Claims

1. A pharmaceutical composition containing, as active principles, aprocitentan, or a pharmaceutically acceptable salt thereof, in combination with an SGLT-2 inhibitor, which is canagliflozin, dapagliflozin, or empagliflozin, or a pharmaceutically acceptable salt thereof, as well as at least one pharmaceutically acceptable excipient;

wherein said pharmaceutical composition is

- for preventing or treating chronic kidney disease (CKD), including CKD caused by / associated with hypertension, and/or caused by / associated with diabetes; acute or chronic renal failure; diabetic nephropathy; or glomerulonephritis;
- for reducing the risk of developing a major cardiovascular event in patients who have diabetes, wherein said diabetes is accompanied by at least one other cardiovascular risk factor comprising hypertension; or
- for treating hypertension including resistant hypertension.

2. The pharmaceutical composition according to claim 1, wherein said composition is

- for preventing or treating CKD caused by / associated with hypertension;
- for preventing or treating diabetic kidney disease (DKD)) associated, in addition, with hypertension;
- for preventing or treating chronic renal failure caused by / associated with hypertension or caused by / associated with diabetes; diabetic nephropathy; or glomerulonephritis caused by / associated with hypertension; or
- for reducing the risk of developing a major cardiovascular event in patients who have diabetes, wherein said diabetes is accompanied by at least one other cardiovascular risk factor comprising hypertension.

3. The pharmaceutical composition according to claim 1 or 2, wherein the SGLT-2 inhibitor is canagliflozin, or a pharmaceutically acceptable salt thereof.

4. The pharmaceutical composition according to claim 1 or 2, wherein the SGLT-2 inhibitor is dapagliflozin, or a pharmaceutically acceptable salt thereof.

5. The pharmaceutical composition according to claim 1 or 2, wherein the SGLT-2 inhibitor is c empagliflozin, or a pharmaceutically acceptable salt thereof.

6. The pharmaceutical composition according to claims 1 or 2, wherein aprocitentan, or a pharmaceutically acceptable salt thereof, is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 10 to 50 mg per day of aprocitentan.

7. The pharmaceutical composition according to claim 1, wherein

- aprocitentan, or a pharmaceutically acceptable salt thereof, is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 10 to 50 mg per day of aprocitentan;
- canagliflozin, or a pharmaceutically acceptable salt thereof, if present, is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 50 to 400 mg per day of canagliflozin;
- dapagliflozin, or a pharmaceutically acceptable salt thereof, if present, is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 1 to 20 mg per day of dapagliflozin; and
- empagliflozin, or a pharmaceutically acceptable salt thereof, if present, is comprised in a pharmaceutical unit dosage form suitable for the oral administration of 5 to 50 mg per day of empagliflozin.

8. The pharmaceutical composition according to any one of claims 1 to 8, said composition comprising aprocitentan in crystalline form, wherein said crystalline form 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°.

9. Use of aprocitentan, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament

- for preventing or treating chronic kidney disease (CKD), including CKD caused by / associated with hypertension, and/or caused by / associated with diabetes; acute or chronic renal failure; diabetic nephropathy; or glomerulonephritis;
- for reducing the risk of developing a major cardiovascular event in patients who have diabetes, wherein said diabetes is accompanied by at least one other cardiovascular risk factor comprising hypertension;
- for treating hypertension including resistant hypertension;

wherein aprocitentan is to be administered in combination with an SGLT-2 inhibitor which is canagliflozin, dapagliflozin, or empagliflozin, or a pharmaceutically acceptable salt thereof.

10. The use according to claim 9, wherein said medicament is

- for preventing or treating CKD caused by / associated with hypertension;
- for preventing or treating diabetic kidney disease (DKD) associated, in addition, with hypertension;
- for preventing or treating chronic renal failure caused by / associated with hypertension or caused by / associated with diabetes; diabetic nephropathy; or glomerulonephritis caused by / associated with hypertension; or

- for reducing the risk of developing a major cardiovascular event in patients who have diabetes, wherein said diabetes is accompanied by at least one other cardiovascular risk factor comprising hypertension.

11. The use according to claim 9 wherein said medicament is for treating diabetic kidney disease (DKD) associated, in addition, with hypertension.

12. The use according to any one of claims 9, 10, or 11, wherein said SGLT-2 inhibitor is canagliflozin, or a pharmaceutically acceptable salt thereof.

13. The use according to any one of claims 9, 10 or 11, wherein said SGLT-2 inhibitor is dapagliflozin, or a pharmaceutically acceptable salt thereof.

14. The use according to any one of claims 9, 10 or 11, wherein said SGLT-2 inhibitor is empagliflozin, or a pharmaceutically acceptable salt thereof.

15. The use according to any one of claims 9, 10 or 11; wherein said medicament comprises aprocitentan, or a pharmaceutically acceptable salt thereof, in a pharmaceutical unit dosage form suitable for the oral administration of 10 to 50 mg per day of aprocitentan.

16. The use according to any one of claims 9, 10 or 11; wherein said medicament comprises aprocitentan, or a pharmaceutically acceptable salt thereof, in a pharmaceutical unit dosage form suitable for the oral administration of 10 to 50 mg per day of aprocitentan; and wherein

- canagliflozin, or a pharmaceutically acceptable salt thereof, if present, is to be administered in a pharmaceutical unit dosage form suitable for the oral administration of 50 to 400 mg per day of canagliflozin;
- dapagliflozin, or a pharmaceutically acceptable salt thereof, if present, is to be administered in a pharmaceutical unit dosage form suitable for the oral administration of 1 to 20 mg per day of dapagliflozin; and
- empagliflozin, 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 50 mg per day of empagliflozin.

17. The use according to any one of claims 9, 10 or 11, wherein said medicament is further to be administered in combination / as co-therapy to conventional background therapy suitable for the prevention or treatment of hypertension; chronic kidney disease (CKD); or diabetes.

18. The use according to claim 17, wherein said conventional background therapy comprises

- an angiotensin converting enzyme (ACE) inhibitor, or a pharmaceutically acceptable salt thereof; and/or
- an angiotensin receptor blocker (ARB), or a pharmaceutically acceptable salt thereof; and/or

- a calcium channel blocker, or a pharmaceutically acceptable salt thereof;
- and/or metformin; and/or
- insulin; and/or
- a sulfonylurea, or a pharmaceutically acceptable salt thereof; and/or
- a DPP-4 inhibitor, or a pharmaceutically acceptable salt thereof; and/or
- a GLP-1 receptor agonist; and/or
- a thiazolidinedione, or a pharmaceutically acceptable salt thereof.