Claims

1. An orally dispersible composition of vortioxetine hemihydrobromide, which comprises vortioxetine hemihydrobromide and pharmaceutically acceptable excipients.
2. The orally dispersible composition according to claim 1, which is tablet, granule, capsule, powder, suspension, dry suspension or solution; preferably, the tablet is an orally disintegrating tablet or a dispersible tablet; more preferably, the tablet is orally disintegrating tablet.
3. An orally dispersible taste masking composition of vortioxetine hemihydrobromide or vortioxetine hydrobromide, which comprises vortioxetine hemihydrobromide or vortioxetine hydrobromide and pharmaceutically acceptable taste masking excipients.
4. The orally dispersible taste masking composition according to claim 3, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is coated with the taste masking excipient to form coated granules; preferably, the taste masking excipient is cellulose acetate, ethyl cellulose, hydroxypropyl cellulose, methacrylic acid copolymer, chitosan, copovidone, or polyvinyl alcohol; optionally, the taste masking excipient contains alkaline excipients; optionally, the coated granules contain an anticaking agent.
5. The orally dispersible taste masking composition according to claim 3, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is dispersed in the taste masking excipient to form a solid dispersion; preferably, the taste masking excipient is cellulose acetate, ethyl cellulose, hydroxypropyl cellulose, methacrylic acid copolymer, chitosan, copovidone, povidone, polyvinyl alcohol, or polyethylene glycol; optionally, the taste masking excipient includes an alkaline excipient.
6. The orally dispersible taste masking composition according to claim 3, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is mixed with alkaline excipients, preferably, vortioxetine hemihydrobromide or vortioxetine hydrobromide is mixed with at least one of trisodium phosphate, disodium hydrogen phosphate, disodium hydrogen phosphate, potassium carbonate, sodium carbonate, sodium bicarbonate, potassium citrate, sodium acetate, calcium hydroxide, sodium hydroxide, potassium hydroxide, or meglumine, then form a composition.

7. A taste masking coated granule of vortioxetine hemihydrobromide or vortioxetine hydrobromide, wherein the taste masking coating excipient is cellulose acetate, ethyl cellulose, hydroxypropyl cellulose, methacrylic acid copolymer, chitosan, copovidone, or polyvinyl alcohol; optionally, the taste masking coating excipient includes an alkaline excipient; optionally, the taste masking coating excipient includes an anticaking agent.
8. A taste masking solid dispersion of vortioxetine hemihydrobromide or vortioxetine hydrobromide, wherein the taste masking excipient is cellulose acetate, ethyl cellulose, hydroxypropyl cellulose, methacrylic acid copolymer, chitosan, copovidone, povidone, polyvinyl alcohol, or polyethylene glycols; optionally, the taste masking excipient includes alkaline excipient.
9. A taste masking combination of vortioxetine hemihydrobromide or vortioxetine hydrobromide, which comprises vortioxetine hemihydrobromide or vortioxetine hydrobromide and an alkaline excipient; preferably, the alkaline excipient is at least one of trisodium phosphate, disodium hydrogen phosphate, dipotassium hydrogen phosphate, potassium carbonate, sodium carbonate, sodium hydrogen carbonate, potassium citrate, sodium acetate, calcium hydroxide, sodium hydroxide, potassium hydroxide, or meglumine.
10. The orally dispersible taste masking composition according to claim 4 or claim 5, the taste masking coating granule according to claim 7, or the taste masking solid dispersion according to claim 8, wherein the methacrylic copolymer is polyacrylic resin, preferably polyacrylic resin is polyacrylic resin II or polyacrylic resin IV.
11. The orally dispersible taste masking composition according to claim 4 or the taste masking coated granule according claim 7, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is coated with the taste masking excipient to form coated granules, and the coated granules are further dispersed in the taste masking excipient to form a solid dispersion; optionally; the formed solid dispersion is further mixed with alkaline excipient.
12. The orally dispersible taste masking composition according to claim 5 or the solid dispersion according to claim 8, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is dispersed in the taste masking excipient to form a solid dispersion, and the solid dispersion is further coated with the taste masking excipient to form a coated granule; optionally; the formed coated granule is further mixed with alkaline excipient.

