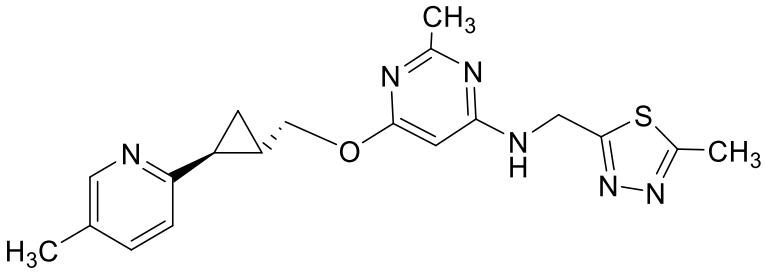
CLAIMS

What is claimed is:

1. A controlled-release tablet formulation comprising a:

1) first layer having about 1%-25% by weight of pharmaceutically acceptable Compound A, represented by structural formula I:



I

or a pharmaceutically acceptable salt, ester derivative, geometric isomer, stereoisomer, or optical isomer thereof and about 60-90% by weight low viscosity polyethylene oxide (PEO) polymer;

2) second layer comprising about 50%-70% by weight high viscosity polyethylene oxide polymer, about 10%-40% by weight metal halide and about 5%-30% by weight tableting agent; and

3) semipermeable coating wherein the coating comprises about 1%-15% by weight of the tablet, said tablet having an orifice in the first layer, wherein said formulation induces no dystonia after administration.

2. The formulation according to claim 1 wherein the low viscosity polyethylene oxide has a molecular weight range (g/mol) of about 100, 000 to 300,000 and is present in the first layer at about 65%-88% by weight.

3. The formulation of claims 1 or 2 wherein the high viscosity polyethylene oxide has a molecular weight range (g/mol) of about 4,000,000 to 7,000,000 and is present in the second layer at about 50%-70% by weight.

4. The formulation of any one of claims 1 to 3, wherein the tableting agent is selected from lactose, spray dried lactose, microcrystalline cellulose, mannitol, sorbitol, dibasic calcium phosphate dehydrate, and calcium sulphate dehydrate.

5. The formulation of claim 4 wherein the tableting agent is microcrystalline cellulose, present at about 10%-20% by weight.

6. The formulation of any one of claims 1 to 5, wherein the metal halide selected from sodium chloride, potassium chloride, calcium chloride, and potassium iodide, or a mixture thereof, and is present at about 15%-25% by weight.

7. The formulation any one of claims 1 to 6, wherein the semipermeable coating comprises cellulose acetate, ethyl cellulose, or a combination thereof and low molecular weight polyethylene glycol.

8. The formulation of any one of claims 1 to 7, wherein Compound A, or a pharmaceutically acceptable salt, ester derivative, geometric isomer, stereoisomer, or optical isomer thereof is present at about 4%-25% by weight, and low viscosity polyethylene oxide has a molecular weight range (g/mol) of about 100,000 to 300,000 and is present at about 65%-88% by weight of total first layer weight.

9. The formulation of any one of claims 1 to 8,

a) the high viscosity polyethylene oxide has a molecular weight range (g/mol) of about 4,000,000 to 7,000,000 and is present at about 60%-68% by weight,

b) the tableting agent is present up to10%-20% by weight, and

c) the metal halide is present at about 15%-25% by weight

of total weight of the second layer.

10. The formulation of any one of claims 1 to 9, wherein 5%-15% of the semipermeable coating comprises cellulose acetate, ethyl cellulose, or mixture thereof, wherein the cellulose acetate, ethyl cellulose, or mixture thereof contains about 5%-20%, by weight, of low molecular weight polyethylene glycol.

11. The formulation of any one of claims 1 to 10, further comprising a sugar alcohol selected from mannitol, sucrose, and lactose.

12. The formulation of any one of claims 1 to 11, that exhibits peak to trough concentration levels of Compound A from about 1.0 to about 3.5.

13. The formulation of any one of claims 1 to 12, comprising from about 17 mg to about 47 mg of Compound A which can be administered once daily with no incidence of dystonia.

14. The formulation of any one of claims 1 to 13, comprising Compound A at doses at 16mg or higher which exhibits sustained muscarinic enzyme occupancy at both peak and trough of about 65% or higher.

15. The formulation according to claim 14, wherein when administered in a patient population suffering from schizophrenia there are no reported incidents of dystonia.

16. Use of a controlled-release formulation of Compound A according to any one of claims 1 to 16 in the manufacture of a medicament for the treatment of schizophrenia or other psychiatric disorders in a patient in need thereof, wherein the Compound A is to be administered at doses of 16mg or higher without inducing dystonia in the patient.

17. A controlled-release formulation of Compound A according to any one of claims 1 to 16 for use in therapy.