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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, IR, IS, JP, KE, KG, 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, SA, 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.

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Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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- *with international search report (Art. 21(3))*

(54) **Title:** STABILISED AMORPHOUS FORMS OF SAXAGLIPTIN

(57) **Abstract:** Glass solution or glass suspension of saxagliptin base, or pharmaceutically acceptable salt thereof, dispersed within a polymer matrix, wherein the polymer is selected from polyvinylpyrrolidone, hydroxypropyl methylcellulose and hydroxypropylcellulose.



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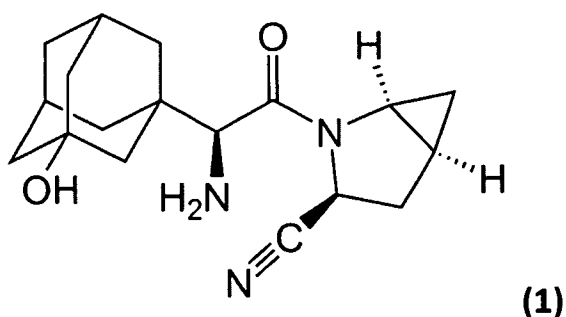
Stabilised amorphous forms of Saxagliptin

Technical Field

The present invention relates to novel stabilised amorphous forms of Saxagliptin, methods of preparation as well as use in pharmaceutical compositions.

Background Art

The compound (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxy-1-adamantyl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile (Saxagliptin) of formula 1



is known to be a new oral hypoglycemic (anti-diabetic drug) of the new dipeptidyl peptidase-4 (DPP-4) inhibitor class of drugs. It is a therapeutic agent for treatment of Type-2 diabetes mellitus, obesity and related diseases as shown in U.S. Patent No.6,395,767, example 60.

As has been described in WO2008/131149 and US2012/0083517, Saxagliptin can exist as hydrate, solvate, free base or pharmaceutically acceptable salts. Also amorphous form of Saxagliptin was described as well as process for preparation of individual forms and use thereof in pharmaceutical formulation. For preparation of pharmaceutical composition however, predominantly crystalline forms of Saxagliptin are used due to the lower stability and usually higher content of impurities present in amorphous form.

Subject matter of the invention

Glass solution or glass suspension of saxagliptin base, or pharmaceutically acceptable salt thereof, dispersed within a polymer matrix, wherein the polymer is selected from polyvinylpyrrolidone, hydroxypropyl methylcellulose and hydroxypropylcellulose, process for its the preparation and its use for the preparation of the pharmaceutical composition.

Detailed description of the invention

The present invention relates to the solid state structures of (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxy-1-adamantyl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile (hereafter referred to as Saxagliptin) in the form of a stable amorphs and their preparation.

Crystalline solid is characterised by its long-range order. On the other hand, amorphous solids lack the long-range order. The molecular arrangement in the amorphous solid may be represented by a frozen liquid with the rheological properties of a solid.

As used herein, the term „solid dispersion“ means any solid composition having at least two components. In certain embodiments, a solid dispersion as disclosed herein includes an active pharmaceutical ingredients -API (saxagliptin) dispersed among at least one other component, for example a polymer.

The term „molecularly dispersed“, as used herein, refers to the random distribution of a compound (e.g. saxagliptin) with a polymer. In some embodiments, saxagliptin may be dispersed within a matrix formed by the polymer in its solid state such that the saxagliptin is immobilised in its amorphous form. When saxagliptin is molecularly dispersed in a polymer the resulting solid dispersion is having a single glass transition temperature (T_g) and its herein referred to as a glass solution.

On the other hand if a compound (e.g. saxagliptin) is transformed into an amorphous state but is not molecularly dispersed in a polymer matrix because amorphous saxagliptin clusters are incorporated in a polymer instead, the solid dispersion used herein is called a glass suspension. The resulting glass

suspension having two glass transition temperatures; one results from the amorphous API and the other one results from a polymer.

As it is known in the art, because of the lack of a long-range order and usually high surface area, amorphous solids typically exhibit higher solubility than crystalline form. In order to increase solubility of a crystalline solid, it is thus beneficial to prepare active pharmaceutical ingredient in an amorphous form.

If a crystalline material is heated until its melting point is reached (T_m), the material is transformed from solid to liquid state. This is reversible, so upon cooling, the molten liquid rearranges back to crystal lattice. If, however, the liquid is cooled sufficiently fast below its melting point, crystallisation may be prevented forming a super-cooled liquid. In the super-cooled liquid is cooled enough to reach glass transition temperature (T_g), the molecules are kinetically frozen and the super-cooled liquid solidifies into a glass. In general, molecules in a super-cooled liquid state have much higher mobility as in a glassy state as described in Remington: The Science and Practice of Pharmacy, Pharmaceutical Press, 21st edition.