13. The orally dispersible taste masking composition according to claim 4 or the taste masking coated granule according claim 7, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is coated with the taste masking excipient to form a coated granule, and the coated granule is further mixed with alkaline excipient.
14. The orally dispersible taste masking composition according to claim 5 or the solid dispersion according to claim 8, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is dispersed in the taste masking excipient to form a solid dispersion, and the solid dispersion is further mixed with alkaline excipient.
15. The orally dispersible taste masking composition according to claim 3, the taste masking coated granule according claim 7, the taste masking solid dispersion according to claim 8 or the taste masking combination according to claim 9, wherein the weight ratio of vortioxetine hemihydrobromide or vortioxetine hydrobromide to pharmaceutically acceptable taste masking excipient is 1:0.1-1:5, preferably, 1:0.3-1:3, more preferably, 1:0.5-1:1.5; wherein the weight ratio of vortioxetine hemihydrobromide or vortioxetine hydrobromide to pharmaceutically acceptable alkaline excipient is 1:0.01-1:1.1, preferably, 1:0.03-1:1.
16. The orally dispersible taste masking composition according to claim 3, the taste masking coated granule according claim 7, the taste masking solid dispersion according to claim 8 or the taste masking combination according to claim 9, which is crystalline or amorphous substance.
17. The orally dispersible taste masking composition according to claim 3, the taste masking coated granule according claim 7, the taste masking solid dispersion according to claim 8, the taste masking combination according to claim 9, or the orally dispersible taste masking composition according to claim 15, which further comprises a filler, a flavoring agent, a release regulator agent, a plasticizer, an anticaking agent, and/or a disintegrant agent; preferably, the anticaking agent is talc, which accounts for 5%-25% of the total weight of the taste masking coated granule, for example, 10%-20%; wherein the disintegrant agent is sodium starch glycolate, croscarmellose sodium, crospovidone, and combinations thereof, which accounts for 1%-8% of the total weight of the orally dispersible taste masking composition, preferably, 2%-6%; preferably, wherein the flavoring agent is neotame, which accounts for 0.05%-0.5% of the total weight of the orally dispersible taste masking composition, preferably, 0.1%-0.3%.

18. The orally dispersible taste masking composition according to claim 3, the taste masking coated granule according claim 7, the taste masking solid dispersion according to claim 8 or the taste masking combination according to claim 9, which is (or is prepared as) tablets, granules, capsules, powders, suspensions, dry suspensions, solutions; preferably, wherein the tablets are orally disintegrating tablets or dispersible tablets, more preferably, the tablets are orally disintegrating tablets.
19. The orally dispersible composition according to claim 1 or claim 2, the orally dispersible taste masking composition according to claim 3, the taste masking coated granule according claim 7, the taste masking solid dispersion according to claim 8 or the taste masking combination according to claim 9, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide is amorphous or crystal.
20. Use of vortioxetine hemihydrobromide in the preparation of orally dispersible composition, taste masking coated granule, taste masking solid dispersion, taste masking combination or orally dispersible taste masking composition, preferably, wherein the orally dispersible preparation or the orally dispersible taste masking preparation is tablets, granules, capsules, powders, suspensions, dry suspensions, and solutions, preferably, wherein the tablets are orally disintegrating tablets or dispersible tablets, more preferably, the tablets are orally disintegrating tablets.
21. Use of vortioxetine hydrobromide in the preparation of orally dispersible composition, taste masking coated granule, taste masking solid dispersion, taste masking combination or orally dispersible taste masking composition, preferably, wherein the orally dispersible composition or the orally dispersible taste masking composition is tablets, granules, capsules, powders, suspensions, dry suspensions, and solutions, preferably, wherein the tablets are orally disintegrating tablets or dispersible tablets, more preferably, the tablets are orally disintegrating tablets.
22. A method for preparing taste masking coated granules of vortioxetine hemihydrobromide or vortioxetine hydrobromide or their compositions thereof, which comprises:

    (1) crushing vortioxetine hemihydrobromide or vortioxetine hydrobromide to obtain vortioxetine hydrobromide half salt or one salt powder; preferably, sieving of materials through a 20-300 mesh sieve after crushing, more preferably, sieving through a 100-200 mesh;

(2a) dispersing the taste masking excipients in a solvent, coating the vortioxetine hemihydrobromide or vortioxetine hydrobromide powder with the taste masking excipients through a fluid bed and removing the solvent to obtain the vortioxetine hemihydrobromide or vortioxetine hydrobromide coated with the taste masking excipients; preferably, dispersing taste masking excipient and release regulator agent in a solvent; more preferably, wherein the release regulator agent is polyethylene glycol or alkaline excipient; preferably, wherein the solvent is water, ethanol or dichloromethane; or

