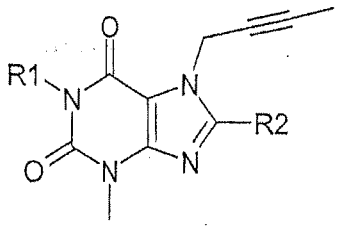
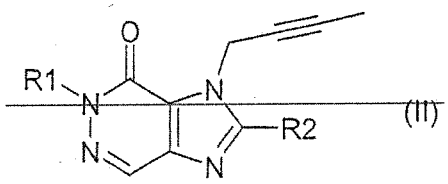
CLAIMS:

1. Use of a DPP IV inhibitor of formula (I)



(I)

~~or of formula (II)~~



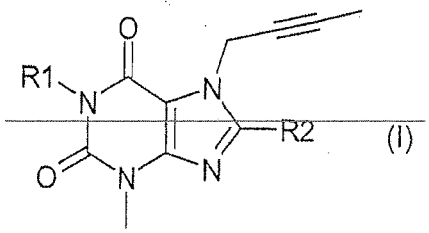
~~(II)~~

or one of the salts thereof, characterised in that

R1 denotes ([1,5]naphthyridin-2-yl)methyl, (quinazolin-2-yl)methyl], (quinoxalin-6-yl)methyl, (4-methyl-quinazolin-2-yl)methyl, 2-cyano-benzyl, (3-cyano-quinolin-2-yl)methyl, (3-cyano-pyridin-2-yl)methyl, (4-methyl-pyrimidin-2-yl)methyl, or (4,6-dimethyl-pyrimidin-2-yl)methyl and
R2 denotes 3-(R)-amino-piperidin-1-yl, (2-amino-2-methyl-propyl)-methylamino or (2-(S)-amino-propyl)-methylamino,

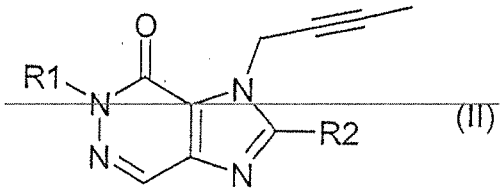
for preparing a medicament for the therapeutic treatment of a patient who has been diagnosed with a physiological functional disorder selected from among ~~pre-diabetes, glucose intolerance, pathological fasting glucose, diabetic hyperlipidaemia, diabetic dyslipidaemia, newly diagnosed type 1 diabetes,~~ hyperglycaemia, and heart failure.

2. Use of a DPP IV inhibitor of formula (I)



(I)

or of formula (II)



(II)

or one of the salts thereof, characterised in that

R1 denotes ([1,5]naphthyridin-2-yl)methyl, (quinazolin-2-yl)methyl, (quinoxalin-6-yl)methyl, (4-methyl-quinazolin-2-yl)methyl, 2-cyano-benzyl, (3-cyano-quinolin-2-yl)methyl, (3-cyano-pyridin-2-yl)methyl, (4-methyl-pyrimidin-2-yl)methyl, or (4,6-dimethyl-pyrimidin-2-yl)methyl and

R2 denotes 3-(*R*)-amino-piperidin-1-yl, (2-amino-2-methyl-propyl)-methylamino or (2-(S)-amino-propyl)-methylamino.

for preparing a medicament for the treatment of patients who have been diagnosed with pre-diabetes, characterised in that by using the medicament the risk of impaired glucose metabolism despite treatment, an elevated HbA1c value despite treatment, an impaired fasting glucose value despite treatment, the need for insulin treatment, manifest type 2 diabetes, a diabetic foot, a diabetes-associated ulcer, diabetic hyperlipidaemia, diabetic dyslipidaemia or a macrovascular complication is reduced; or for preparing a medicament for the treatment of patients who have been diagnosed with manifest type 2 diabetes characterised in that by using the medicament the risk of diabetic hyperlipidaemia or diabetic dyslipidaemia is reduced.

3. Use according to claim 2, characterised in that the macrovascular complication is selected from among myocardial infarct, acute coronary syndrome, unstable angina pectoris, stable angina pectoris, haemorrhagic or ischaemic stroke,

peripheral arterial occlusive disease, cardiomyopathy, left heart insufficiency, right heart insufficiency, global heart failure, heart rhythm disorders and vascular restenosis.

