



(51) International Patent Classification:

A61K 9/16 (2006.01) *A61K 9/50* (2006.01)
A61K 9/20 (2006.01) *A61K 31/403* (2006.01)

(21) International Application Number:

PCT/IB2013/053527

(22) International Filing Date:

3 May 2013 (03.05.2013)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

3584/MUM/2012 21 December 2012 (21.12.2012) IN

(71) Applicant: **WOCKHARDT LIMITED** [IN/IN]; D-4, MIDC Area, Chikalthana, Aurangabad 431210 (IN).

(72) Inventors: **JAIN, Girish Kumar**; 4, Sharada Niketan, Teacher's Colony, Pitam Pura, Delhi 110034 (IN). **NAIDU, Venkataramana**; Flat No 15, Srinidhi Apartments, Maharaja Colony, Sikhvillage, Secunderabad - 500009, Andhra Pradesh (IN). **WAGH, Balasaheb Parshuram**; At Post. Kasbe Tadawale, Tal and Dist : Osmanabad - 413405, Maharashtra (IN). **SUGGALA, Vijay**; H.No.7-1-144, Dwaraka Nagar, Khammam - 507002, Andhra Pradesh (IN).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: STABLE PHARMACEUTICAL COMPOSITIONS OF SAXAGLIPTIN OR SALTS THEREOF

(57) Abstract: The present invention refers to a stable pharmaceutical composition of saxagliptin or salts thereof. In particular, the invention relates to composition comprising plurality of saxagliptin components. Such composition of saxagliptin exhibit relatively improved storage stability and particularly, levels of degradants in the formulation during storage can be effectively controlled. The invention also includes a process of preparing such compositions and method of treating type-II diabetes mellitus by administering the composition to a patient in need thereof.



WO 2014/096983 A1

STABLE PHARMACEUTICAL COMPOSITIONS OF SAXAGLIPTIN OR SALTS
THEREOF

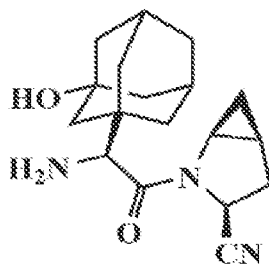
Field Of The Invention

The present invention relates to a stable pharmaceutical composition of saxagliptin or salts thereof. In particular, the invention relates to composition comprising plurality of saxagliptin components. Such composition of saxagliptin exhibit relatively improved storage stability and particularly, levels of degradants in the formulation during storage can be effectively controlled. The invention also includes a process of preparing such compositions and method of treating type-II diabetes mellitus by administering the composition to a patient in need thereof.

Background Of The Invention

Saxagliptin is an orally active inhibitor of the dipeptidyl peptidase-4 (DPP4) enzyme. After a meal intake, insulinotropic hormone glucagon-like peptide-1 (GLP-1) is released which in turn induces insulin release from the pancreas. Some of the GLP-1 is inactivated by the DPP4 present in plasma and intestinal capillary endothelium. Therefore, if the DPP4 is inhibited, more GLP-1 will be available to activate insulin release from the pancreas. The advantage of this mechanism of insulin release is that insulin is secreted only in response to a meal. Therefore, problems of hypoglycemia associated with other diabetes drugs are less likely with a DPP4 inhibitor.

Chemically saxagliptin is (1S,3S,5S)-2-[(2S)-2-Amino-2-(3-hydroxytricyclo[3.3.1.1]dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile, monohydrate or (1S,3S,5S)-2-[(2S)-2-Amino-2-(3-hydroxyadamantan-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile with the structure



Saxagliptin alone or in combination with other anti-diabetic agents are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type-II diabetes mellitus in multiple clinical conditions. It is marketed in the United States in the form of tablets under the brand name Onglyza®.

It is well known in the art that saxagliptin is an unstable compound and it is prone to an intra-molecular cyclization. The resultant degradant, cyclic amidine (mainly cis-cyclic amidine) is not therapeutically active and therefore, its formation is not desirable. This cyclization reaction can occur both in solid state and solution state. The rate of intra-molecular cyclization of saxagliptin is accelerated when formulations are subject to commonly used processing activities such as wet granulation, roller compaction, or tableting. In addition, most commonly used excipients, when mixed with saxagliptin, can accelerate the rate of cyclization. Moreover, the level of cis-cyclic amidine increases when the drug to excipient ratio increases posing more challenges for low strength dosage forms. Thus, these properties of saxagliptin poses major challenge in devising conventional and stable dosage form with ease of manufacture.

