This compound and methods for its preparation are disclosed in WO 2005/075421, US 2008/146818 and WO 2008/114857. For details, e.g. on a process to manufacture, to formulate or to use this compound or a salt thereof, reference is thus made to these documents.

- 2-({6-[(3R)-3-amino-3-methylpiperidin-1-yl]-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-5H-pyrrolo[3,2-d]pyrimidin-5-yl}methyl)-4-fluorobenzonitrile or a pharmaceutically acceptable salt thereof, or 6-[(3R)-3-amino-piperidin-1-yl]-5-(2-chloro-5-fluoro-benzyl)-1,3-dimethyl-1,5-dihydro-pyrrolo[3,2-d]pyrimidine-2,4-dione or a pharmaceutically acceptable salt thereof:

These compounds and methods for their preparation are disclosed in WO 2009/084497 and WO 2006/068163, respectively. For details, e.g. on a process to manufacture, to formulate or to use these compounds or salts thereof, reference is thus made to these documents.

For avoidance of any doubt, the disclosure of each of the foregoing documents cited above is specifically incorporated herein by reference in its entirety.

Within the scope of the present invention it has now surprisingly been found that certain DPP-4 inhibitors as defined herein have surprising and particularly advantageous properties, which make them particularly suitable for use in wound healing, especially in diabetic patients (particularly in type 2 diabetes patients).

Thus, the present ~~invention~~disclosure provides a DPP-4 inhibitor as defined herein for use in healing of diabetic or non-diabetic wounds.

In a first aspect, there is provided the use of a DPP-4 inhibitor for preparing a pharmaceutical composition for use in wound healing in diabetic patients, wherein said DPP-4 inhibitor is
1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine, or
1-[(3-cyano-pyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
or a pharmaceutically acceptable salt thereof.

In a second aspect, there is provided the use of a tablet for oral use or a topical preparation for preparing a medicament for use in wound healing in diabetic patients, said tablet or topical preparation comprising 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine.

In a third aspect, there is provided the use of 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine for preparing a medicament for topical use for wound healing in diabetic patients.

In a fourth aspect, there is provided the use of 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine, for the manufacture of a pharmaceutical composition for wound healing in diabetic patients.

In a fifth aspect, there is provided the use of a DPP-4 inhibitor for preparing a pharmaceutical composition for treating skin diseases and/or wounds in diabetic patients, wherein said DPP-4 inhibitor is

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

or a pharmaceutically acceptable salt thereof;

wherein the pharmaceutical composition is administered topically.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for promoting or improving wound healing in diabetic and non-diabetic patients, especially in diabetic patients.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for use in the treatment and/or prevention (including preventing or slowing the progression or reducing the occurrence or delaying the onset) of wound healing deficit or impairments in the wound healing process, especially in diabetic patients.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for treating and/or preventing (including preventing or slowing the progression or reducing the occurrence or

delaying the onset) of skin diseases, wounds and/or wound healing disturbances including, but not limited to, those which are associated with diabetes.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for use in the treatment and/or prevention (including preventing or slowing the progression or reducing the occurrence or delaying the onset) of chronic skin ulcerations, wounds or sores, destructive wound inflammation (e.g. infiltration of neutrophils), delayed or impaired wound healing or closure, or disturbed tissue regeneration, formation or remodeling, especially in diabetic patients.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for diminishing wound size and/or for improving wound closure, particularly of diabetes-associated wounds.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for improving wound epithelialization, wound morphology and/or tissue regeneration, particularly of diabetes-associated wounds.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for promoting neo-or re-epithelialization, particularly of diabetes-associated wounds.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for reducing destructive wound inflammation, such as e.g. for reducing the number of polymorphonuclear neutrophils (PMN), particularly in diabetes-associated wounds.

The present ~~invention~~disclosure further provides a DPP-4 inhibitor as defined herein for treating and/or preventing (including reducing the risk of developing or progressing) metabolic disorders or diseases, especially diabetes (particularly type 2 diabetes), in patients with or at risk of skin diseases, wounds and/or wound healing disturbances or impairments (in particular which are associated with diabetes), such as e.g. those described herein (e.g. chronic skin ulcerations, wounds or sores, destructive wound inflammation (e.g. infiltration of neutrophils), delayed or impaired wound healing or closure, or disturbed tissue regeneration, formation or remodeling).

Further, according to ~~another aspect of~~ the ~~invention~~disclosure, there is provided the use of a DPP-4 inhibitor as defined herein for the manufacture of a medicament for one or more of the following purposes:

- preventing, slowing the progression of, delaying or treating a metabolic disorder or disease, such as e.g. type 1 diabetes mellitus, type 2 diabetes mellitus, impaired glucose tolerance (IGT), impaired fasting blood glucose (IFG), hyperglycemia, postprandial hyperglycemia, overweight, obesity, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertension, atherosclerosis, endothelial dysfunction, osteoporosis, chronic systemic inflammation, retinopathy, neuropathy, nephropathy and/or metabolic syndrome;
- improving glycemic control and/or for reducing of fasting plasma glucose, of postprandial plasma glucose and/or of glycosylated hemoglobin HbA1c;
- preventing, slowing, delaying or reversing progression from impaired glucose tolerance (IGT), impaired fasting blood glucose (IFG), insulin resistance and/or from metabolic syndrome to type 2 diabetes mellitus;
- preventing, reducing the risk of, slowing the progression of, delaying or treating of complications of diabetes mellitus such as micro- and macrovascular diseases, such as nephropathy, micro- or macroalbuminuria, proteinuria, retinopathy, cataracts, neuropathy, learning or memory impairment, neurodegenerative or cognitive disorders, cardio- or cerebrovascular diseases, tissue ischaemia, diabetic foot or ulcus, atherosclerosis, hypertension, endothelial dysfunction, myocardial infarction, acute coronary syndrome, unstable angina pectoris, stable angina pectoris, peripheral arterial occlusive disease, cardiomyopathy, heart failure, heart rhythm disorders, vascular restenosis, and/or stroke;
- reducing body weight or preventing an increase in body weight or facilitating a reduction in body weight;
- preventing, slowing, delaying or treating the degeneration of pancreatic beta cells and/or the decline of the functionality of pancreatic beta cells and/or for improving and/or restoring the functionality of pancreatic beta cells and/or stimulating and/or restoring the functionality of pancreatic insulin secretion;
- preventing, slowing, delaying or treating non alcoholic fatty liver disease (NAFLD) including hepatic steatosis, non-alcoholic steatohepatitis (NASH) and/or liver fibrosis;
- preventing, slowing the progression of, delaying or treating type 2 diabetes with primary or secondary failure to conventional (oral) antihyperglycemic mono- or combination therapy;
- achieving a reduction in the dose of conventional antihyperglycemic medication required for adequate therapeutic effect;

- reducing the risk for adverse effects associated with conventional (oral or non-oral) antihyperglycemic medication; and/or
- maintaining and/or improving the insulin sensitivity and/or for treating or preventing hyperinsulinemia and/or insulin resistance;

particularly in a patient having (or being at risk of) a skin disease, wound and/or wound healing disturbance or impairment, in particular associated with diabetes, such as e.g. any of those wound and/or skin disorders described herein (e.g. chronic skin ulcerations, wounds or sores, destructive wound inflammation (e.g. infiltration of neutrophils), delayed or impaired wound healing or closure, or disturbed tissue regeneration, formation or remodeling); optionally in combination with one or more other active substances, such as e.g. any of those mentioned herein.

The present ~~invention~~disclosure further provides a pharmaceutical composition for use in wound healing, especially in diabetic patients, said pharmaceutical composition comprising a DPP-4 inhibitor as defined herein and optionally one or more pharmaceutically acceptable carriers and/or diluents.

The present ~~invention~~disclosure further provides a fixed or non-fixed combination including a kit-of-parts for use in wound healing, especially in diabetic patients, said combination comprising a DPP-4 inhibitor as defined herein and one or more other active substances, e.g. any of those mentioned herein.

The present ~~invention~~disclosure further provides the use of a DPP-4 inhibitor as defined herein optionally in combination with one or more other active substances, such as e.g. any of those mentioned herein, for the manufacture of a pharmaceutical composition for wound healing, especially in diabetic patients.

The present ~~invention~~disclosure further provides a pharmaceutical composition for use in wound healing, especially in diabetic patients, said pharmaceutical composition comprising a DPP-4 inhibitor as defined herein and optionally one or more other active substances, such as e.g. any of those mentioned herein, such as e.g. for separate, sequential, simultaneous, concurrent or chronologically staggered use of the active ingredients.

The present ~~invention~~disclosure further provides a method of wound healing, especially in diabetic patients, said method comprising administering to a subject in need thereof (particularly a

human patient) an effective amount of a DPP-4 inhibitor as defined herein, optionally alone or in combination, such as e.g. separately, sequentially, simultaneously, concurrently or chronologically staggered with an effective amount of one, two or more other active substances, such as e.g. any of those mentioned herein.

An embodiment of the DPP-4 inhibitors according to this ~~invention~~disclosure refers to those DPP-4 inhibitors which - besides their glycemic action - exert direct favourable (e.g. extraglycemic) effects on the wound repairing process in a type 2 diabetic subject. Beyond improving glycemic control, these DPP-4 inhibitors are suitable for providing additional therapeutic benefits to patients with or at risk of skin diseases, wounds and/or wound healing disturbances or impairments.

An embodiment of the patients described herein, particularly of those having (or being at risk of) skin diseases, wounds and/or wound healing disturbances or impairment, in particular associated with diabetes, being amenable to the therapies of this ~~invention~~disclosure includes, without being limited to, diabetes patients for whom metformin therapy is inappropriate due to intolerability or contraindication against metformin and/or who have renal disease, renal dysfunction, or insufficiency or impairment of renal function (including patients having chronic renal insufficiency, such as e.g. patients with mild, moderate or severe renal impairment or with end stage renal disease, and/or having nephropathy, micro- or macroalbuminuria, or proteinuria).

Other aspects of the present ~~invention~~disclosure become apparent to the skilled person from the foregoing and following remarks.

A DPP-4 inhibitor within the meaning of the present invention includes, without being limited to, any of those DPP-4 inhibitors mentioned hereinabove and hereinbelow, preferably orally active DPP-4 inhibitors.

In a first embodiment (embodiment **A**), a DPP-4 inhibitor in the context of the present invention is any DPP-4 inhibitor of
formula (I)

5. Use of a tablet for oral use or a topical preparation for preparing a medicament for use in wound healing in diabetic patients, said tablet or topical preparation comprising 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine.

6. ~~A~~ The use according to claim 5, wherein the medicament is a topical preparation comprising 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine, ,
with suitable carrier materials for topical preparations.

7. The use according to claim 6, wherein the topical preparation ~~according to claim 6, which~~ is an ointment.

8. Use of 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine for preparing a medicament for topical use for wound healing in diabetic patients.

9. Use of 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine, for the manufacture of a pharmaceutical composition for wound healing in diabetic patients.

14. Use of a DPP-4 inhibitor for preparing a pharmaceutical composition for treating skin diseases and/or wounds in diabetic patients, wherein said DPP-4 inhibitor is

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

~~1-[(3-cyano-pyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,~~

or a pharmaceutically acceptable salt thereof;

wherein the pharmaceutical composition is administered topically.

15. The use according to claim 14, wherein a chronic wound, sore, ulcer or diabetic foot is treated.