Claims

1. A pharmaceutical composition in solid dosage form comprising, as active ingredient, Methylthioninium chloride (MTC), said composition further comprising at least one diluent suitable for direct compression,

characterised in that said dosage form is obtained by a process of dry compression of an intimate powder mixture of MTC in a substantially pure polymorphic form with said diluent, and optionally one or more other excipients,

wherein the MTC exists in the composition in a substantially pure and stable polymorphic form, and

wherein the amount of MTC in the composition is more than 10% w/w.

2. A composition as claimed in Claim 1, wherein the MTC is in polymorph Form A.

3. A composition as claimed in Claim 1 or Claim 2, wherein:
(i) the amount of MTC in the composition is ~~more than about 10% w/w, or~~ more than 20%, or more than 30% w/w, and optionally ~~.~~

~~4. A composition as claimed in Claim 3, wherein the amount of MTC is~~ less than ~~about~~ 75% w/w, or less than 60% or less than 50% w/w,
for example ~~.~~

~~5. A composition as claimed in Claim 4, wherein the amount of MTC in the composition is~~ from ~~about~~ 10% w/w (or 20% or 30%) to ~~about~~ 70% w/w (or 60% or 50%); and\or~~.~~

(ii)~~6. A~~ the composition ~~as claimed in any preceding claim, which~~ comprises at least 15% w/w, at least 20%, at least 30%, at least 40% or at least 50% w/w of diluent(s).

~~4~~7. A composition as claimed in any preceding claim, wherein the diluent(s) are selected from the group consisting of microcrystalline cellulose, lactose or~~,~~ mannitol~~, calcium salts such as calcium phosphate dibasic, calcium sulphate and calcium carbonate, and sugars such as lactose, sucrose, dextrose and maltodextrin~~.

~~5~~8. A composition as claimed in any preceding claim, which further comprises a lubricant, optionally 0.5 to 5.0% w/w lubricant,
~~.~~

~~9. A composition as claimed in Claim 8,~~ wherein the lubricant is optionally selected from the group consisting of magnesium stearate, calcium stearate, sodium stearyl fumarate, stearic acid, glycerylbehaptate, polyethylene glycol, ethylene oxide polymers, sodium lauryl sulphate, magnesium lauryl stearate, mixtures of magnesium stearate with sodium lauryl sulphate, and hydrogenated vegetable oil.

~~10. A composition as claimed in Claim 8, wherein the lubricant is magnesium stearate.~~

~~11. A composition as claimed in any one of Claims 8 to 10, which comprises from about 0.5 to about 5.0% w/w lubricant.~~

~~6~~12. A composition as claimed in any preceding claim, which further comprises:

(i) one or more disintegrants selected from the group consisting of crosslinked polyvinylpyrrolidone,

sodium starch glycolate, crosslinked sodium carboxymethyl cellulose (sodium croscarmellose), and pregelatinized starch; and\or

~~13. A composition as claimed in any preceding claim, which further comprises~~ (ii) a binder selected from the group consisting of cellulose derivatives (carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxyethylcellulose, ethylcellulose, microcrystalline cellulose) and sugars such as lactose, sucrose, dextrose, glucose, maltodextrin, and mannitol, xylitol, polymethacrylates, polyvinylpyrrolidone, sorbitol, pregelatinized starch, alginic acids, and salts thereof such as sodium alginate, magnesium aluminum silicate, polyethylene glycol~~, and the like~~.

7~~14~~. A composition as claimed in any preceding claim, which is a tablet, wherein optionally a film coating has been applied, wherein optionally the film coating comprises hydroxypropylmethylcellulose (HPMC) or polyvinyl alcohol-part hydrolysed (PVA).

8~~15~~. A composition as claimed in any one of claims 1 to 6~~preceding claim~~, which is a capsule~~.~~

~~16. A composition as claimed in claim 14, to which a film coating has been applied.~~

~~17. A composition as claimed in Claim 14, wherein the film coating comprises hydroxypropylmethylcellulose (HPMC) or polyvinyl alcohol-part hydrolysed (PVA).~~

~~18. A composition as claimed in Claim 14~~, wherein optionally the capsule is an HPMC or Gelatin capsule.

~~19. A free-flowing, cohesive powder, comprising MTC in a substantially pure polymorphic form, at least one diluent suitable for direct compression, and optionally one or more other excipients, said powder being capable of being directly compressed into a pharmaceutical composition according to any preceding claim.~~

9~~20~~. A process for the manufacture of a pharmaceutical composition according to claim 1, which process comprises the dry compression ~~process~~ of an intimate powder mixture of Methylthioninium chloride (MTC) in a substantially pure polymorphic form with at least one diluent suitable for direct compression, and optionally one or more other excipients.

10~~21~~. A process according to claim 9~~20~~, which process comprises the direct compression of an intimate powder mixture of MTC in a substantially pure polymorphic form with at least one diluent suitable for direct compression, and optionally one or more other excipients.

11~~22~~. A process as claimed in Claim 9~~20~~, which is a direct compression process in which MTC, diluent(s) and other optional excipients are blended together in solid, particulate form to create an intimate mixture, and then compressed using a tablet machine.

1223. A process as claimed in Claim 920, which is a dry granulation process in which MTC, diluent(s) and other optional excipients are formed into a compressed mass, milled and then compressed using a tablet machine.

1324. A process as claimed in Claim 920, which is a moist granulation process in which the diluent(s) are wet massed using a granulating fluid and the wet mass is then dried to form granules which are subsequently blended with MTC and compressed to form tablets.

1425. A process as claimed in any one of Claims 920 to 1324, which further comprises the step of applying a film coating to the tablets.

~~26. A process as claimed in Claim 25,~~
wherein the step of applying a film coating is carried out in a coating pan and comprises pre-heating of the coating pan, prior to introduction of the tablets to be coated.

~~27. A process as claimed in Claim 26,~~
wherein optionally the temperature of the tablets is maintained during coating at a temperature of 38-48°C, more preferably 42-44°C.

1528. The use of a solid dosage form composition as claimed in any one of claims 1 to 8 in the manufacture of a medicament for the treatment or prophylaxis of a disease condition in a patient.

1629. The use of claim 1528 wherein the disease is a tauopathy.

~~30 A drug product for the treatment of a disease state associated with tau protein aggregation in a mammal suffering therefrom, comprising a container labeled or accompanied by a label indicating that the drug product is for the treatment of said disease, the container containing one or more dosage units each comprising a solid dosage form composition as claimed in any one of claims 1 to 18.~~

17. A substantially moisture impervious blister pack comprising a composition as claimed in any one of claims 1 to 8.

1831. Use of system comprising a diluent and direct compression for enhancing the stability of a substantially pure Methylthioninium chloride (MTC) polymorph in a pharmaceutical composition.

~~32. Use as claimed in claim 31,~~
wherein the pharmaceutical composition is the solid dosage form composition as claimed in any one of claims 1 to 814 ~~or claim 16 or claim 17~~.