

Claims

1. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients, wherein the dosage of macitentan is from 20 mg per day to 300 mg per day.
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2. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 1, wherein the treatment means the reduction of morbidity and/or mortality risk of pulmonary vascular disease and/or cardiac dysfunction
10 in functional single ventricular heart disease patients, especially in Fontan-palliated patients.
3. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 1 or 2, wherein the dosage of macitentan is 20 mg per day to 250 mg per day.
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4. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 3, wherein the dosage of macitentan is 60 to 90 mg per day, preferably 65 to 85 mg per day, more preferably 70 to 80 mg per day and most preferably 75 mg per day.
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5. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 3, wherein the dosage of macitentan is 25 to 50 mg per day, preferably 30 to 45 mg per day, more preferably 35 to 40 mg per day and most preferably 37.5 mg per day.
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6. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 3, wherein the dosage of macitentan is 110 to 200 mg per day, preferably 125 to 175 mg per day, more preferably 140 to 160 mg per day and most preferably 150 mg per day.
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7. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-

palliated patients according to any one of claims 1 to 3, wherein the dosage of macitentan is 60 to 90 mg twice per day, preferably 65 to 85 mg twice per day, more preferably 70 to 80 mg twice per day and most preferably 75 mg twice per day.

8. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 3, wherein the dosage of macitentan is 25 to 50 mg twice per day, preferably 30 to 45 mg twice per day, more preferably 35 to 40 mg twice per day and most preferably 37.5 mg twice per day.

9. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 3, wherein the dosage of macitentan is escalated from 10 mg per day, followed by 25 to 50 mg per day, preferably 37.5 mg per day, and optionally followed by 60 to 90 mg per day, preferably 75 mg per day.

10. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 3, wherein the dosage of macitentan is escalated from 10 mg per day, followed by 60 to 90 mg per day, preferably 75 mg once per day or 37.5 mg twice a day.

11. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 9, wherein the dosage of macitentan is escalated from 10 mg once per day, preferably for 15 to 45 days; followed by 25 to 50 mg per day, preferably 37.5 mg once per day, preferably for 15 to 45 days; and optionally followed by 60 to 90 mg per day, preferably by 75 mg once per day or 37.5 mg twice per day.

12. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 10, wherein the dosage of macitentan is escalated from 10 mg once per day, preferably for 15 to 45 days; followed by 60 to 90 mg per day, preferably by 75 mg once per day or 37.5 mg twice per day.

13. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 4, wherein the dosage of macitentan

is escalated from 25 to 50 mg per day, preferably 37.5 mg per day, preferably for 15 to 45 days; optionally followed by 60 to 90 mg per day, preferably by 75 mg per day; provided that the patient is already treated with an endothelin receptor antagonist preferably selected from bosentan and ambrisentan.

5 14. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 4, wherein the dosage of macitentan is 60 to 90 mg per day, preferably 75 mg per day; provided that the patient is already
10 treated with an endothelin receptor antagonist preferably selected from bosentan and ambrisentan.

15 15. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 1 to 14, wherein macitentan is combined with a PDE5 inhibitor and/or a prostacyclin analogue, and/or a prostacyclin receptor
agonist and/or a soluble guanylate cyclase stimulator.

16. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 15, wherein the PDE5 inhibitor is selected from sildenafil, tadalafil, vardenafil, and udenafil; the prostacyclin analogue is selected from
20 epoprostenol, treprostinil, iloprost, and beraprost; the prostacyclin receptor agonist is selected from selexipag and ralinepag; and the soluble guanylate cyclase stimulator is selected from riociguat and vericiguat.

17. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 15 or 16, wherein macitentan is combined with
25 tadalafil and/or selexipag or ralinepag, preferably with tadalafil and/or selexipag.

18. Macitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 17, wherein tadalafil, if applicable, has a dose of 20
30 to 40 mg per day, preferably 40 mg per day, selexipag, if applicable, has a dose of 0.2 to 1.6 mg twice per day and ralinepag, if applicable, has a dose of 0.05 to 1.45 mg per day.

19. A pharmaceutical composition for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients comprising macitentan and at least a pharmaceutically acceptable excipient, containing macitentan in an amount of 20 mg to 300 mg.
20. A pharmaceutical composition according to claim 19, which contains macitentan in an amount of 20 mg to 250 mg, preferably 37.5 mg, 75 mg or 150 mg, more preferably 37.5 mg or 75 mg, most preferably 75 mg.
21. The pharmaceutical composition according to claim 19 or 20, which comprises
- (i) macitentan in a total amount of 10 to 50% in weight based on the total weight of the pharmaceutical composition,
- (ii) a filler, consisting of lactose monohydrate with microcrystalline cellulose, in a total amount of 10 to 85% in weight based on the total weight of the pharmaceutical composition,
- (iii) a disintegrant, consisting of sodium starch glycolate or a combination of sodium starch glycolate and polyvinylpyrrolidone, in a total amount of 1 to 10% in weight based on the total weight of the pharmaceutical composition,
- (iv) a surfactant, consisting of a polysorbate, in a total amount of 0.1 to 1% in weight based on the total weight of the pharmaceutical composition, and
- (v) a lubricant, consisting of magnesium stearate, in a total amount of 0.05 to 5% in weight based on the total weight of the pharmaceutical composition.
22. The pharmaceutical composition according to any one of claims 19 to 21, which is in the form of a capsule or a tablet.
23. Aprocitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients, wherein the dosage of aprocitentan is 100 mg per day to 1500 mg per day.
24. Aprocitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 23, wherein the treatment means the reduction of morbidity and/or mortality risk of pulmonary vascular disease and/or cardiac dysfunction

in functional single ventricular heart disease patients, especially in Fontan-palliated patients.

25. Aprocitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to claim 23 or 24, wherein the dosage of aprocitentan is 100 mg per day to 1250 mg per day.

26. Aprocitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 23 to 25, wherein the dosage of aprocitentan is 300 to 450 mg per day, preferably 325 to 425 mg per day, more preferably 350 to 400 mg per day and most preferably 375 mg per day.

27. Aprocitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 23 to 26, wherein the dosage of aprocitentan is 125 to 250 mg per day, preferably 150 to 225 mg per day, more preferably 175 to 200 mg per day and most preferably 187.5 mg per day.

28. Aprocitentan for use in the treatment of pulmonary vascular disease and/or cardiac dysfunction in functional single ventricular heart disease patients, especially in Fontan-palliated patients according to any one of claims 23 to 27, wherein the dosage of aprocitentan is escalated from 50 mg per day, followed by 125 to 250 mg per day, preferably 187.5 mg per day, and optionally followed by 300 to 450 mg per day, preferably 375 mg per day.