4. Use according to claim 1, characterised in that the medicament is used for the therapeutic treatment of a patient in whom pre-diabetes, glucose intolerance or pathological fasting glucose has been diagnosed.

5. Use according to claim 1, characterised in that the medicament is used for the therapeutic treatment of a patient in whom diabetic hyperlipidaemia or diabetic dyslipidaemia has been diagnosed.

6. Use according to claim 1, characterised in that the medicament is used for the therapeutic treatment of a hyperglycaemia.

7. 2. Use of a DPP-IV inhibitor selected from

- 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine,
- 1-[([1,5]naphthyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(Quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 2-((R)-3-Amino-piperidin-1-yl)-3-(but-2-yinyl)-5-(4-methyl-quinazolin-2-ylmethyl)-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one,
- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(2-amino-2-methyl-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-quinolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-(2-Cyano-benzyl)-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(*S*)-(2-amino-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-pyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4-Methyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

- 1-[(4,6-Dimethyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine, and
- 1-[(Quinoxalin-6-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

or a therapeutically active salt thereof, for preparing ~~a~~~~according to claim 1, characterised in that the~~ medicament ~~is used~~ for the therapeutic treatment of heart failure.

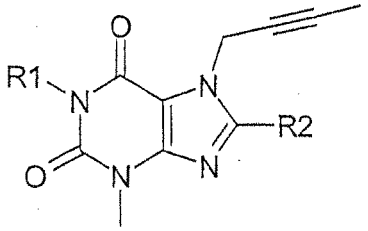
~~8. Use according to claim 2, characterised in that by using the medicament the risk of a further rise in the HbA1c value, a deterioration in the fasting glucose and the need for insulin treatment is reduced.~~

~~9~~3. The use according to any of the preceding claims, wherein the DPP IV inhibitor is combined with an active substance selected from among the other antidiabetics; active substances that lower the blood sugar level; active substances that lower the lipid level in the blood; active substances that raise the HDL level in the blood; active substances that lower blood pressure; ~~and~~ active substances that are indicated in the treatment of atherosclerosis or obesity; and active substances for the treatment of heart failure.

~~104~~. The use according to claim ~~93~~, wherein the DPP IV inhibitor is combined with another antidiabetic or a blood pressure-lowering active substance.

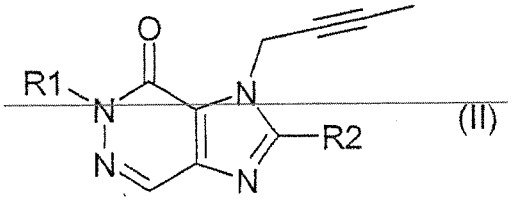
~~11.~~ 5. The use according to claim ~~104~~, wherein the DPP IV inhibitor is combined with metformin, pioglitazone, miglitol, atorvastatin, metoprolol, amlodipin, ramipril, valsartan or telmisartan.

~~12.~~ 6. Use of a DPP IV inhibitor of (I)



(I)

~~or of formula (II)~~



(II)

~~and~~ or one of the salts thereof, characterised in that

R1 denotes ([1,5]naphthyridin-2-yl)methyl, (quinazolin-2-yl)methyl, (quinoxalin-6-yl)methyl, (4-methyl-quinazolin-2-yl)methyl, 2-cyano-benzyl, (3-cyano-quinolin-2-yl)methyl, (3-cyano-pyridin-2-yl)methyl, (4-methyl-pyrimidin-2-yl)methyl, or (4,6-dimethyl-pyrimidin-2-yl)methyl and

R2 denotes 3-(*R*)-amino-piperidin-1-yl, (2-amino-2-methyl-propyl)-methylamino or (2-(S)-amino-propyl)-methylamino,

for preparing a medicament combination with an active substance selected from among the other antidiabetics; active substances that lower the blood sugar level; active substances that lower the lipid level in the blood; active substances that raise the HDL level in the blood; active substances that lower blood pressure; and active substances that are indicated in the treatment of atherosclerosis or obesity;

for the therapeutic treatment of a patient in whom a physiological functional disorder has been diagnosed, selected from among ~~pre-diabetes, glucose intolerance, pathological fasting glucose, diabetic hyperlipidaemia, diabetic dyslipidaemia, newly diagnosed type 1 diabetes,~~ heart failure ~~and hyperglycaemia; or~~

