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(54) Benævnelse: **Solid dosage form of olmesartan medoxomil and amlodipine**

(57) Sammendrag:

The invention relates to a stable solid dosage form comprising olmesartan medoxomil and amlodipine or a pharmacologically acceptable salt thereof. In particular, it relates to solid dosage forms free from reducing sugars. The stable solid dosage form may optionally further comprise hydrochlorothiazide or a pharmacologically acceptable salt thereof.

CLAIMS

1. A solid dosage form comprising olmesartan medoxomil and amlodipine or a pharmacologically acceptable salt thereof, having less than 2.5 % concentration (w/w) of 4-(1-hydroxy-1-methylethyl)-2-propyl-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-imidazol-5-carboxylic acid (RNH-6270).

2. A solid dosage form comprising olmesartan medoxomil and amlodipine or a pharmacologically acceptable salt thereof, having less than 0.4 % concentration (w/w) of 3-ethyl-5-methyl-2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methylpyridine-3,5-dicarboxylate (Impurity D).

3. A solid dosage form comprising olmesartan medoxomil and amlodipine or a pharmacologically acceptable salt thereof, having less than 5.1 % concentration (w/w) of total impurities.

4. A solid dosage form comprising olmesartan medoxomil and amlodipine or a pharmacologically acceptable salt thereof, having less than 2.5 % concentration (w/w) of RNH-6270 and less than 5.1 % concentration (w/w) of total impurities.

5. A solid dosage form according to claim 1 or claim 2, further comprising hydrochlorothiazide or a pharmacologically acceptable salt thereof.

6. A solid dosage form according to claim 5, having less than 7.3% concentration (w/w) of total impurities.

7. A solid dosage form comprising olmesartan medoxomil and amlodipine or a pharmacologically acceptable salt thereof, wherein said solid dosage form is substantially free of reducing sugars.

8. A solid dosage form according to claim 1, wherein said solid dosage form is substantially free of a reducing sugars.

9. A solid dosage form according to claim 2, wherein said solid dosage form is substantially free of reducing sugars.

10. A solid dosage form according to claim 3, wherein said solid dosage form is substantially free of reducing sugars.

11. A solid dosage form according to claim 4, wherein said solid dosage form is substantially free of reducing sugars.

12. A solid dosage form according to claim 5 or claim 6, wherein said solid dosage form is substantially free of reducing sugars.

13. A solid dosage form according to any one of claims 7 to 12, wherein said solid dosage form has less than 2.0 % (w/w) of reducing sugars.

14. A solid dosage form according to any one of claims 7 to 12, wherein said solid dosage form has less than 0.3 % (w/w) of reducing sugars.

15. A solid dosage form according to any one of claims 7 to 12, wherein said solid dosage form has less than 0.05 % (w/w) of reducing sugars.

16. The solid dosage form according to any one of claims 1, 5 and 7 to 15 having less than 0.5 % concentration (w/w) of RNH-6270.

17. The solid dosage form according to any one of claims 1, 5 and 7 to 15 having less than 0.4 % concentration (w/w) of RNH-6270.

18. The solid dosage form according to any one of claims 2, 5 and 7 to 15, having less than 0.3 % concentration (w/w) of Impurity D.

19. The solid dosage form according to any one of claims 2, 5 and 7 to 15, having less than 0.05 % concentration (w/w) of Impurity D.

20. The solid dosage form according to any one of claims 3 and 5 to 15, having less than 1.5 % concentration (w/w) of total impurities.

21. The solid dosage form according to any one of claims 4 to 15, having less than 0.5 % concentration (w/w) of RNH-6270 and less than 1.5 % concentration (w/w) of total impurities.

22. The solid dosage form according to any one of claims 4 to 15, having less than 0.4 % concentration (w/w) of RNH-6270 and less than 1.5 % concentration (w/w) of total impurities.

23. The solid dosage form according to any one of claims 1 to 6 and 16 to 22 wherein the concentration of said impurity or impurities is that measured after accelerated testing of said solid dosage form for three months at 40°C and 75% relative humidity.

24. The solid dosage form according to any one of claims 1 to 23 wherein the amlodipine is present in the form of its besylate salt.

25. The solid dosage form according to any one of claims 1 to 24, further comprising one or more pharmacologically acceptable additives.