Since the molecules even in a glassy state have some mobility, it is known in the art that it is beneficial that the glass transition temperature of active pharmaceutical ingredient is at least 20 °C higher, more preferably at least 30 °C higher and most preferably at least 40 °C higher than the actual storage conditions.

Amorphous Saxagliptin has relatively low glass transition temperature (T_g), which is about 54 °C. Therefore, the amorphous form undergoes recrystallisation upon storage conditions. It is therefore highly beneficial to stabilise amorphous form of Saxagliptin by increasing the glass transition temperature (T_g) in order to prevent recrystallisation.

Amorphous form of Saxagliptin can be stabilised by mixing the API with a second component. There are a number of different second components that can be used. In general, all second components used to stabilise Saxagliptin have a common characteristic, which is that they decrease mobility of Saxagliptin molecules and thus prevent the recrystallisation.

One type of the second component used for stabilisation of amorphous Saxagliptin are polymers. Suitable polymers used may be selected from, but not restricted to water soluble as well as water insoluble polymers. Typical water soluble polymers suitable to stabilise amorphous Saxagliptin are
5 polyvinylpyrrolidone (povidone), copovidone, polyvinyl alcohol, hydroxypropyl methylcellulose (hypromellose), hydroxypropylcellulose, polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft co-polymer (Soluplus™), and similar. Typical water insoluble polymers suitable to stabilise amorphous Saxagliptin are
10 methylcellulose, ethylcellulose, polymethacrylates, hypromellose phthalate, hypromellose acetate succinate, cellulose acetate phthalate, carboxymethyl ethyl cellulose and crospovidone.

There exist a number of possible processes to prepare the stabilised amorphous form of Saxagliptin.

One possible process is the so-called solvent processes. What is common to all
15 solvent processes is that the active ingredient is dissolved in a solvent or in any mixture thereof. Solvents can be water or any organic solvents. Some examples of possible organic solvents are methanol, ethanol, ethyl acetate, isopropanol, acetone, dichloromethane, tetrahydrofuran etc. In the next step, a second component to stabilise Saxagliptin is added forming either solution or
20 suspension. The solvent is then quickly removed and a super-cooled glassy solid remains. Some concrete solvent processes used to prepare composition of Saxagliptin in stabilised amorphous form may be selected from, but not restricted to removal of a solvent in a rotary evaporator, fluid bed granulation, spray drying, electrospinning, freeze drying and similar.

25 The second possible process is the process without the use of a solvent. In this process, Saxagliptin is mixed directly with the second component to stabilise amorphous form and melted in order to form a melt. In general, the melt is heated to approximately 20-40 °C above the Tg of the melted system in order to decrease the viscosity of a system to such a degree that it is possible to process
30 the system. The melt is subsequently cooled in order to form a super-cooled glassy solid. Some concrete examples of this process may be selected from, but not restricted to hot melt extrusion, hot melt granulation in a high shear mixer, solvent-free melt granulation in a fluid bed granulator and the like.

The invention relates to a solid pharmaceutical composition comprising Saxagliptin and at least one second component used to stabilise amorphous Saxagliptin, preferably polymer selected from a group comprising polyvinylpyrrolidone, hydroxypropyl methylcellulose and hydroxypropylcellulose, more preferably PVP K30, PVP K25, Methocel E5 and Klucel EF polymers.

PVP K30 is polyvinylpyrrolidone polymer with molecular weight about 50,000 Da (g/mol).

PVP K25 is polyvinylpyrrolidone polymer with molecular weight about 30,000 Da (g/mol).

Methocel E5 is hydroxypropyl methylcellulose polymer with molecular weight about 22,000 Da (g/mol).

Klucel EF is hydroxypropylcellulose polymer with molecular weight about 80,000 Da (g/mol).

Two approaches can be applied for preparation of glass solutions by spray drying technique. Saxagliptin can be used either as a salt or as a free base *in situ* with an acid, yielding Saxagliptin dispersed in a matrix formed by the polymer.

The spray dried products were assessed by XRPD and DSC analysis and the results are summarised in Table 1.

The XRPD results demonstrated that Saxagliptin with PVP K30, Klucel EF, Methocel E5 and PVP K25 polymers formed amorphous solid dispersions. All diffractograms displayed a broad amorphous halo with the absence of sharp signals as shown in Figure 1 as a representative example.

In differential scanning calorimetry (DSC) measurements, solid dispersions of saxagliptin and polymer selected from PVP K30, Klucel EF, Methocel E5 exhibited a single glass transition temperature (T_g) indicating complete miscibility between the API and polymer.

It is known that the physical stability of the glass solution is increased with a higher glass transition temperature (Hancock and Zografi, 1997). Comparing all

recorded Tg values, the highest glass transition temperature was observed for the PVP K30 glass solution as shown in Figure 2.