~~for the treatment of patients who have been diagnosed with pre-diabetes,~~

~~characteristised in that by using the medicament the risk of impaired glucose metabolism despite treatment, an elevated HbA1c value despite treatment, an impaired fasting glucose value despite treatment, the need for insulin treatment, manifest type 2 diabetes, a diabetic foot, a diabetes-associated ulcer, diabetic hyperlipidaemia, diabetic dyslipidaemia or a macrovascular complication is reduced; or~~

~~for the treatment of patients who have been diagnosed with manifest type 2 diabetes, characterized in that by using the medicament the risk of diabetic hyperlipidaemia or diabetic dyslipidaemia is reduced~~.

~~137~~. Use according to claim ~~126~~, characterised in that a medicament combination of a DPP IV inhibitors with another antidiabetic or a biood pressure-lowering active substance is prepared.

~~148~~. Use according to claim ~~126~~, characterised in that a medicament combination of a DPP IV inhibitor with metformin, pioglitazone, miglitol, atorvastatin, metoprolol, amlodipin, ramipril, valsartan or telmisartan is prepared.

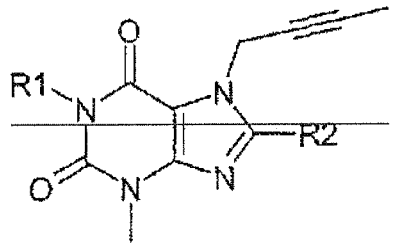
~~15.~~ 9. Use according to claim ~~12~~6, characterised in that a medicament combination of a DPP IV inhibitor with metformin, pioglitazone, miglitol, atorvastatin, valsartan or telmisartan is prepared.

~~16. Use according to claim 12, wherein the macrovascular complication is selected from among myocardial infarct, acute coronary syndrome, unstable angina pectoris, stable angina pectoris, hemorrhagic or ischaemic stroke, peripheral arterial occlusive disease, cardiomyopathy, left heart insufficiency, right heart insufficiency, global heart failure, heart rhythm disorders and vascular restenosis.~~

~~17. Isolation or storage medium for islets of Langerhans or beta cells, characterised in that the medium contains 1 nmol/l to 1 µmol/l of a DPP IV inhibitor for enhancing the vitality and secretion capacity of the cells.~~

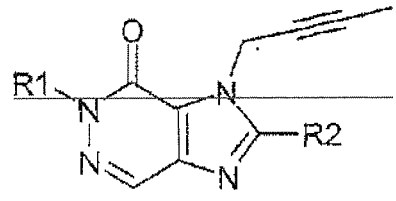
~~18. Medium according to claim 17, characterised in that the structure of the DPP IV inhibitor is described by the formula (I)~~

~~(I)~~



~~or the formula (II)~~

~~(II)~~



~~and one of the salts thereof, characterised in that~~

~~R1 denotes ([1,5]naphthyridin-2-yl)methyl, (quinazolin-2-yl)methyl, (quinoxaiin-6-yl)methyl, (4-methyl-quinazolin-2-yl)methyl, 2-cyano-benzyl, (3-cyano-~~

~~quinolin-2-yl)methyl, (3-cyano-pyridin-2-yl)methyl, (4-methyl-pyrimidin-2-yl)methyl, or(4,6-dimethyl-pyrimidin-2-yl)methyl and~~

~~**R2** denotes 3-(R)-amino-piperidin-1-yl, (2-amino-2-methyl-propyl)-methylamino or (2-(S)-amino-propyl)-methylamino.~~

~~19. Method of enhancing the vitality and secretion capacity of islets of Langerhans or beta-cells, characterised in that during the isolation and transplantation phase of the islets of Langerhans or beta-cells a DPP IV inhibitor is added to the isolation and storage medium in a concentration of between 1 nmol/l and 1 µmol/l.~~

~~20. Use of a DPP IV inhibitory in the manufacture of a medicament for treating a patient suffering from heart failure.~~

~~21~~10. Use according to any one of the preceding claims, wherein the DPP IV inhibitor is selected from

- 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine,
- 1-[([1,5]naphthyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

- 1-[(Quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 2-((R)-3-Amino-piperidin-1-yl)-3-(but-2-yinyl)-5-(4-methyl-quinazolin-2-ylmethyl)-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one,
- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(2-amino-2-methyl-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-quinolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-(2-Cyano-benzyl)-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(*S*)-(2-amino-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-pyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4-Methyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4,6-Dimethyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine, and
- 1-[(Quinoxalin-6-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

or a therapeutically active salt thereof.

