

**CLAIMS:**

1. A lyophilised formulation obtained by freeze drying a pharmaceutical aqueous solution formulation comprising

1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, or a lactate salt thereof, lactic acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 6mg/ml and sufficient lactic acid is present to provide a clear solution; or

1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, or a phosphate salt thereof, orthophosphoric acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 4mg/ml and sufficient orthophosphoric acid is present to provide a clear solution.

2. A lyophilised formulation as claimed in claim 1, the pharmaceutical aqueous solution formulation comprising 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, or a lactate salt thereof, lactic acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 6mg/ml and sufficient lactic acid is present to provide a clear solution.

3. A lyophilised formulation as claimed in claim 1 or 2, the pharmaceutical aqueous solution formulation comprising 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, lactic acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 6mg/ml and sufficient lactic acid is present to provide a clear solution.

4. A lyophilised formulation as claimed in any one of claims 1 to 3 wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present in the pharmaceutical aqueous solution formulation at a solution concentration of from 2.5 to 5.5mg/ml.

5. A lyophilised formulation as claimed in any one of claims 1 to 4 wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present in the pharmaceutical aqueous solution formulation at a solution concentration of from 5.0 to 5.5mg/ml and at least 2.5 mole equivalents of lactic acid are present.

6. A lyophilised formulation as claimed in claim 4 wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present in the pharmaceutical aqueous solution formulation at a solution concentration of about 5mg/ml.

7. A lyophilised formulation as claimed in claim 6 wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present in the pharmaceutical aqueous solution formulation at a solution concentration of about 5mg/ml and at least 2.5 mole equivalents of lactic acid are present.

8. A lyophilised formulation as claimed in any one of claims 1 to 3, the pharmaceutical aqueous solution formulation comprising 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, lactic acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of about 5mg/ml, and at least 2.5 mole equivalents of lactic acid are present and in an amount sufficient to ensure a clear solution is formed.

9. A lyophilised formulation as claimed in claim 1 or 2, the pharmaceutical aqueous solution formulation comprising 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea lactate, lactic acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of about 5mg/ml, and at least 1.5 mole equivalents of lactic acid are present and in an amount sufficient to ensure a clear solution is formed.

10. A lyophilised formulation as claimed in claim 8, the pharmaceutical aqueous solution formulation comprising 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, lactic acid and water, wherein 1-(4-([4-

(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of about 5mg/ml, and about 4.1 mole equivalents of lactic acid are present and in an amount sufficient to ensure a clear solution is formed with a pH of no greater than 3.7.

11. A lyophilised formulation as claimed in claim 1 or 2, the pharmaceutical aqueous solution formulation comprising 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, lactic acid and water, wherein 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of from 2.5 to 5.5mg/ml, and from above 2.5 to 8.0 mole equivalents of lactic acid are present and in an amount sufficient to ensure a clear solution is formed.

12. A lyophilised formulation as claimed in any one of claims 1 to 11 wherein DL-lactic acid, L-lactic acid or D-lactic acid is used in the pharmaceutical aqueous solution formulation.

13. A lyophilised formulation as claimed in any one of claims 1 to 12 wherein DL-lactic acid is used in the pharmaceutical aqueous solution formulation.

14. A lyophilised formulation as claimed in claim 1, the pharmaceutical aqueous solution formulation comprising 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, or a phosphate salt thereof, orthophosphoric acid and water, wherein 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 4 mg/ml and sufficient orthophosphoric acid is present to provide a clear solution.

15. A lyophilised formulation as claimed in claim 1 or 14, the pharmaceutical aqueous solution formulation comprising 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, orthophosphoric acid and water, wherein 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 4 mg/ml and sufficient orthophosphoric acid is present to provide a clear solution.

16. A lyophilised formulation as claimed in claim 15 wherein 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-

yl)phenyl]urea is present in the pharmaceutical aqueous solution formulation at a solution concentration of from 3.0 to 3.5mg/ml.

17. A lyophilised formulation as claimed in claim 15 or 16 wherein at least 5 mole equivalents of orthophosphoric acid are used in the pharmaceutical aqueous solution formulation.
18. A lyophilised formulation as claimed in claim 17 wherein from 5 to 7 mole equivalents of orthophosphoric acid are used in the pharmaceutical aqueous solution formulation.
19. A lyophilised formulation as claimed in any one of claims 1 to 18 additionally containing a bulking agent.
20. A lyophilised formulation as claimed in claim 19 wherein the bulking agent is mannitol.
21. A process for the preparation of a pharmaceutical aqueous clear solution formulation by reconstitution or constitution of a lyophilized formulation as claimed in any one of claims 1 to 20 using water or an aqueous solution comprising a tonicity modifier.
22. A process as claimed in claim 21 wherein the tonicity modifier is dextrose, sucrose or mannitol, or is a mixture of any 2 or more thereof.
23. A process as claimed in claim 21 or 22, that is adjusted, as necessary, to have a pH suitable for intravenous or parenteral administration.
24. A process as claimed in claim 23 wherein the pH is from 3 to 4.5.
25. A pharmaceutical aqueous solution formulation comprising 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, or a phosphate salt thereof, orthophosphoric acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 4 mg/ml and sufficient orthophosphoric acid is present to provide a clear solution.
26. A pharmaceutical aqueous solution formulation as claimed in claim 25 comprising 1-(4-([4-(dimethylamino)piperidin-1-yl]carbonyl)phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, orthophosphoric acid and water, wherein 1-(4-([4-(dimethylamino)piperidin-

1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of less than 4 mg/ml and sufficient orthophosphoric acid is present to provide a clear solution.

27. A pharmaceutical aqueous solution formulation as claimed in claim 26 wherein 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea is present at a solution concentration of from 3.0 to 3.5mg/ml.

28. A pharmaceutical aqueous solution formulation as claimed in claim 26 or 27 wherein at least 5 mole equivalents of orthophosphoric acid are used.

29. A pharmaceutical aqueous solution formulation as claimed in claim 28 wherein from 5 to 7 mole equivalents of orthophosphoric acid are used.

30. A formulation as claimed in any one of claims 1 to 20 and 25 to 29 for use in the treatment of cancer.