Numerous studies have been conducted to address the formulation and drug release systems of DPP4 inhibitor's and several attempts have also been made to improve the formulation stability.

U.S. Patent No. 6,395,767 discloses a DPP4 inhibiting compound, saxagliptin and its use in treating type-II diabetes mellitus.

PCT Publication No. WO 2011/052825 discloses a composition of DPP4 inhibitors and anti-diabetic compounds for use in the treatment of diabetes.

U.S. Patent Application Publication No. 2005/0208133 discloses a multiple drug release systems, its composition and methods of its preparation.

PCT Publication No. WO 2002/085335 discloses a composition providing control release of medicament. The composition contains several coatings, which controls the release of the medicament.

U.S. Patent No. 7,951,400 discloses a saxagliptin tablet containing several coating layers of polyvinyl alcohol.

The compositions disclosed in the prior art suggests that stable formulations of saxagliptin can be prepared by applying drug in the form of a coating along with several polymer coatings. However, apart from its complex structure, the process of preparing such formulations requires critical optimization and control of several processing steps such as layer coating, drying temperature, which are detrimental for drug release pattern and the stability of the end formulation.

The prior art also suggests that when saxagliptin is placed in the core of the formulation, the resulting formulations would have compromised stability.

Thus, there still exists an enduring need for alternative, improved and stable pharmaceutical composition of saxagliptin, involving simple manufacturing process, which is suitable for commercial production.

Summary Of The Invention

In one aspect, the present invention provides a stable pharmaceutical composition comprising plurality of saxagliptin components, which comprises of particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof and optionally, one or more pharmaceutical excipients.

In another aspect, the present invention provides a stable pharmaceutical composition comprising plurality of saxagliptin components, which comprises of particles of one or

more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof, optionally with one or more pharmaceutical excipients, wherein said components are further coated with one or more polymers.

In another general aspect, the saxagliptin components are in the form of solid particles, granules, beads, or pellets.

In another general aspect, the saxagliptin components are completely or partially coated saxagliptin or salts, hydrates, anhydrate thereof.

In another aspect, the present invention provides a stable pharmaceutical composition comprising plurality of saxagliptin components, which comprises of particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof.

In another aspect, the present invention provides a stable pharmaceutical composition comprising plurality of saxagliptin components, which comprises of particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof and a polymer selected from hydroxypropyl methylcellulose, polyvinyl alcohol, or mixtures thereof.

In another aspect, the present invention provides a process for the preparation of plurality of saxagliptin components, which process comprises of: coating particles of one or more pharmaceutical excipients completely or partially with saxagliptin or salts, hydrates, anhydrate thereof.

In another aspect, the present invention provides a process for preparation of a stable pharmaceutical composition comprising saxagliptin or salts, hydrates, anhydrate thereof, which process comprises of:

(a) providing plurality of saxagliptin components comprising one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof and optionally, with one or more polymers and one or more pharmaceutical excipients;

- (b) optionally, mixing the saxagliptin components with one or more pharmaceutical excipients to form a blend;
- (c) formulating the saxagliptin components prepared in step (a) or the blend prepared in step (b) in a suitable dosage form.

In another general aspect, the coating of saxagliptin or salts, hydrates, anhydrate thereof on the particles of the pharmaceutical excipients is applied by spray coating. Perforated pan coaters and fluid bed coaters can be used for the coating.

In another general aspect, in the process for preparation of saxagliptin components, the saxagliptin coating is applied as a suspension of saxagliptin or salts, hydrates, anhydrate thereof and optionally with one or more polymers in a coating solvent.

In another general aspect, the stable pharmaceutical composition of saxagliptin or salts, hydrates thereof retains at least 90% w/w of total potency of saxagliptin after storage at 40°C and 75% relative humidity for at least 3 months.

In another aspect, the present invention provides a method of treating type-II diabetes mellitus in a patient which method comprising administering the pharmaceutical composition as substantially described herein to the patient.

Embodiments of the pharmaceutical composition may include one or more of the following features. For example, the pharmaceutically acceptable excipients may include diluents, disintegrants, binders, bulking agents, anti-adherents, anti-oxidants, buffering agents, colorants, flavoring agents, coating agents, plasticizers, stabilizers, preservatives, lubricants, glidants, chelating agents, and the like known to the art used either alone or in combination thereof.

