Claims

1. Crystalline methylthioninium chloride dihydrate as Form C.

2. The compound of claim 1 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	8.1
2	11.1
3	17.6
4	25.9
5	27.2

3. The compound of claim 1 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	8.1
2	11.1
3	17.6
4	25.9
5	27.2
6	16.2
7	17.8
8	24.4
9	30.8
10	31.3
11	33.0

4. The compound of any one of claims 1 to 3, which has two endothermic maxima at 151°C and 183°C when heated at a rate of 100°C per minute in Differential Scanning Calorimetry.

5. A process for the preparation of methylthioninium chloride dihydrate substantially in form C according to any one of claims 1 to 4, wherein a water-containing methylthioninium chloride or a mixture of various hydrates or a specific hydrate thereof is suspended and stirred at ambient temperature in a solvent selected from the group comprising isopropanol, 1-propanol, 1-butanol, 2-butanol, tert.-butanol, tetrahydrofurane, dioxane, acetone, 2-butanone, and acetonitrile containing a small amount of water, for a time sufficient to generate form C; the solid is then isolated; and the solvent is removed from the solid.

6. Crystalline methylthioninium chloride monohydrate as Form E.

7. The compound of claim 6 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	9.0
2	12.5
3	14.1
4	14.4
5	18.1
6	23.2
7	24.1
8	26.0

8. The compound of claim 6 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	9.0
2	12.5
3	14.1
4	14.4
5	18.1
6	23.2
7	24.1
8	26.0
9	24.5
10	27.2

9. The compound of any one of claims 6 to 8, which shows no thermal event up to the decomposition temperature near 220°C when heated at a rate of 100°C per minute in Differential Scanning Calorimetry.

10. A process for the preparation of methylthioninium chloride monohydrate substantially in form E according to any one of claims 6 to 9, wherein:
water-containing methylthioninium chloride or a mixture of various hydrates or a specific hydrate of methylthioninium chloride is suspended and stirred at ambient temperature in a dry solvent, preferably isopropanol, for a time sufficient to generate form E; the solid is isolated by filtration; and residual solvent is removed from the solid by either vacuum drying or purging with dry gas.

11. Crystalline methylthioninium chloride dihydrate as Form D.

12. The compound of claim 11 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	7.0
2	8.5
3	12.0
4	14.4
5	25.3
6	25.7
7	27.5

13. The compound of claim 11 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	7.0
2	8.5
3	12.0
4	14.4
5	25.3
6	25.7
7	27.5
8	6.0
9	10.4
10	20.9
11	21.1
12	21.7
13	22.3
14	23.7
15	24.5
16	26.9
17	28.5
18	29.0
19	30.4
20	31.8

14. The compound of any one of claims 11 to 13, which has two endothermic peak maxima at 164°C and 185°C and a step in the baseline near 63°C when heated at a rate of 100°C per minute in Differential Scanning Calorimetry.

15. A process for the preparation of methylthioninium chloride dihydrate substantially in form D according to any one of claims 11 to 14, comprising: dissolving methylthioninium chloride pentahydrate in acetic acid and combining the solution with toluene, either by adding toluene to the acetic acid solution or by adding the acetic acid solution to toluene; isolating the solid by filtration shortly after precipitation; and removing the solvent by vacuum drying or in an inert gas flow, whereby the relative air humidity in all process steps is less than 50%.

16. Crystalline methylthioninium chloride dihydrate substantially as Form B.

17. The compound of claim 16 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	5.8
2	11.2
3	25.3
4	26.8

18. The compound of claim 16 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	5.8
2	11.2
3	25.3
4	26.8
5	15.6
6	16.9
7	20.3
8	28.3

19. The compound of any one of claims 16 to 18, which has a melting peak at 186°C with a shoulder towards lower temperature when heated at a rate of 100°C per minute in Differential Scanning Calorimetry.

20. A process for the preparation of methylthioninium chloride dihydrate substantially in form B, which comprises exposing solid methylthioninium chloride pentahydrate at about room temperature to an inert gas flow having a relative humidity from 8 to 15% for a time sufficient to generate essentially pure form B.

21. A pharmaceutical composition comprising methylthioninium chloride dihydrate form B, C or D or methylthioninium chloride monohydrate form E according to any one of claims 1 to 4, 5 to 9, 11 to 14 or 16 to 19.

22. A pharmaceutical composition comprising methylthioninium chloride dihydrate form B, C or D or methylthioninium chloride monohydrate form E according to any one of claims 1 to 4, 5 to 9, 11 to 14 or 16 to 19 and a pharmaceutically acceptable carrier, excipient or diluent.

23. Methylthioninium chloride dihydrate form B, C or D or methylthioninium chloride monohydrate form E according to to any one of claims 1 to 4, 5 to 9, 11 to 14 or 16 to 19 for use in a method of treatment of the human or animal body by therapy.

24. Use of methylthioninium chloride dihydrate form B, C or D or methylthioninium chloride monohydrate form E according to to any one of claims 1 to 4, 5 to 9, 11 to 14 or 16 to 19 in the treatment of a disease condition.

