Claims

1. A pharmaceutical composition containing, as active principles, aprocitentan, or a pharmaceutically acceptable salt thereof, in combination with an angiotensin receptor blocker which is valsartan, or a pharmaceutically acceptable salt thereof;

as well as at least one pharmaceutically acceptable excipient

2. A pharmaceutical composition according to claim 1 containing, as active principles, aprocitentan, or a pharmaceutically acceptable salt thereof, in combination with

- an angiotensin receptor blocker which is valsartan, or a pharmaceutically acceptable salt thereof;
- a calcium channel blocker which is amlodipine, or a pharmaceutically acceptable salt thereof; and
- a diuretic which is a thiazide-like diuretic, or a pharmaceutically acceptable salt thereof;

as well as at least one pharmaceutically acceptable excipient.

3. A pharmaceutical composition according to claim 2 wherein the diuretic is hydrochlorothiazide or chlorthalidone.

4. A pharmaceutical composition according to claim 3 wherein

- aprocitentan is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 2.5 to 100 mg per day of aprocitentan;
- valsartan or a pharmaceutically acceptable salt thereof is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 100 to 320 mg per day of valsartan;
- amlodipine or a pharmaceutically acceptable salt thereof is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 2 to 10 mg per day of amlodipine; and
- hydrochlorothiazide or a pharmaceutically acceptable salt thereof, if present, is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 5 to 25 mg per day of hydrochlorothiazide; and chlorthalidone or a pharmaceutically acceptable salt thereof, if present, is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 10 to 150 mg per day of chlorthalidone.

5. A pharmaceutical composition according to claim 4, wherein the diuretic is hydrochlorothiazide.

6. A pharmaceutical composition according to claim 5 wherein

- aprocitentan is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 2.5 to 100 mg per day of aprocitentan;
- valsartan or a pharmaceutically acceptable salt thereof is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 100 to 320 mg per day of valsartan;

- amlodipine or a pharmaceutically acceptable salt thereof is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 2 to 10 mg per day of amlodipine; and
- hydrochlorothiazide or a pharmaceutically acceptable salt thereof is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 5 to 25 mg per day of hydrochlorothiazide.

7. A pharmaceutical composition according to any one of claims 1 to 6, said composition comprising aprocitentan in crystalline Form A characterized by the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ: 17.8°, 18.6°, 20.0°, 23.2° and 23.5°; wherein said X-ray powder diffraction diagram is obtained by using combined Cu Kα1 and Kα2 radiation, without Kα2 stripping; and the accuracy of the 2θ values is in the range of 2θ +/- 0.2°.

8. A pharmaceutical composition containing, as active principles, aprocitentan in crystalline Form A characterized by the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ: 17.8°, 18.6°, 20.0°, 23.2° and 23.5°; wherein said X-ray powder diffraction diagram is obtained by using combined Cu Kα1 and Kα2 radiation, without Kα2 stripping; and the accuracy of the 2θ values is in the range of 2θ +/- 0.2°;
in combination with an angiotensin receptor blocker, or a pharmaceutically acceptable salt thereof; as well as at least one pharmaceutically acceptable excipient.

9. A pharmaceutical composition according to claim 8, containing, as active principles, aprocitentan in crystalline Form A, in combination with

- an angiotensin receptor blocker, or a pharmaceutically acceptable salt thereof;
- a calcium channel blocker, or a pharmaceutically acceptable salt thereof; and
- a diuretic which is a thiazide-like diuretic, or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition according to claim 2 wherein the diuretic is hydrochlorothiazide or chlorthalidone.

11. The use of aprocitentan, or of a pharmaceutically acceptable salt thereof, in the preparation of a medicament for use in the treatment of hypertension including resistant hypertension; heart failure including chronic heart failure; diastolic dysfunction; chronic kidney disease (CKD) including CKD of stages 1 to 4 caused by or associated with essential hypertension; or for use in the reduction of the risk of developing a major cardiovascular event in patients who have diabetes that is accompanied by at least one other cardiovascular risk factor comprising hypertension;
wherein said medicament is to be administered in combination with an angiotensin receptor blocker which is valsartan, or a pharmaceutically acceptable salt thereof.