11. Use of a DPP IV inhibitory which is 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine (linagliptin), or a therapeutically active salt thereof; in the manufacture of a medicament for treating a patient suffering from heart failure.

~~22.~~ 12. Use of a DPP IV inhibitor selected from

- 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine,
- 1-[([1,5]naphthyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(Quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 2-((R)-3-Amino-piperidin-1-yl)-3-(but-2-yinyl)-5-(4-methyl-quinazolin-2-ylmethyl)-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one,

- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(2-amino-2-methyl-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-quinolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-(2-Cyano-benzyl)-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(*S*)-(2-amino-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-pyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4-Methyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4,6-Dimethyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine, and
- 1-[(Quinoxalin-6-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

or a therapeutically active salt thereof, for preparing a medicament for treating a patient with heart failure, wherein the DPP IV inhibitor may be combined with an ACE-inhibitor (e.g. 2.5 mg to 15 mg ramipril), AT1-receptor-antagonist (e.g. 20 mg to 160 mg telmisartan), beta-blocker (e.g. 50 mg to 200 mg metoprolol), combined alpha/beta blocker (e.g. 3.25 mg to 100 mg carvedilol), diuretic (e.g. 12.5 mg to 25 mg hydrochlorothiazide), mineralocorticoid receptor antagonist (e.g. 25 mg to 100 mg eplerenone; and/or B-type natriuretic peptide (BNP) (e.g. 2 µg/kg as a bolus followed by 0.01 µg/kg/min nesiritide), a BNP – derived peptide or a BNP-fusion product, either in a free combination or in a fixed combination in a tablet.

~~23.~~ 13. Use of a DPP IV inhibitor selected from

- 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine,
- 1-[([1,5]naphthyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(Quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 2-((R)-3-Amino-piperidin-1-yl)-3-(but-2-yinyl)-5-(4-methyl-quinazolin-2-ylmethyl)-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one,
- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(2-amino-2-methyl-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-quinolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-(2-Cyano-benzyl)-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4-Methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(*S*)-(2-amino-propyl)-methylamino]-xanthine,
- 1-[(3-Cyano-pyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

- 1-[(4-Methyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
- 1-[(4,6-Dimethyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine, and
- 1-[(Quinoxalin-6-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

or a therapeutically active salt thereof,

in a dosage of ~~0.5 mg to 50 mg for oral administration, preferably 2.5 mg to 50 mg, particularly~~ 0.5 mg to 10 mg (such as e.g. 0.5 mg, 1 mg, 2.5 mg, 5 mg or 10 mg) for oral administration, for preparing a medicament for use in the treatment of type 2 diabetes.

14. The use according to claim 13, wherein the DPP IV inhibitor is combined with / is used in combination with metformin.

15. The use according to claim 14, wherein the dose of metformin is from 300 mg to 1000 mg once or twice a day, or delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day or 500 mg to 2000 mg once a day.

16. The use according to 14, wherein the dose of metformin is 500 mg, 850 mg or 1000 mg metformin as a single dose with a total daily dose of metformin of 500-2850 mg, or 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form.

17. The use according to any one of the preceding claims, wherein the DPP IV inhibitor is used in a dosage of 0.5 mg to 10 mg (such as e.g. 0.5 mg, 1 mg, 2.5 mg, 5 mg or 10 mg) for oral administration.

18. The use according to any one of the preceding claims, wherein the DPP IV inhibitor is used in a dosage of 2.5 mg or 5 mg.

19. The use according to any one of the preceding claims, wherein daily oral dose of the DPP IV inhibitor is 5 mg.

20. The use according to any of the preceding claims, wherein the DPP-IV inhibitor is 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine.