CLAIMS

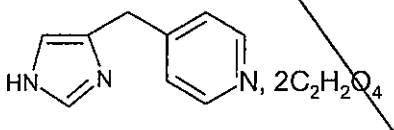
1. A pharmaceutical composition comprising immethridine or one of its pharmaceutically acceptable salts, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated (including hydrated) forms, suitable for administration of 0.001 to 0.1 mg/kg of bodyweight per day in human.

2. A pharmaceutical composition according to claim 1, wherein immethridine is in the form of a pharmaceutically acceptable salt.

3. The pharmaceutical composition according to claim 1 or 2, wherein the salts of immethridine are chosen from the dihydrobromide, dihydrochloride, dihydrogenosulfate, toluenesulfonate, ditoluenesulfonate, dicamphorsulfonate, dibenzenesulfonate, phosphate, dimethanesulfonate, alpha-ketoglutarate, oxalate, monosulfate salts of immethridine, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated including hydrated forms.

4. The pharmaceutical composition according to claim 1, 2 or 3, wherein immethridine is in the form of an oxalate salt.

5. A pharmaceutical composition according to anyone of the preceding claims, wherein immethridine is in the form of the dioxalate salt, of formula:



6. The pharmaceutical composition according to anyone of the preceding claims, wherein the salt is the dioxalate salt of immethridine in its polymorphic form III comprising a characterizing peak at 16.6° by X ray diffraction.

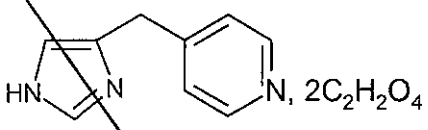
7. The pharmaceutical composition according to anyone of the preceding claims, wherein the immethridine salt is the compound having the the X-ray powder diffraction spectrum as shown in figure 1 referred to as BP1.5375L phase 3.

8. The pharmaceutical composition according to anyone of the preceding claims, wherein the immethridine salt is the compound obtainable by the process according to claim 17.

9. The salts of immethridine chosen from the dihydrochloride, dihydrogenosulfate, toluenesulfonate, ditoluenesulfonate, dicamphorsulfonate, dibenzenesulfonate, phosphate, dimethanesulfonate, alpha-ketoglutarate, oxalate, monosulfate salts of immethridine, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated including hydrated forms.

10. The salts of immethridine according to claim 9 which are oxalate salts of immethridine.

11. The compound according to claim 9 or 10, which is the dioxalate salt of immethridine, of formula (I):

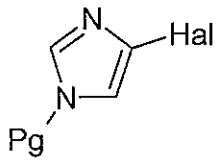


12. The compound according to claim 9, 10 or 11 which is the dioxalate salt of immethridine in its polymorphic form III comprising a characterizing peak at 16.6° by X ray diffraction.

13. The compound according to claim 9, which has the X-ray powder diffraction spectrum as shown in figure 1 referred to as BP1.5375L phase 3.

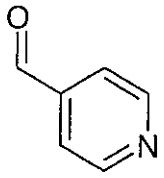
14. A process of preparation of the compound according to anyone of claims 9 to 13 comprising the step of reacting immethridine with the corresponding acid in an organic solvent.

15. The process according to claim 14, which further comprises the steps of preparing immethridine by coupling a compound of formula (II)



(II)

with a compound of formula (III)



(III)

where Hal represents a halogen atom, Pg represents a protecting group followed by dexoxygenating/deprotecting said protecting group Pg.

16. The process according to claim 14 or 15 comprising the step of reacting immethridine with oxalic acid.

17. Process according to anyone of claims 14 to 16 comprising:

- slowly adding acetone to a 10% (wt/wt) solution of immethridine dioxalate in water at 20°C to a final composition water/acetone 10/90 wt/wt;
- stirring for 24 hours at room temperature ;
- filtering, rinsing the solid with acetone ;
- drying.

18. The compound obtainable by the process according to claim 17.

19. Use of immethridine or one of its pharmaceutically acceptable salts as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated (including hydrated) forms for for the preparation of a medicament for preventing and/or treating H3R related disorders chosen from stress, pain, psychosomatic disorders, insomnia, migraines, respiratory, allergic or inflammatory conditions (asthma, bronchitis, rhinitis, tracheitis), cardiac conditions (myocardial dysfunction and infarction), gastrointestinal conditions as a result of their antisecretory and anti-inflammatory actions (gastric and duodenal ulcers, gastro-esophageal reflux, ulcerative colitis, Crohn's disease, irritable bowel, faecal incontinence), conditions of the urogenital system (cystitis, metritis, premenstrual syndrome, prostatic inflammations, urinary incontinence, genital disorders) and conditions of the cutaneous system (urticaria, itching), arthritis and other rheumatic conditions, conjunctivitis and other ocular inflammations, sialorrhoea, secretion, inflammation, sleep or circadian rhythm disorders, convulsions, hypothalamohypophyseal secretion disorders, depressive states, cerebral

circulation disorders, immune system disorders, allergic conditions, comprising administration of 0.001 to 0.1 mg/kg of bodyweight per day of immethridine in human.

20. Use according to claim 19, wherein the salts of immethridine chosen from the dihydrobromide, dihydrochloride, dihydrogenosulfate, toluenesulfonate, ditoluenesulfonate, dicamphorsulfonate, dibenzenesulfonate, phosphate, dimethanesulfonate, alpha-ketoglutarate, oxalate, monosulfate salts of immethridine, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated including hydrated forms.

21. Use according to claim 19 or 20, which is in the form of oxalate salts.

22. Use according to claim 20 or 21, which is the dioxalate salt of immethridine.

23. Use according to anyone of claims 19 to 22, wherein the salt is the dioxalate salt of immethridine in its polymorphic form III comprising a characterizing peak at 16.6° by X ray diffraction.

24. Use according to anyone of claims 19 to 23 as a psychotropic, hypnotic, sleep regulator agent and/or as an anaesthesia adjuvant.

25. Use according to anyone of claims 19 to 24 for the prevention or treatment of abstinence symptoms, withdrawal syndrome, and dependence from drugs, benzodiazepine receptor agonists, and/or alcohol.

26. Use according to anyone to claims 19 to 25 where the compound is the compound of claim 13 or 18.

27. Combinations comprising immethridine or a pharmaceutically acceptable salt of immethridine as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated (including hydrated) forms with a GABA-A positive modulator.

CLAIMS

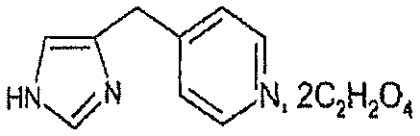
1. A pharmaceutical composition comprising immethridine or one of its pharmaceutically acceptable salts, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated (including hydrated) forms, suitable for administration of 0.001 to 0.1 mg/kg of bodyweight per day in human.

2. A pharmaceutical composition according to claim 1, wherein immethridine is in the form of a pharmaceutically acceptable salt.

3. The pharmaceutical composition according to claim 1 or 2, wherein the salts of immethridine are chosen from the dihydrobromide, dihydrochloride, dihydrogenosulfate, toluenesulfonate, ditoluenesulfonate, dicamphorsulfonate, dibenzenesulfonate, phosphate, dimethanesulfonate, alpha-ketoglutarate, oxalate, monosulfate salts of immethridine, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated including hydrated forms.

4. The pharmaceutical composition according to claim 1, 2 or 3, wherein immethridine is in the form of an oxalate salt.

5. A pharmaceutical composition according to anyone of the preceding claims, wherein immethridine is in the form of the dioxalate salt, of formula:



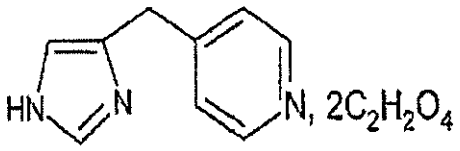
6. The pharmaceutical composition according to anyone of the preceding claims, wherein the immethridine salt is an oxalate salt having the X-ray powder diffraction spectrum as shown in figure 1 referred to as BP1.5375L phase 3.

7. The pharmaceutical composition according to anyone of the preceding claims, wherein the immethridine salt is the compound obtainable by the process according to claim 15.

8. The salts of immethridine chosen from the dihydrochloride, dihydrogenosulfate, toluenesulfonate, ditoluenesulfonate, dicamphorsulfonate, dibenzenesulfonate, phosphate, dimethanesulfonate, alpha·ketoglutarate, oxalate, · monosulfate salts of immethridine, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated including hydrated forms.

