

Metabolites of the Pyrimidine Amine Preladenant as Adenosine A_{2a} Receptor Antagonists

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Title: Metabolites of the Pyrimidine Amine Preladenant as Adenosine A_{2a} Receptor Antagonists

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Inventors:

Ting, P.; Ma, S.; Blumenkrantz, N.; Chowdbury, S.; Neustadt, B. R.

Assignee Company:

Merck Sharp & Dohme Corp., USA

Disease Area:

Central Nervous System Disorders

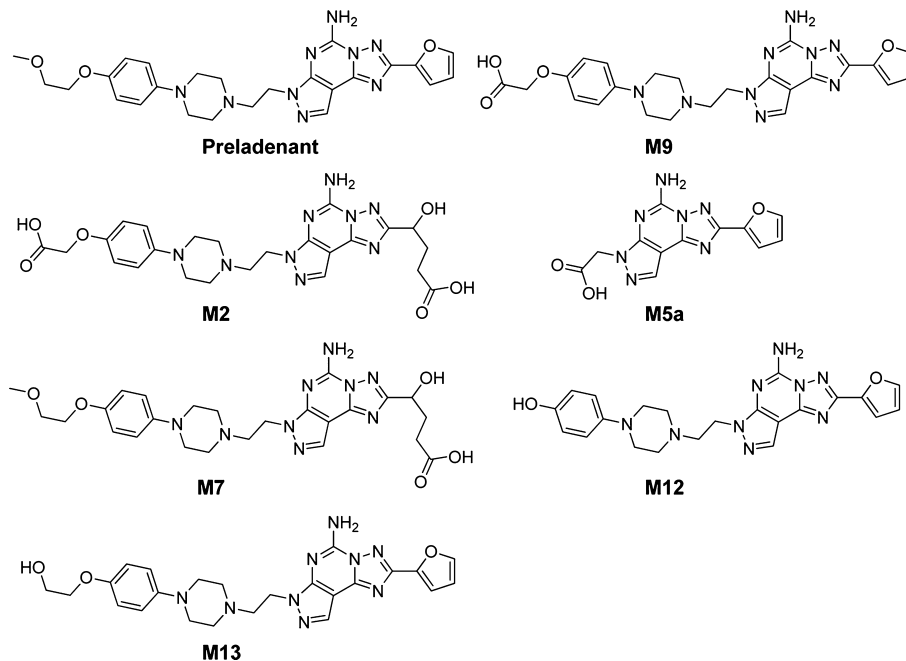
Biological Target:

Adenosine A_{2a} Receptor

Summary:

The application claims a single compound, **M9**, an adenosine A_{2a} receptor antagonist, which is a metabolite of 2-(furan-2-yl)-7-(2-(4-(4-(2-methoxyethoxy)phenyl)piperazin-1-yl)ethyl)-7H-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine-5-amine (Preladenant). Preladenant is currently in phase III clinical trials for the treatment of Parkinson's disease. In addition, the invention describes a method of determining if a subject has been administered Preladenant and of identifying its metabolites after administration to rat, dog, and human.

Key Structures:



Recent Review Articles:

Xu, F.; Wu, H.; Katritch, V.; Han, G. W.; Jacobson, K. A.; Gao, Z. G.; Cherezov, V.; Stevens, R. C. Structure of an Agonist-Bound Human A_{2a} Adenosine Receptor. *Science*, **2011**, *15 April*, 322–327.

Biological Assays (Description):

Human adenosine A_{2a} receptor competition binding assay.

Pharmacological Data:

Adenosine A_{2a} receptor binding assay

Compound	Human A _{2a} receptor K _i (nM)
M2	>1000
M5a	>1000
M7	>1000
M9	1.4
M12	1.3
M13	0.6

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- Synthesis:** Synthesis of Preladenant metabolites and [¹⁴C] labeled Preladenant are described.
- Claims:** Claims 2–4, 9–11: Use of compound of the invention in combination with another compound useful in treating Parkinson's disease or selected from L-DOPA, dopaminergic agonists, MAO-B inhibitors, COMT inhibitors, typical/atypical antipsychotic agent.
- Claims 5–8: Use of the compound or the combination for the treatment of a variety of central nervous system diseases, stroke, depression, cognitive disease, Parkinson's disease, Extra-Pyramidal Syndrome (EPS).
- Claim 14: Method of determining if a subject has been administered Preladenant.

■ AUTHOR INFORMATION

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Notes

The author declares no competing financial interest.