(2b) adding the vortioxetine hemihydrobromide or vortioxetine hydrobromide powder and taste masking excipients to solvent to form a suspension, removing the solvent through a fluid bed, spray drying or evaporation, then obtaining the vortioxetine hemihydrobromide or vortioxetine hydrobromide coated with the taste masking excipients; preferably, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide, taste masking excipient, release regulator agent and/or plasticizer are added to solvent to form suspension of vortioxetine hemihydrobromide or vortioxetine hydrobromide; preferably, wherein the plasticizer is polyethylene glycol or triethyl citrate; preferably, wherein the solvent is water, ethanol or dichloromethane.

(3) optionally, the coated vortioxetine hemihydrobromide or vortioxetine hydrobromide is prepared as a composition.

23. A method for preparing taste masking coated granules of vortioxetine hemihydrobromide or vortioxetine hydrobromide or their compositions thereof, which comprises:

(1) crushing vortioxetine hemihydrobromide or vortioxetine hydrobromide to obtain vortioxetine hydrobromide half salt or one salt powder; preferably, sieving of materials through a 20-300 mesh sieve after crushing, more preferably, sieving through a 100-200 mesh;

(2a) mixing the vortioxetine hemihydrobromide or vortioxetine hydrobromide powder with taste masking excipients, heating at 50-150°C to soften or liquefy, cooling to solidify, and crushing to obtain powder; preferably, wherein the vortioxetine hemihydrobromide or vortioxetine hydrobromide powder, the taste masking excipient and release regulator agent are mixed; or

(2b) dissolving the vortioxetine hemihydrobromide or vortioxetine hydrobromide powder and taste masking excipients in a solvent, and removing the solvent by

distillation, fluid bed or spray drying to obtain powder; preferably, wherein the solvent is water, ethanol or dichloromethane;

(3) optionally, the powder obtained in step (2a) or (2b) is prepared as a composition.

24. The preparation method according to claim 22 or claim 23, wherein the taste masking excipients are cellulose acetate, ethyl cellulose, hydroxypropyl cellulose, methacrylic acid copolymer, chitosan, copovidone, povidone, polyvinyl alcohol, or polyethylene glycols; preferably, wherein the methacrylic acid copolymer is a polyacrylic resin; more preferably, the polyacrylic resin is polyacrylic resin II or polyacrylic resin IV.

25. A method for preparing taste masking coated granules of vortioxetine hemihydrobromide or vortioxetine hydrobromide or their compositions thereof, which comprises:

(1) crushing vortioxetine hemihydrobromide or vortioxetine hydrobromide to obtain vortioxetine hemihydrobromide or vortioxetine hydrobromide powder; preferably, sieving of materials through a 50-300 mesh sieve after crushing, more preferably, 100-200 mesh sieve;

(2) mixing the vortioxetine hemihydrobromide or vortioxetine hydrobromide powder with the alkaline excipients to obtain taste masking composition; preferably, wherein the alkaline excipients are trisodium phosphate, disodium hydrogen phosphate, dipotassium hydrogen phosphate, potassium carbonate, sodium carbonate, sodium bicarbonate, potassium citrate, sodium acetate, calcium hydroxide, sodium hydroxide, potassium hydroxide, or meglumine;

(3) optionally, the taste masking combination is prepared as a composition.

26. The preparation method according to any of claim 22-25, wherein the weight ratio of vortioxetine hemihydrobromide or vortioxetine hydrobromide to pharmaceutically acceptable taste masking excipient for forming a coating or solid dispersion is 1:0.1-1:5, preferably, 1:0.3-1:3, more preferably, 1:0.3-1:1.5; wherein the weight ratio of vortioxetine hemihydrobromide or vortioxetine hydrobromide to pharmaceutically acceptable alkaline excipient is 1:0.01-1:1.1, preferably, 1:0.01-1:1.