9. The salts of immethridine according to claim 8 which are oxalate salts of immethridine.

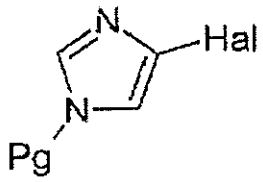
10. The compound according to claim 8 or 9, which is the dioxalate salt of immethridine, of formula (I):



11. The compound according to claim 8, which is an oxalate salt and has the X-ray powder diffraction spectrum as shown in figure 1 referred to as BP1.5375L phase 3.

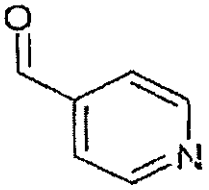
12. A process of preparation of the compound according to anyone of claims 8 to 11 comprising the step of reacting immethridine with the corresponding acid in an organic solvent.

13. The process according to claim 12, which further comprises the steps of preparing immethridine by coupling a compound of formula (II)



(II)

with a compound of formula (III)



(III)

where Hal represents a halogen atom, Pg represents a protecting group followed by dexoxygenating/deprotecting said protecting group Pg.

14. The process according to claim 12 or 13 comprising the step of reacting immethridine with oxalic acid.

15. Process according to anyone of claims 12 to 14 comprising:

- slowly adding acetone to a 10% (wt/wt) solution of immethridine dioxalate in water at 20°C to a final composition water/acetone 10/90 wt/wt;

- stirring for 24 hours at room temperature;
- filtering, rinsing the solid with acetone:
- drying.

16. The compound obtainable by the process according to claim 15.

17. Use of immethridine or one of its pharmaceutically acceptable salts as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated (including hydrated) forms for for the preparation of a medicament for preventing and/or treating H3R related disorders chosen from stress, pain, psychosomatic disorders, insomnia, migraines, respiratory, allergic or inflammatory conditions (asthma, bronchitis, rhinitis, tracheitis), cardiac conditions (myocardial dysfunction and infarction), gastrointestinal conditions as a result of their antisecretory and anti-inflammatory actions (gastric and duodenal ulcers, gastro-esophageal reflux, ulcerative colitis, Crohn's disease, irritable bowel, faecal incontinence), conditions of the urogenital system (cystitis, metritis, premenstrual syndrome, prostatic inflammations, urinary incontinence, genital disorders) and conditions of the cutaneous system (urticaria, itching). arthritis and other rheumatic conditions, conjunctivitis and other ocular inflammations, sialorrhoea, secretion, inflammation, sleep or circadian rhythm disorders, convulsions, hypothalamohypophyseal secretion disorders, depressive states, cerebral circulation disorders, immune system disorders, allergic conditions, comprising administration of 0.001 to 0.1 mg/kg of bodyweight per day of immethridine in human.

18. Use according to claim 17, wherein the salts of immethridine chosen from the dihydrobromide, dihydrochloride, dihydrogenosulfate, toluenesulfonate, ditoluenesulfonate, dicamphorsulfonate, dibenzenesulfonate, phosphate, dimethanesulfonate, alpha-ketoglutarate, oxalate, monosulfate salts of immethridine, as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated including hydrated forms.

19. Use according to claim 17 or 18, which is the dioxalate salt of immethridine.

20. Use according to claim 18 or 19, which is the dioxalate salt of immethridine.

21. Use according to anyone of claims 17 to 20, wherein the salt is the dioxalate salt of immethridine in its polymorphic form III comprising a characterizing peak at 16.6° by X ray diffraction.

22. Use according to anyone of claims 17 to 21 as a psychotropic, hypnotic, sleep regulator agent and/or as an anaesthesia adjuvant.

23. Use according to anyone of claims 17 to 22 for the prevention or treatment of abstinence symptoms, withdrawal syndrome, and dependence from drugs,

benzodiazepine receptor agonists, and/or alcohol.

24. Use according to anyone to claims 17 to 23 where the compound is the compound of claim 13 or 18.

25. Combinations comprising immethridine or a pharmaceutically acceptable salt of immethridine as well as their solvated, including hydrated forms, and polymorphic forms of said salts and/or polymorphic forms of said solvated (including hydrated) forms with a GABA-A positive modulator.