Claims

1. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the concentration of the prostacyclin compound is sufficient to maintain a therapeutically effective level of prostacyclin in blood plasma for at least 12 hours after a single subcutaneous or intramuscular injection.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises the prostacyclin compound in a concentration of at least 0.05 mg/ml.

3. The pharmaceutical composition comprising a prostacyclin compound of claim 1 or 2 in a concentration of at least 0.05 mg/ml, and wherein a single dose of the pharmaceutical composition comprises at least 0.05 mg of the prostacyclin compound.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein the time period between administration of a pharmaceutical composition is at least about 12 hours, such as at least 16 hours, typically at least one day.

5. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the pharmaceutical composition is characterized by having a pharmacokinetic profile in vivo in a mammal, in particular in a human, with substantially no burst of the prostacyclin compound.

6. The pharmaceutical composition of any one of claims 1 to 4, wherein the pharmaceutical composition is characterized by having a pharmacokinetic profile in vivo in a mammal, in particular in a human, with substantially no burst of the prostacyclin compound.

7. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the pharmaceutical composition is characterized by exhibiting a peak to trough ratio of the prostacyclin

compound in a mammal, in particular in a human, of less than 5, such as less than 3, or less than 2.

8. The pharmaceutical composition of any one of claims 1 to 6, wherein the pharmaceutical composition is characterized by exhibiting a peak to trough ratio of the prostacyclin compound in a mammal, in particular in a human, of less than 5, such as less than 3, or less than 2.

9. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the prostacyclin compound has an activity of < 20%, preferably < 10%, more preferably < 5% of the activity of free prostacyclin.

10. The pharmaceutical composition of any one of claims 1 to 8, wherein the prostacyclin compound has an activity of < 20%, preferably < 10%, more preferably < 5% of the activity of free prostacyclin.

11. A pharmaceutical composition comprising a prostacyclin prodrug, and optionally one or more pharmaceutically acceptable excipients, wherein the pharmaceutical composition is characterized in that after subcutaneous or intramuscular administration of said prostacyclin prodrug more than 50% of the administered prostacyclin dose is releasable within the blood compartment.

12. The pharmaceutical composition of any one of claims 1 to 10 wherein the prostacylin compound is a prostacyclin prodrug characterized in that after subcutaneous or intramuscular administration of said prostacyclin prodrug more than 50% of the administered prostacyclin dose is releasable within the blood compartment.

13. The pharmaceutical composition of any one of claims 1 to 10, wherein the prostacyclin compound is in a depot, preferably a polymer gel, even more preferably a hydrogel, most preferably a hydrated polymer matrix.

14. The pharmaceutical composition of claim 13, wherein the prostacyclin compound is covalently linked to a compound in the depot, preferably to the polymer gel, even more preferably to the hydrogel, most preferably tothe well hydrated polymer matrix.

15. The pharmaceutical composition of any of claims 1 to 15, wherein the prostacyclin compound is a prodrug of prostacyclin.

16. The pharmaceutical composition of claim 15, wherein the promoiety of the prodrug comprises a linear or branched PEG moiety.

17. A pharmaceutical composition comprising a prostacyclin prodrug, wherein said pharmaceutical composition is characterized in that the prostacyclin compound releases prostacyclin in a plasma-independet manner.

18. The pharmaceutical composition of any one of claims 5 to 17, characterized by being administered by injection, preferably subcutaneous or intramuscular injection.

19. A pharmaceutical composition of any of claims 1 to 18, for use in the treatment or prevention of pulmonary hypertension, ischemic diseases, preferably peripheral vascular disease including peripheral arterial disease, Raynaud's phenomenon including Raynaud's disease and Raynaud's syndrome, scleroderma including systemic sclerosis, myocardial ischemia, ischemic stroke, renal insufficiency, ischemic ulcers including digital ulcers, heart failure, in particular congestive heart failure, portopulmonary hypertension, interstitial lung disease, idiopathic pulmonary fibrosis, conditions requiring anticoagulation, in particular post MI, post cardiac surgery, thrombotic microangiopathy, extracorporeal circulation, central retinal vein occlusion, atherosclerosis, inflammatory diseases, in particular COPD, psoriasis, hypertension, in particular preeclampsia, reproduction and parturition, cancer or other conditions of unregulated cell growth, cell/tissue preservation and other emerging therapeutic areas where prostacyclin treatment appears to have a beneficial role.

20. A method for treating pulmonary hypertension, wherein the method comprises the step of subcutaneous or intramuscular administration, to a patient with pulmonary hypertension, of a pharmaceutical composition comprising

(a) a polymer carrier-linked prostacyclin prodrug, and optionally one or more pharmaceutically acceptable excipients, or

(b) a prostacyclin compound and at least one polymer, and optionally one or more pharmaceutically acceptable excipients,

wherein the pharmaceutical composition releases therapeutically effective amounts of free prostacyclin compound for a period of time of at least 12 hours.

21. The method of claim 20, wherein the pharmaceutical composition of (b) comprises from about 0.05 to about 10weight percent the prostacyclin compound and from about 0.5 to about 20 weight percent total polymer content.

Claims

1. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the concentration of the prostacyclin compound is sufficient to maintain a therapeutically effective level of prostacyclin in blood plasma for at least 12 hours after a single subcutaneous or intramuscular injection.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises the prostacyclin compound in a concentration of at least 0.05 mg/ml.

3. The pharmaceutical composition comprising a prostacyclin compound of claim 1 or 2 in a concentration of at least 0.05 mg/ml, and wherein a single dose of the pharmaceutical composition comprises at least 0.05 mg of the prostacyclin compound.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein the time period between administration of a pharmaceutical composition is at least about 12 hours, such as at least 16 hours, typically at least one day.

5. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the pharmaceutical composition is characterized by having a pharmacokinetic profile in vivo in a mammal, in particular in a human, with substantially no burst of the prostacyclin compound.

6. The pharmaceutical composition of any one of claims 1 to 4, wherein the pharmaceutical composition is characterized by having a pharmacokinetic profile in vivo in a mammal, in particular in a human, with substantially no burst of the prostacyclin compound.

7. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the pharmaceutical composition is characterized by exhibiting a peak to trough ratio of the prostacyclin

compound in a mammal, in particular in a human, of less than 5, such as less than 3, or less than 2.

8. The pharmaceutical composition of any one of claims 1 to 6, wherein the pharmaceutical composition is characterized by exhibiting a peak to trough ratio of the prostacyclin compound in a mammal, in particular in a human, of less than 5, such as less than 3, or less than 2.

9. A pharmaceutical composition comprising a prostacyclin compound, and optionally one or more pharmaceutically acceptable excipients, wherein the prostacyclin compound has an activity of < 20%, preferably < 10%, more preferably < 5% of the activity of free prostacyclin.

10. The pharmaceutical composition of any one of claims 1 to 8, wherein the prostacyclin compound has an activity of < 20%, preferably < 10%, more preferably < 5% of the activity of free prostacyclin.

11. A pharmaceutical composition comprising a prostacyclin prodrug, and optionally one or more pharmaceutically acceptable excipients, wherein the pharmaceutical composition is characterized in that after subcutaneous or intramuscular administration of said prostacyclin prodrug more than 50% of the administered prostacyclin dose is releasable within the blood compartment.

12. The pharmaceutical composition of any one of claims 1 to 10 wherein the prostacylin compound is a prostacyclin prodrug characterized in that after subcutaneous or intramuscular administration of said prostacyclin prodrug more than 50% of the administered prostacyclin dose is releasable within the blood compartment.

13. The pharmaceutical composition of any one of claims 1 to 10, wherein the prostacyclin compound is in a depot, preferably a polymer gel, even more preferably a hydrogel, most preferably a hydrated polymer matrix.

14. The pharmaceutical composition of claim 13, wherein the prostacyclin compound is covalently linked to a compound in the depot, preferably to the polymer gel, even more preferably to the hydrogel, most preferably tothe well hydrated polymer matrix.

15. The pharmaceutical composition of any of claims 1 to 15, wherein the prostacyclin compound is a prodrug of prostacyclin.

16. The pharmaceutical composition of claim 15, wherein the promoiety of the prodrug comprises a linear or branched PEG moiety.

17. A pharmaceutical composition comprising a prostacyclin prodrug, wherein said pharmaceutical composition is characterized in that the prostacyclin compound releases prostacyclin in a plasma-independet manner

18. The pharmaceutical composition of any one of claims 5 to 17, characterized by being administered by injection, preferably subcutaneous or intramuscular injection.

19. A pharmaceutical composition of any of claims 1 to 18, for use in the treatment or prevention of pulmonary hypertension, ischemic diseases, preferably peripheral vascular disease including peripheral arterial disease, Raynaud's phenomenon including Raynaud's disease and Raynaud's syndrome, scleroderma including systemic sclerosis, myocardial ischemia, ischemic stroke, renal insufficiency, ischemic ulcers including digital ulcers, heart failure, in particular congestive heart failure, portopulmonary hypertension, interstitial lung disease, idiopathic pulmonary fibrosis, conditions requiring anticoagulation, in particular post MI, post cardiac surgery, thrombotic microangiopathy, extracorporeal circulation, central retinal vein occlusion, atherosclerosis, inflammatory diseases, in particular COPD, psoriasis, hypertension, in particular preeclampsia, reproduction and parturition, cancer or other conditions of unregulated cell growth, cell/tissue preservation and other emerging therapeutic areas where prostacyclin treatment appears to have a beneficial role.

20. A pharmaceutical composition for use in the treatment of prevention of pulmonary hypertension, wherein the method comprises the step of subcutaneous or intramuscular

administration, to a patient with pulmonary hypertension, of a pharmaceutical composition comprising

(a) a polymer carrier-linked prostacyclin prodrug, and optionally one or more pharmaceutically acceptable excipients, or

(b) a prostacyclin compound and at least one polymer, and optionally one or more pharmaceutically acceptable excipients,

wherein the pharmaceutical composition releases therapeutically effective amounts of free prostacyclin compound for a period of time of at least 12 hours.

21. The pharmaceutical composition of claim 20, wherein the pharmaceutical composition of (b) comprises from about 0.05 to about 10weight percent the prostacyclin compound and from about 0.5 to about 20 weight percent total polymer content.