Detailed Description Of The Invention

The inventors of the present invention have surprisingly found that it is possible to formulate pharmaceutical compositions of saxagliptin, which can exhibit superior chemical and physical stability and involve simple manufacturing process.

The stable pharmaceutical composition of the present invention comprises plurality of saxagliptin components comprising particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof optionally with one or more pharmaceutical excipients and one or more polymers.

The pharmaceutical composition of the present invention exhibits excellent storage stability over the storage period.

In an embodiment, the stable pharmaceutical composition of the present invention may be characterized by lower level of degradant cis-cyclic amidine.

In another embodiment, the stable pharmaceutical composition of saxagliptin or salts, hydrates thereof retains at least 90% w/w of the total potency of saxagliptin after storage at 30°C and 60% relative humidity, at 40°C and 75% relative humidity, or at 25°C and 60% relative humidity for at least 3 months.

The term "saxagliptin" used throughout the specification refers to not only saxagliptin per se, but also various pharmaceutically acceptable salts and pharmaceutically acceptable hydrates thereof.

The term "saxagliptin component" used throughout the specification refers to particles, agglomerates, granules, pellets, microspheres, liposomes, sphericles, or any solid physical form known to the person skilled in the art of one or more pharmaceutical excipients partially or completely coated or complexed with saxagliptin or salts, hydrates, anhydrate thereof and optionally one or more pharmaceutical excipients and polymers. The present invention also embraces the dosage forms prepared by processing the components as defined herein (for instance, tablets prepared by compressing the saxagliptin components). It should be understood that the components in the final dosage form of the present invention may or may not be physically separated.

The term "particles of pharmaceutical excipients" as used throughout the specification refers to as a single or an aggregate of all physical forms of pharmaceutical excipients.

The saxagliptin components of the present invention comprise particles of one or more pharmaceutical excipients completely or partially coated with saxagliptin or salts, hydrates, anhydrate thereof optionally with one or more pharmaceutical excipients and one or more polymers.

Particles of the pharmaceutical excipients in the saxagliptin components of the present invention are selected from the group consisting of fillers/diluents, binders, glidants, lubricants, disintegrants, and plasticizers.

The bulking agents or fillers may be present in the core in an amount within the range from about 1 to about 95% w/w and preferably from about 10 to about 85% w/w of the composition. Examples of bulking agents or fillers suitable for use herein include, but are not limited to, cellulose derivatives such as microcrystalline cellulose or wood cellulose, lactose, sucrose, starch, pregelatinized starch, dextrose, mannitol, fructose, xylitol, sorbitol, corn starch, modified corn starch, inorganic salts such as calcium carbonate, calcium phosphate, dicalcium phosphate, calcium sulfate, dextrin/dextrates, maltodextrin, compressible sugars, and other known bulking agents or fillers, and/or mixtures thereof, preferably microcrystalline cellulose.

The binder may be present in the core in an amount within the range from about 0 to about 20% w/w, preferably from about 1 to about 10% w/w of the composition. Examples of binders suitable for use herein include, but are not limited to, hydroxypropyl cellulose, corn starch, pregelatinized starch, modified corn starch, polyvinyl pyrrolidone (PVP) (molecular weight ranging from about 5,000 to about 1,000,000, preferably about 40,000), hydroxypropyl methylcellulose (HPMC), lactose, gum acacia, ethyl cellulose, cellulose acetate, as well as a wax binder such as carnauba wax, paraffin, spermaceti, polyethylenes or microcrystalline wax, as well as other conventional binding agent and/or mixtures thereof, preferably hydroxypropyl cellulose.

The disintegrant may be present in the core in an amount within the range from about 0 to about 20% w/w, preferably from about 0.25 to about 10% w/w of the composition. Examples of disintegrants suitable for use herein include, but are not limited to, croscarmellose sodium, crospovidone, starch, potato starch, pregelatinized starch, corn starch, sodium starch glycolate, microcrystalline cellulose, low substituted hydroxypropyl cellulose or other known disintegrant, preferably croscarmellose sodium.

