Claims

1. A tablet comprising:

(1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclo-pentane-1,2-diol; and

at least one disintegrating excipient;

wherein the tablet has a hardness of from 50 to 150N and a disintegration time of less than 3 minutes;

wherein the at least one disintegrating excipient comprises mannitol, xylitol, anhydrous dibasic calcium phosphate, crospovidone and microcrystalline cellulose.

2. The tablet according to Claim 1, wherein the tablet has a disintegration time of less than about 60 seconds.

3. The tablet according to claim 1 or claim 2, wherein the at least one disintegrating excipient is a disintegrating excipient pre-mix that is present in an amount ranging from 50% to 80% by weight of the tablet.

4. The tablet according to any one of the preceding claims, wherein the (1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-

hydroxyethoxy)cyclopentane-1,2-diol is present in an amount of from 10 to 18% by weight.

5. The tablet according to any one of the preceding claims, wherein the tablet comprises 60 mg or 90 mg of (1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol.

6. The tablet according to Claim 5, wherein the tablet comprises about 90 mg of (1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol.

7. The tablet according to any one of the preceding claims, wherein the tablet has a hardness of from 55 to 90N.

8. The tablet according to any one of the preceding claims, wherein the tablet further comprises at least one anti-caking agent.

9. The tablet according to Claim 8, wherein the at least one anti-caking agent is present in an amount of from 0.5 to 1% by weight of the tablet.

10. The tablet according to any one of the preceding claims, wherein the tablet is obtainable by a process comprising wet granulation of:

(1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclo-pentane-1,2-diol; and

an anti-caking agent.

11. The tablet according to Claim 10, wherein the wet granulation process involves the wet granulation of a mixture comprising (1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol in an amount of at least about 35% of by weight of the dry ingredients in the mixture.

12. The tablet according to Claim 10 or Claim 11, wherein the wet granulation process involves the wet granulation of a mixture comprising (1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-

2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol in an amount of up to about 70% by weight of the dry ingredients in the mixture.

13. The tablet according to any one of Claims 10 to 12, wherein the mixture used in the wet granulation process comprises said anti-caking agent in an amount ranging from 0.1 to 1% by weight of the dry ingredients in the mixture.

14. The tablet according to any one of Claims 10 to 13, wherein the product of the wet granulation process comprises granules having a D (v, 0.9) value of less than about 1600 µm.

15. The tablet according to any one of Claims 10 to 14, wherein, after completion of the wet granulation step, the product is mixed with a second amount of an anti-caking agent or a glidant.

16. The tablet according to Claim 15 wherein the second amount of an anti-caking agent or the glidant is present at from 0.2 to 0.6%, preferably from 0.3 to 0.6%, by weight of the tablet.

17. The tablet according to any one of Claims 10 to 16, wherein the tablet is obtainable by a process comprising wet granulation of:

(1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol;

an anti-caking agent; and

a binder.

18. The tablet according to Claim 17, wherein the binder is present in the wet granulation mixture at an amount ranging from 2 to 6%, preferably from 3 to 6%, by weight of the dry ingredients in the mixture.

19. The tablet according to any one of the preceding claims, wherein the tablet comprises one or more lubricants.

20. The tablet according to Claim 19, wherein the lubricant is present in an amount of from 1 to 2% by weight.

21. The tablet according to any one of the preceding claims, wherein the tablet comprises:

(1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol at from 10 to 18% by weight of the tablet;

hydroxypropyl cellulose at from 0.9 to 2% by weight of the tablet;

colloidal anhydrous silica at from 0.5 to 1% by weight of the tablet;

mannitol at from 47 to 67% by weight of the tablet;

xylitol at from 2.5 to 4% by weight of the tablet;

anhydrous dibasic calcium phosphate at from 2 to 3.5% by weight of the tablet;

microcrystalline cellulose at from 9 to 15% by weight of the tablet;

crospovidone at from 5 to 9% by weight of the tablet; and

sodium stearyl fumarate at from 1 to 2% by weight of the tablet.

22. The tablet according to any of the preceding claims, wherein the (1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol has a D (v, 0.9) particle size distribution of from 5 µm to 50 µm.

23. A process for the preparation of a tablet as defined in any one of the preceding claims which comprises the step of mixing together (1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol and at least one anti-caking agent along with, or in, a liquid, so providing a wet granulate.

24. The process according to Claim 23, which further comprises:
(I) drying the wet granulate mixture,
(II) adding one or more excipients to the dried granulates, and then
(III) forming the mixture into tablets.

25. The process according to Claim 24, wherein the one or more excipients includes at least one disintegrating excipient as defined in any one of Claims 1 to 3, a second amount of an anti-caking agent as defined in Claim 15 or Claim 16, and/or a lubricant as defined in Claim 19 or Claim 20.

26. Use of a composition comprising:

(1*S*,2*S*,3*R*,5*S*)-3-[7-{[(1*R*,2*S*)-2-(3,4-difluorophenyl)cyclopropyl]amino}-5-(propylthio)-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidin-3-yl]-5-(2-hydroxyethoxy)cyclopentane-1,2-diol; and

at least one disintegrating excipient;

in the manufacture of a medicament for use in treating or preventing atherothrombotic events in patients with cardiovascular disease, wherein the medicament is in the form of a tablet as defined in any one of Claims 1 to 22.

27. The use according to Claim 26, wherein the atherothrombotic events are selected from the group consisting of cardiovascular death, myocardial infarction, stroke and peripheral arterial disease.

28. The use according to any one of Claims 26 to 27, wherein said medicament is to be administered to an elderly patient.

29. The use according to any one of Claims 26 to 28, wherein said medicament is to be administered to a patient that has suffered a myocardial infarction or a stroke.