2345-2349
1-Aryl-4-(biaryl)methylene)piperazines were prepared and their affinity for D₂ and 5-HT_{1A} receptors was determined. A selection of these compounds was evaluated in vivo, resulting in the identification of a drug candidate **Bifeprunox** which is being clinically evaluated as a potential atypical antipsychotic with reduced extrapyrimidal side effects.

Ref. 2: Watanabe, Mark D. **Bifeprunox. A partial dopamine-receptor agonist for the treatment of schizophrenia.** *Formulary* (2007), 42, 371-377
A review. Schizophrenia is a chronic psychiatric disorder that affects an estimated 1% of the population. This disorder may be treated with typical (first-generation) or atypical (second-generation) agents; a recognized concern regarding these agents is that long-term use has been associated with increased risks of serious side effects, either neurologic or metabolic in nature. **Bifeprunox** is a partial dopamine-receptor agonist under investigation for the treatment of patients with schizophrenia. As a partial dopamine-receptor agonist, **bifeprunox** acts as a dopamine-system stabilizer. This proposed mechanism of action is similar to that of aripiprazole but different from that of the other currently marketed antipsychotic medications. Available clinical and safety data are limited but describe positive effects in treating acute psychotic symptoms and prolonging time to deterioration, with a generally tolerable side-effect profile. If approved, **bifeprunox** may serve as an additional option for the acute and maintenance treatment of schizophrenia.

Ref. 3: Newman-Tancredi et al. **Neuropharmacological profile of bifeprunox: merits and limitations in comparison with other third-generation antipsychotics.** *Current Opinion in Investigational Drugs (Thomson Scientific)* (2007), 8, 539-554
A review. Schizophrenia is characterized by a range of positive and negative symptoms, and cognitive deficits. While positive symptoms respond to current antipsychotic agents, negative symptoms and cognitive deficits are often resistant to pharmacopeia. Thus research is now focused on developing third-generation antipsychotics that combine antagonism or partial agonism at dopamine D(2)-like receptors with agonism at serotonin 5-HT(1A) receptors. Such an association is anticipated to provide therapeutic benefits against a broader range of schizophrenia symptoms. **Bifeprunox** is one such third-generation antipsychotic agent which acts as a partial agonist at D(2)-like receptors and is an efficacious agonist at 5-HT(1A) receptors, with little interaction at 5HT(2A/2C), muscarinic or histaminergic H(1) receptors. This review summarizes the pharmacological profiles of the current antipsychotic agents and describes the rationale behind the development of third-generation antipsychotics. It also evaluates current data concerning **bifeprunox** in comparison with currently available antipsychotics, as well as those that are still under clinical development.