12. The use of aprocitentan, or a pharmaceutically acceptable salt thereof, according to claim 10; wherein said medicament is to be administered in combination with

- an angiotensin receptor blocker which is valsartan or a pharmaceutically acceptable salt thereof,

- a calcium channel blocker which is amlodipine, or a pharmaceutically acceptable salt thereof; and
- a diuretic which is a thiazide-like diuretic wherein said diuretic is hydrochlorothiazide or a pharmaceutically acceptable salt thereof, or chlorthalidone or a pharmaceutically acceptable salt thereof.

13. The use of aprocitentan, or of a pharmaceutically acceptable salt thereof, according to claim 12; wherein • said medicament is to be administered in a pharmaceutical unit dosage form suitable for the oral administration of 10 to 50 mg per day of aprocitentan;

wherein

• valsartan or a pharmaceutically acceptable salt thereof is is to be administered in a pharmaceutical unit dosage form suitable for the oral administration of 100 to 320 mg per day of valsartan;

• amlodipine or a pharmaceutically acceptable salt thereof is is to be administered in a pharmaceutical unit dosage form suitable for the oral administration of 2 to 10 mg per day of amlodipine; and

• hydrochlorothiazide or a pharmaceutically acceptable salt thereof, if present, is to be administered in a pharmaceutical unit dosage form suitable for the oral administration of 5 to 25 mg per day of hydrochlorothiazide; and chlorthalidone or a pharmaceutically acceptable salt thereof, if present, is to be administered in a pharmaceutical unit dosage form suitable for the oral administration of 10 to 150 mg per day of chlorthalidone.

14. The use of aprocitentan, or of a pharmaceutically acceptable salt thereof, according to claim 12 or 13; wherein said diuretic is hydrochlorothiazide or a pharmaceutically acceptable salt thereof.

15. The use of aprocitentan, or of a pharmaceutically acceptable salt thereof, according to claim 13; wherein said medicament is for the treatment of resistant hypertension.

16. The use of aprocitentan, or of a pharmaceutically acceptable salt thereof, according to claim 14; wherein said medicament is for the treatment of resistant hypertension.

17. The use of aprocitentan, or of a pharmaceutically acceptable salt thereof, according to any one of claims claim 11 to 13; wherein said medicament is for the treatment of CKD of stages 1 to 4 caused by essential hypertension; or for use in the reduction of the risk of developing a major cardiovascular event in patients who have diabetes that is accompanied by at least one other cardiovascular risk factor comprising hypertension.

18. The use of aprocitentan in the preparation of a medicament for use in the treatment of hypertension including resistant hypertension; heart failure including chronic heart failure; diastolic dysfunction; chronic kidney disease (CKD) including CKD of stages 1 to 4 caused by or associated with essential hypertension; or for use in the reduction of the risk of developing a major cardiovascular event in patients who have diabetes that is accompanied by at least one other cardiovascular risk factor comprising hypertension;

wherein aprocitentan in crystalline Form A is used in the preparation of said medicament;

wherein said crystalline Form A is characterized by the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ: 17.8°, 18.6°, 20.0°, 23.2° and 23.5°; wherein said X-ray powder diffraction diagram is obtained by using combined Cu Kα1 and Kα2 radiation, without Kα2 stripping; and the accuracy of the 2θ values is in the range of 2θ +/- 0.2°;

wherein said medicament is to be administered in combination with an angiotensin receptor blocker, or a pharmaceutically acceptable salt thereof.

19. The use of aprocitentan in crystalline Form A according to claim 18;

wherein said medicament is to be administered in combination with

- an angiotensin receptor blocker, or a pharmaceutically acceptable salt thereof;
- a calcium channel blocker, or a pharmaceutically acceptable salt thereof; and
- a diuretic which is a thiazide-like diuretic, or a pharmaceutically acceptable salt thereof.

20. The use of aprocitentan in crystalline Form A according to claim 19 wherein the diuretic is hydrochlorothiazide or chlorthalidone.

21. The use of aprocitentan in crystalline Form A according to any one of claims 18 to 20; wherein said medicament is for the treatment of resistant hypertension.

22. The use of aprocitentan in crystalline Form A according to any one of claims 18 to 20; wherein said medicament is for the treatment of CKD of stages 1 to 4 caused by with essential hypertension; or for use in the reduction of the risk of developing a major cardiovascular event in patients who have diabetes that is accompanied by at least one other cardiovascular risk factor comprising hypertension.