The lubricant may be present in the core in an amount within the range from about 0.1 to about 5% w/w, preferably from about 0.2 to about 2% w/w of the composition. Examples of tableting lubricants suitable for use herein include, but are not limited to, magnesium stearate, zinc stearate, calcium stearate, talc, carnauba wax, stearic acid, palmitic acid, sodium stearyl fumarate or hydrogenated vegetable oils and fats, or mixtures thereof, preferably magnesium stearate.

In an embodiment, the saxagliptin component of the present invention comprises plurality of particles of lactose, microcrystalline cellulose and croscarmellose sodium coated with saxagliptin or salts, hydrates, anhydrate thereof and one or more polymers.

The amount of saxagliptin in the components may range from about 1% to about 99% w/w of the component.

In an embodiment, the stable pharmaceutical composition of the present invention comprises plurality of saxagliptin components comprising particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof and one or more polymers.

The saxagliptin and polymer coating may comprise at least one polymer and a coating solvent, which preferably is water, which is used for processing and removed by drying. Suitable polymer may be selected from, but not limited water-soluble polymer, water-insoluble polymer, or mixtures thereof. Particularly, water-soluble polymers are preferred.

Examples of polymers suitable for first coating layer include, but not limited to hydroxypropyl methylcellulose, ethyl cellulose, methacrylic polymers or hydroxypropyl cellulose, preferably hydroxypropyl methylcellulose. The coating layer may also optionally include a plasticizer such as triacetin, diethyl phthalate, tributyl sebacate or polyethylene glycol (PEG), preferably PEG; and an anti-adherent or glidant such as talc, fumed silica or magnesium stearate. The amount of polymer in the components may range from about 0.5% to about 50% w/w of the component.

Examples of suitable coating solvents includes, but not limited to water, ethanol, methanol, and isopropyl alcohol, with water being preferred.

The saxagliptin and polymer coating composition may comprise one or more plasticizers in an amount sufficient to minimize effect of the formulation processing (e.g. upon compression into tablet dosage form) on the coating integrity. The composition of the coating also provides advantageous mechanical properties to the coating.

The amount of plasticizer in the coating composition may range from about 5 to about 50%, preferably from about 5 to about 30% w/w of the coating layer.

The coating layer will preferably be formed by coating polymer layer in an amount within the range from about 10 to about 99%, preferably from about 20 to about 99% w/w of the component, plasticizer in an amount within the range from about 1 to about 30%, preferably from about 5 to about 20% w/w of the component, and anti-adherent or glidant in an amount within the range for about 15 to about 30%, preferably from about 10 to about 15% w/w of the component.

In an embodiment, the pharmaceutical composition of the present invention comprises a core comprising plurality of saxagliptin components and optionally one or more pharmaceutical excipients.

The core employed in the composition of the invention may include conventional pharmaceutical excipients to enable formation of a pharmaceutically acceptable solid core. The core may be in the form of a tablet, bead, beadlet, or pill.

In an embodiment, the core may contain one or more additional anti-diabetic agents, other than saxagliptin, in an amount within the range from about 0.1 to about 70% wt/wt and preferably from about 1 to about 50% w/w of the composition.

The core may be formed of one or more pharmaceutical excipients selected from, but not limited to one or more of bulking agents or fillers, binders, disintegrants, and lubricants.

In an embodiment, the core preferably contain a) at least one bulking agent or filler; b) optionally at least one binder; c) optionally at least one disintegrant; and d) preferably but optionally at least one lubricant, wherein a) the bulking agent or filler is present in an amount within the range from about 1 to about 95% w/w, preferably from about 10 to about 85% w/w; b) the binder is present in an amount within the range from about 0 to about 20% w/w, preferably from about 1 to about 10% w/w; c) the disintegrant is present in an amount within the range from about 0 to about 20% w/w, and preferably from about 0.25 to about 10% w/w; and d) the lubricant is present in an amount within the range from about 0 to about 5% w/w, preferably from about 0.2 to about 2% w/w of the composition.

In another embodiment, the bulking agents are microcrystalline cellulose and lactose monohydrate; the disintegrant is croscarmellose sodium; and the lubricant is magnesium stearate.

The cores present in the composition of the invention can be prepared by a variety of processes and order of addition of excipients. The utility of these formulations is not limited to a specific dosage form or manufacturing process. The cores may be manufactured by wet granulation, dry granulation, direct blending or any other pharmaceutically acceptable process using saxagliptin components.