27. A solid dispersion comprising vortioxetine hemihydrobromide and polyacrylic resin IV, wherein the weight ratio of vortioxetine hemihydrobromide to polyacrylic resin IV is 1:0.1-1:5, preferably, 1:0.3-1:2, more preferably, 1:0.3-

~~1:1.5; preferably, wherein the solid dispersion has characteristic peaks as shown in Figure 20.~~

~~28. A solid dispersion comprising vortioxetine hydrobromide and polyacrylic resin IV, wherein the weight ratio of vortioxetine hydrobromide to polyacrylic resin IV is 1:0.1-1:5, preferably, 1:0.3-1:3, more preferably, 1:0.3-1:1.5; preferably, wherein the solid dispersion has characteristic peaks as shown in Figure 22.~~

~~29. The solid dispersion according to claim 27 or claim 28, wherein Cu-Kα radiation is used, and the X-ray powder diffraction pattern expressed at 2θ angles has characteristic peaks at the following positions: 4.2±0.2°, 14.5±0.2°, 17.4±0.2°, 19.2±0.2°, and 22.6±0.2°.~~

~~30. The solid dispersion according to claim 27 or claim 28, wherein Cu-Kα radiation is used, and the X-ray powder diffraction pattern expressed at 2θ angles has characteristic peaks at the following positions: 4.2±0.2°, 14.5±0.2°, 16.6±0.2°, 17.4±0.2°, 19.2±0.2°, 21.5±0.2°, 22.6±0.2°, 24.4±0.2°, 26.0±0.2°, 28.2±0.2°, and 29.0±0.2°.~~

~~31. The solid dispersion according to claim 27 or claim 28, which further comprises at least one of PEG 4000, PEG 6000 and PEG 8000; preferably, wherein the weight ratio of polyacrylic resin IV to at least one of PEG 4000, PEG 6000, and PEG 8000 is 1:0.05-1:2.~~

~~32. According to any one of the above claims, vortioxetine hemihydrobromide or vortioxetine hydrobromide orally dispersible taste masking compositions, taste masking coated granules, taste masking solid dispersions and taste masking combination in the use of preparing antidepressant drug.~~

~~33. According to any one of the above claims, vortioxetine hemihydrobromide or vortioxetine hydrobromide orally dispersible taste masking compositions, taste masking coated granules, taste masking solid dispersions and taste masking combination, which are used for the treatment of depression disorder or preparing antidepressant drug.~~

~~34. A method for the treatment of depression disorder, which comprises administering the vortioxetine hemihydrobromide or vortioxetine hydrobromide orally dispersible taste masking compositions, taste masking coated granules, taste masking solid dispersions, or taste masking combinations to a subject in need.~~

1. An orally dispersible taste masking composition, comprising vortioxetine hemihydrobromide and pharmaceutically acceptable taste masking

excipients.

2. The orally dispersible taste masking composition according to claim 1, further comprising granules in which the vortioxetine hemihydrobromide is coated with the taste masking excipients.

3. The orally dispersible taste masking composition according to claim 1, further comprising a solid dispersion in which the vortioxetine hemihydrobromide is dispersed in the taste masking excipients.

4. The orally dispersible taste masking composition according to claim 1, wherein the taste masking excipients comprise alkaline excipients selected from the group consisting of trisodium phosphate, disodium hydrogen phosphate, disodium hydrogen phosphate, potassium carbonate, sodium carbonate, sodium bicarbonate, potassium citrate, sodium acetate, calcium hydroxide, sodium hydroxide, potassium hydroxide, and meglumine.

5. The orally dispersible taste masking composition according to claim 2, wherein the taste masking excipients comprise alkaline excipients, the weight ratio of the vortioxetine hemihydrobromide to the taste masking excipients is 1:0.1-1:5, and the weight ratio of the vortioxetine hemihydrobromide to the alkaline excipient is 1:0.01-1:1.1.

6. The orally dispersible taste masking composition according to claim 3, wherein the taste masking excipients comprise alkaline excipients, the weight ratio of the vortioxetine hemihydrobromide to the taste masking excipients is 1:0.1-1:5, and the weight ratio of the vortioxetine hemihydrobromide to the alkaline excipient is 1:0.01-1:1.1.

7. The orally dispersible taste masking composition according to claim 4, wherein the weight ratio of the vortioxetine hemihydrobromide to the alkaline excipients is 1:0.01-1:1.1.

8. The orally dispersible taste masking composition according to claim 5, further comprising a solid dispersion in which the granules are dispersed in the

taste masking excipients.

9. The orally dispersible taste masking composition according to claim 6, further comprising granules in which the solid dispersion is coated with the taste masking excipient.