25. Use of methylthioninium chloride dihydrate form B, C or D or methylthioninium chloride monohydrate form E according to to any one of claims 1 to 4, 5 to 9, 11 to 14 or 16 to 19 in the treatment of a tauopathy, Alzheimer's disease (AD), skin cancer, melanoma, Hepatitis C, HIV or West Nile virus.

26. A method of treatment of a tauopathy, Alzheimer's disease (AD), skin cancer, melanoma, Hepatitis C, HIV or West Nile virus in a patient, comprising administering to said patient a therapeutically-effective amount of methylthioninium chloride dihydrate form B, C or D or methylthioninium chloride monohydrate form E according to to any one of claims 1 to 4, 5 to 9, 11 to 14 or 16 to 19.

Claims

1. Crystalline methylthioninium chloride monohydrate as Form E, having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	9.0
2	12.5
3	14.1
4	14.4
5	18.1
6	23.2
7	24.1
8	26.0

2. The compound of claim 1 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	9.0
2	12.5
3	14.1
4	14.4
5	18.1
6	23.2
7	24.1
8	26.0
9	24.5
10	27.2

3. The compound of any one of claims 1 to 2, which shows no thermal event up to the decomposition temperature near 220°C when heated at a rate of 100°C per minute in Differential Scanning Calorimetry.

4. A process for the preparation of methylthioninium chloride monohydrate substantially in form E according to any one of claims 1 to 3, wherein:
water-containing methylthioninium chloride or a mixture of various hydrates or a specific hydrate of methylthioninium chloride is suspended and stirred at ambient temperature in a dry solvent, preferably isopropanol, for a time sufficient to generate form E; the solid is

isolated by filtration; and residual solvent is removed from the solid by either vacuum drying or purging with dry gas.

5. Crystalline methylthioninium chloride dihydrate as Form D, having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	7.0
2	8.5
3	12.0
4	14.4
5	25.3
6	25.7
7	27.5

6. The compound of claim 5 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	7.0
2	8.5
3	12.0
4	14.4
5	25.3
6	25.7
7	27.5
8	6.0
9	10.4
10	20.9
11	21.1
12	21.7
13	22.3
14	23.7
15	24.5
16	26.9
17	28.5
18	29.0

19	30.4
20	31.8

7. The compound of any one of claims 5 to 6, which has two endothermic peak maxima at 164°C and 185°C and a step in the baseline near 63°C when heated at a rate of 100°C per minute in Differential Scanning Calorimetry.

8. A process for the preparation of methylthioninium chloride dihydrate substantially in form D according to any one of claims 5 to 7, comprising: dissolving methylthioninium chloride pentahydrate in acetic acid and combining the solution with toluene, either by adding toluene to the acetic acid solution or by adding the acetic acid solution to toluene; isolating the solid by filtration shortly after precipitation; and removing the solvent by vacuum drying or in an inert gas flow, whereby the relative air humidity in all process steps is less than 50%.

9. Crystalline methylthioninium chloride dihydrate substantially as Form B, having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	5.8
2	11.2
3	25.3
4	26.8

10. The compound of claim 9 having the following characteristic peaks in a powder X-ray diffraction pattern:

Peak	2θ values (± 0.1°)
1	5.8
2	11.2
3	25.3
4	26.8
5	15.6
6	16.9
7	20.3
8	28.3

11. The compound of any one of claims 9 to 10, which has a melting peak at 186°C with a shoulder towards lower temperature when heated at a rate of 100°C per minute in Differential Scanning Calorimetry.

12. A process for the preparation of methylthioninium chloride dihydrate substantially in form B, which comprises exposing solid methylthioninium chloride pentahydrate at about room temperature to an inert gas flow having a relative humidity from 8 to 15% for a time sufficient to generate essentially pure form B.

13. A pharmaceutical composition comprising methylthioninium chloride dihydrate form B according to any one of claims 1 to 3 or methylthioninium chloride dihydrate Form D according to any one of claims 5 to 8, or methylthioninium chloride monohydrate form E according to any one of claims 9 to 11.

14. A pharmaceutical composition comprising methylthioninium chloride dihydrate form B according to any one of claims 1 to 3 or methylthioninium chloride dihydrate Form D according to any one of claims 5 to 8, or methylthioninium chloride monohydrate form E according to any one of claims 9 to 11 and a pharmaceutically acceptable carrier, excipient or diluent.

15. Methylthioninium chloride dihydrate form B or D or methylthioninium chloride monohydrate form E according to any one of claims 1 to 3, 5 to 8, or 9 to 11 for use in therapy.

16. Use of methylthioninium chloride dihydrate form B or D or methylthioninium chloride monohydrate form E according to any one of claims 1 to 3, 5 to 8, or 9 to 11 in the manufacture of a medicament for the treatment of a disease condition.

17. Use of methylthioninium chloride dihydrate form B or D or methylthioninium chloride monohydrate form E according to any one of claims 1 to 3, 5 to 8, or 9 to 11 in the manufacture of a medicament for the treatment of a tauopathy, Alzheimer's disease (AD), skin cancer, melanoma, Hepatitis C, HIV or West Nile virus.