In an embodiment, the process of preparing the cores includes the steps of blending the saxagliptin components with one or more excipients such as bulking agent, optionally

binder and optionally disintegrant followed by formulating the blend in the form of cores. A lubricant will be preferably added to the blend to facilitate tablet formation.

The composition of the present invention further may comprise an outer protective layer comprising one or more polymers and one or more pharmaceutical excipients.

The outer coating layer may include colorant as desired, such as within the range from about 0.5 to about 5.0% w/w, based on the total weight of the outermost coating layer.

The outer protective coating layer may be present in an amount within the range from about 1 to about 10%, preferably from about 1 to about 5% w/w of the composition.

Pharmaceutical excipients suitable for employing in the coating layers of the composition may include, but not limited to, bulking agents or diluents, binders, plasticizers, lubricants, colorants, pH adjusting agents, or mixtures thereof.

The invention further provides a process for preparation of stable pharmaceutical composition of saxagliptin or salts, hydrates thereof, the process comprises of:

- (a) providing plurality of saxagliptin components which comprises of particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof along with one or more polymers and optionally one or more pharmaceutical excipients;
- (b) optionally, mixing the saxagliptin components with one or more pharmaceutical excipients to form a blend;
- (c) formulating the saxagliptin components prepared in step (a) or the blend prepared in step (b) in a suitable dosage form.

The process for the preparation of plurality of saxagliptin components of the present invention comprises a step of coating particles of pharmaceutical excipients completely or partially with saxagliptin or salts, hydrates thereof and one or more polymers. The coated saxagliptin particles may be dried in order to get components suitable for formulating in a solid dosage form.

In a further embodiment, in preparing the saxagliptin components of the invention, coating suspensions including saxagliptin or salts, hydrates thereof and coating polymer are prepared in water. Other coating solvents, which may be employed, include ethanol, methanol, and isopropyl alcohol, with water being preferred.

It has been surprisingly found that the composition of the present invention exhibits superior chemical and physical stability when manufactured using conventional dry granulation, wet granulation, direct compression or slugging.

The composition of the present invention may be formulated in suitable a dosage form including, but not limited to, a tablet, caplet, mini-tablet, pellets, granules, capsule filled with mini-tablets or pellets or combinations thereof.

The present invention further provides a method of treating type-II diabetes mellitus in a patient which method comprising administering the pharmaceutical composition as substantially described herein to the patient.

The present invention is further illustrated by the following examples which are provided merely to be exemplary of the invention and do not limit the scope of the invention. Certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention.

In accordance with the Present Invention coated tablet formulations are set out below.

Example 1: Saxagliptin Tablet**Table 1**

Sr. No.	Ingredients	Qty/Tab
Core Tablets		
Dry Mix		
1	Lactose Monohydrate	98.00
2	Microcrystalline Cellulose	90.00
3	Croscarmellose sodium	10.00
Binder		
4	Saxagliptin HCl	5.60
5	Hypromellose or HPC or PVP or vinylpyrrolidone-vinyl acetate and Glyceryl Caprylocaprate	5.60
6	PEG 6000	1.00
7	Dichloromethane	qs
8	Methanol	qs
Lubricant		
9	Magnesium stearate	2.00
Film Coating		
10	Opadry	5.00
Total		220.2

Process: Mixture of lactose monohydrate, microcrystalline cellulose and croscarmellose sodium was loaded and blended in the in the fluidized bed processor.

A binder dispersion of drug was prepared by mixing saxagliptin HCl, hypromellose/ HPC/ PVP/ vinylpyrrolidone-vinyl acetate and glyceryl caprylocaprate in PEG 6000, dichloromethane and methanol.

The binder dispersion was then coated on the excipients in the fluidized bed processor to form granules, which were then sifted, milled and lubricated by blending with magnesium stearate.

The lubricated granules were then compressed into tablets and the tablets are coated with opadry coating dispersion.