10. The orally dispersible taste masking composition according to claim 1, wherein the orally dispersible taste masking composition has a crystalline form, and wherein the crystalline form has characteristic peaks at 4.2±0.2° and 17.4±0.2° when Cu-Kα radiation is used and the X-ray powder diffraction pattern is expressed at 2θ angles.

11. The orally dispersible taste masking composition according to claim 1, further comprising a filler, a flavoring agent, a release regulator agent, a plasticizer, an anticaking agent, and/or a disintegrant agent.

12. A method for preparing the orally dispersible taste masking composition according to claim 1, comprising:

(a) dispersing the taste masking excipients in a solvent; coating the vortioxetine hemihydrobromide with the taste masking excipients in the solvent through a fluid bed, whereby a mixture is formed; and removing the solvent from the mixture, whereby vortioxetine hemihydrobromide coated with the taste masking excipients is obtained; or

(b) adding the vortioxetine hemihydrobromide and the taste masking excipients to a solvent to form a suspension; and removing the solvent from the suspension through a fluid bed, spray drying or evaporation, whereby vortioxetine hemihydrobromide coated with the taste masking excipients is obtained;

whereby a composition comprising the coated vortioxetine hemihydrobromide is prepared.

13. A method for preparing the orally dispersible taste masking composition according to claim 1, comprising:

(a) mixing the vortioxetine hemihydrobromide with the taste masking excipients, whereby a combination is formed; heating the combination at 50-150°C, whereby a softened or liquefied mixture is formed; cooling the softened or liquefied mixture, whereby a solidified mixture is formed; and milling the solidified mixture, whereby granules of the vortioxetine hemihydrobromide are obtained; or

(b) dissolving the vortioxetine hemihydrobromide and taste masking excipients in a solvent, whereby a solution is formed; and removing the solvent from the solution by distillation, fluid bed or spray drying, whereby granules of the vortioxetine hemihydrobromide are obtained;

whereby a composition comprising the granules of the vortioxetine hemihydrobromide is obtained.

14. A method for preparing the orally dispersible taste masking composition according to claim 1, wherein the taste masking excipients comprise alkaline excipients, comprising:

(a) mixing the vortioxetine hemihydrobromide with the alkaline excipients, whereby a taste masking combination is obtained; and

(b) preparing the taste masking combination as a composition.

15. The preparation method according to claim 12, wherein the taste masking excipients comprise alkaline excipients, the weight ratio of vortioxetine hemihydrobromide to the taste masking excipients is 1:0.1-1:5, and the weight ratio of vortioxetine hemihydrobromide to alkaline excipient is 1:0.01-1:1.1.

16. The preparation method according to claim 13, wherein the taste masking excipients comprise alkaline excipients, the weight ratio of vortioxetine hemihydrobromide to the taste masking excipients is 1:0.1-1:5, and the weight ratio of vortioxetine hemihydrobromide to alkaline excipient is 1:0.01-1:1.1.

17. The preparation method according to claim 14, wherein the taste masking excipients comprise alkaline excipients, the weight ratio of vortioxetine

hemihydrobromide to the taste masking excipients is 1:0.1-1:5, and the weight ratio of vortioxetine hemihydrobromide to alkaline excipient is 1:0.01-1:1.1.

18. The orally dispersible taste masking composition according to claim 3, wherein the taste masking excipients comprise polyacrylic resin IV, wherein the orally dispersible taste masking composition has a crystalline form, and wherein the crystalline form has characteristic peaks at 4.2±0.2°, 14.5±0.2°, 17.4±0.2°, and 22.6±0.2° when Cu-Kα radiation is used and the X-ray powder diffraction pattern is expressed at 2θ angles.

19. A method for treating a depression disorder in a subject, comprising administering to the subject an effective amount of the orally dispersible taste masking composition according to claim 1.

20. An orally dispersible taste masking composition, comprising vortioxetine hydrobromide and alkaline excipients, wherein the weight ratio of the vortioxetine hydrobromide to the alkaline excipient is 1:0.01-1:1.1, wherein the orally dispersible taste masking composition has a crystalline form, and wherein the crystalline form has characteristic peaks at 4.2±0.2° and 17.4±0.2° when Cu-Kα radiation is used and the X-ray powder diffraction pattern is expressed at 2θ angles.