26. The solid dosage form according to claim 25, wherein the one or more pharmacologically acceptable additives are selected from excipients, lubricants, binders, disintegrants, emulsifiers, stabilizers, correctives and diluents.

27. The solid dosage form according to claim 26, wherein the excipient is silicified microcrystalline cellulose and/or mannitol.

28. The solid dosage form according to claim 26, wherein the lubricant is magnesium stearate.

29. The solid dosage form according to claim 26, wherein the disintegrant is pregelatinised starch and/or croscarmellose sodium.

30. The solid dosage form according to any one of claims 1 to 29, wherein the solid dosage form comprises a tablet.

31. The solid dosage form according to claim 30, wherein the tablet is prepared by direct compression.

32. The solid dosage form according to 30 or claim 31 wherein the tablet is coated with at least one elastic film.

33. The solid dosage form according to claim 32, wherein the elastic film contains at least one hydrophilic polymer.

34. The solid dosage form according to claim 33, wherein the hydrophilic polymer is polyvinyl alcohol and/or macrogol.

35. The solid dosage form according to any one of claims 1 to 34, comprising 20 to 40 mg of olmesartan medoxomil.

36. The solid dosage form according to any one of claims 1 to 35, comprising 5 to 10 mg of amlodipine or a pharmacologically acceptable salt of amlodipine equivalent to 5 to 10 mg of amlodipine.

37. The solid dosage form according to any one of claims 1 to 36, comprising 12.5 to 25 mg of hydrochlorothiazide or a pharmacologically acceptable salt of hydrochlorothiazide equivalent to 12.5 to 25 mg of hydrochlorothiazide.

38. A method for the treatment or prophylaxis of hypertension in a warm-blooded animal in need thereof, comprising administering to said animal an effective amount of a solid dosage form according to any one of claims 1 to 37.

39. Use of a solid dosage form according to any one of claims 1 to 37 in the manufacture of a medicament for the treatment or prophylaxis of hypertension.

40. A solid dosage form according to any one of claims 1 to 37 for use in the treatment or prophylaxis of hypertension.

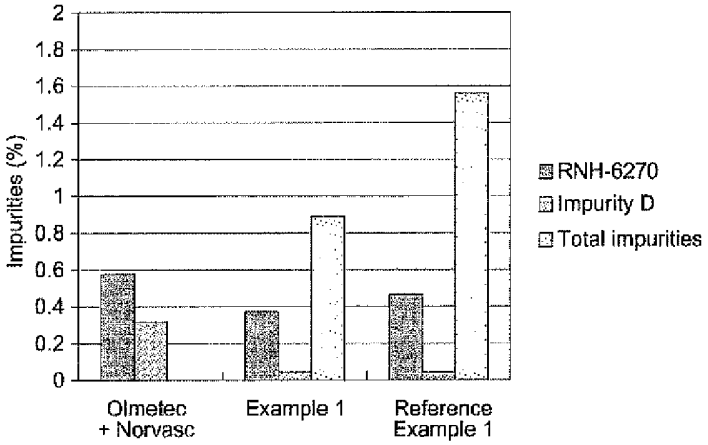

2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Impurities (%)
Olmetec + Norvasc
Example 1
Reference Example 1
RNH-6270
Impurity D
Total impurities

Fig. 1

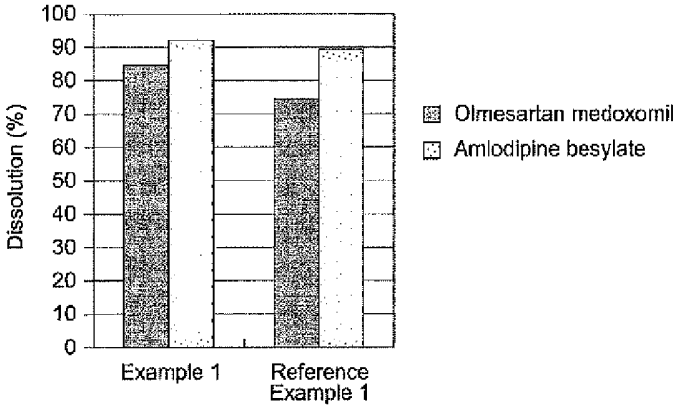

100
90
80
70
60
50
40
30
20
10
0
Dissolution (%)
Example 1
Reference Example 1
Olmesartan medoxomil
Amlodipine besylate

Fig. 2