Claims:

1. A stable pharmaceutical composition comprising plurality of saxagliptin components, which comprises of particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates thereof and optionally, with one or more polymers.
2. The stable pharmaceutical composition of claim 1, wherein the plurality of saxagliptin components forms the core of the composition.
3. The stable pharmaceutical composition of claim 1, wherein the particles of pharmaceutical excipients comprises lactose, microcrystalline cellulose, croscarmellose sodium, and mixture thereof.
4. The stable pharmaceutical composition of claim 1, wherein the polymer comprises one or more water-soluble polymers, water-insoluble polymers, or mixture thereof.
5. The stable pharmaceutical composition of claim 4, wherein the water-soluble polymer comprises hydroxypropyl methylcellulose, polyvinyl alcohol, or mixture thereof.
6. The stable pharmaceutical composition of claim 1, wherein the saxagliptin components comprises from about 1% to about 99% w/w of saxagliptin or salts, hydrates thereof.
7. The stable pharmaceutical composition of claim 1, wherein the saxagliptin components are in the form of solid particles, granules, beads, or pellets.
8. The stable pharmaceutical composition of claim 1, wherein the composition retains at least 90% w/w of the total potency of saxagliptin after storage at 30 °C and 60% relative humidity for at least 3 months.

9. A process for preparation of stable pharmaceutical composition of claim 1, which process comprises of:

- (a) providing plurality of saxagliptin components which comprises of particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof and optionally with one or more pharmaceutical excipients and one or more polymers;
- (b) optionally, mixing the saxagliptin components with one or more pharmaceutical excipients to form a blend;
- (c) formulating the saxagliptin components prepared in step (a) or the blend prepared in step (b) in a suitable dosage form.

10. A tablet comprising:

- (a) a core comprising of plurality of saxagliptin components, which components comprises of particles of one or more pharmaceutical excipients coated with saxagliptin or salts, hydrates, anhydrate thereof and optionally, with one or more pharmaceutical excipients and one or more polymers.
- (b) optionally, an outer protective coating layer coated on the tablet core comprising one or more polymers, and optionally with one or more pharmaceutical excipients.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2013/053527

A. CLASSIFICATION OF SUBJECT MATTER INV. A61K9/16 A61K9/20 A61K9/50 A61K31/403 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data, BIOSIS, EMBASE		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/206766 A1 (FRIEDL THOMAS [DE] ET AL) 25 August 2011 (2011-08-25) paragraphs [0095], [0115]; claim 7 -----	1-10
X	US 7 951 400 B2 (DESAI DIVYAKANT S [US] ET AL) 31 May 2011 (2011-05-31) cited in the application column 5, line 54 - line 56; examples -----	1-10
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 11 July 2013		Date of mailing of the international search report 18/07/2013
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Palma, Vera

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2013/053527

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2011206766	A1	25-08-2011	AR 071175 A1 02-06-2010
			AU 2009232043 A1 08-10-2009
			CA 2720450 A1 08-10-2009
			CN 101983073 A 02-03-2011
			CN 103083672 A 08-05-2013
			CO 6251277 A2 21-02-2011
			EA 201001577 A1 29-04-2011
			EC SP10010489 A 30-10-2010
			EP 2285410 A2 23-02-2011
			JP 2011516456 A 26-05-2011
			KR 20110005690 A 18-01-2011
			NZ 587747 A 25-01-2013
			PE 17302009 A1 10-12-2009
			TW 200946534 A 16-11-2009
			US 2011206766 A1 25-08-2011
			UY 31747 A 10-11-2009
			WO 2009121945 A2 08-10-2009
-----	-----	-----	-----
US 7951400	B2	31-05-2011	AR 049062 A1 21-06-2006
			AU 2005249467 A1 15-12-2005
			BR PI0510419 A 30-10-2007
			CA 2568391 A1 15-12-2005
			CN 1988891 A 27-06-2007
			CN 102895208 A 30-01-2013
			EP 1753406 A1 21-02-2007
			EP 2298288 A1 23-03-2011
			IL 179454 A 29-03-2012
			JP 4901727 B2 21-03-2012
			JP 2008501025 A 17-01-2008
			KR 20070027560 A 09-03-2007
			KR 20120064141 A 18-06-2012
			MY 147639 A 31-12-2012
			NZ 551591 A 26-03-2010
			PE 04252006 A1 01-06-2006
			RU 2372894 C2 20-11-2009
			TW I354569 B 21-12-2011
			TW 201204414 A 01-02-2012
			US 2005266080 A1 01-12-2005
			US 2011200672 A1 18-08-2011
			WO 2005117841 A1 15-12-2005
			ZA 200609541 A 30-01-2008
-----	-----	-----	-----