Saxagliptin is a crystalline drug with a melting point at about 54 °C, while PVP K30 is amorphous solid with Tg value of 167 °C. Therefore, the observed single Tg value of 154°C for this solid dispersion is the indication that the glass solution is consisted of only one phase.

However, in the case of PVP K25 solid dispersion, the DSC curve displayed two glass transition temperatures as shown in Figure 3. One Tg at 55°C resulted from the amorphous API and the other Tg at 167°C resulted from the amorphous polymer PVP K25. This means that saxagliptin was transformed into an amorphous state but was not molecularly dispersed in the polymer matrix. Instead amorphous saxagliptin clusters were incorporated in PVP K25, yielding in formation of a glass suspension not the glass solution.

It was found out that the ratio 1:9 to about 1:1, preferably the 1:2, weight/weight ratio of API and polymer was able to form physically stable glass solutions or suspensions.

Table 1. Amorphous stability evaluation of some solid dispersions prepared by spray drying.

Polymer	XRPD	DSC Tg (°C)	Results after open exposure at 40°C/75% RH
PVP K30	amorph	154	Stable after storage for up to 4 weeks
Klucel EF	amorph	110	Stable after storage for up to 4 weeks
Methocel E5	amorph	140	Stable after storage for up to 4 weeks
PVP K25	amorph	55 & 167	Stable after storage for up to 4 weeks

Solid dispersion prepared by hot melt extrusion process were also analysed by XRPD. Patterns of the X-ray powder diffraction exhibited a broad halo peak characteristic of amorphous glass solutions as shown in Figure 4 as a representative example. Non-occurrence of sharp signals in all diffractograms, which could be allocated to the crystalline form of saxagliptin, confirmed that saxagliptin is molecularly dispersed within the polymers .

The amorphous solid dispersions were characterised by DSC measurements. The glass transition temperature were very similar to those obtained by spray drying technique. Again the highest glass transition temperature of 156 °C was observed for the matrix consist of saxagliptin and PVP K30 polymer. The presence of just one glass transition temperature confirmed that saxagliptin was successfully immobilised in its amorphous form in uniphase matrix as shown in Table 2.

Table 2. Amorphous stability evaluation of some solid dispersions prepared by hot melt extrusion process.

Polymer	XRPD	DSC Tg(°C)	Results after open exposure at 40°C/75% RH
PVP K30	amorph	156	Stable after storage for up to 4 weeks
Klucel EF	amorph	114	Stable after storage for up to 4 weeks
Methocel E5	amorph	142	Stable after storage for up to 4 weeks

The stored samples were evaluated by XRPD and the results did not indicate any crystalline peak in powder XRPD profiles after 4 weeks of open exposure at 40°C and 75% RH.

Glass solutions or glass dispersions of saxagliptin within the polymer matrix according to this invention can be used in the preparation of pharmaceutical composition, especially solid composition, e.g. tablets. Such a solid composition can further comprise at least one pharmaceutical excipient selected from fillers (e.g. lactose), binders (e.g. microcrystalline cellulose), disintegrants (e.g. croscarmellose sodium), lubricants (e.g. MgSt), surfactants, etc. Tablet composition can be optionally coated by any conventional coating, such as polyvinylalcohol or polyethylene glycol.

Brief description of the drawings

1. Figure 1 provides the XRPD pattern of the amorphous glass solution of saxagliptin with PVP K30 polymer.

2. Figure 2 provides the DSC curve of the amorphous glass solution of saxagliptin with PVP K30 polymer.
3. Figure 3 provides the DSC curve of amorphous glass suspension of saxagliptin with PVP K25 polymer.
4. Figure 4 provides the XRPD pattern of the amorphous glass suspension of saxagliptin with PVP K25 polymer.

Characterisation methods and preparation methods

DSC curves were recorded using a Perkin Elmer Pyris 1 differential scanning calorimeter. For the measurements approximately 2 - 6 mg of sample were placed in aluminium pans, accurately weighed and hermetically closed with perforation lids. Prior to measurement the lids were pierced resulting in approximately 1.5 mm pin holes. The samples were then heated under a flow of nitrogen of about 100 mL/min using heating rates of usually 10 K/min.

XRPD patterns were obtained with laboratory X-Ray diffractometer X'PERT PRO MPD PANalytical operating in diffraction mode $\theta - \theta$ with copper radiation $\text{CuK}\alpha$ ($\lambda=1.542 \text{ \AA}$, 45 kV/ 40 mA), in 2-theta range $2 - 40^\circ 2\theta$, with step $0.02^\circ 2\theta$ and step time 3 s. Samples were measured on Si plate (zero-background holder). Primary optics setting: Soller slits 0.02 rad, automatic PDS, 10 mm mask, $1/4^\circ$ anti-scatter slit, irradiated sample area 10 mm. Secondary optics setting: 5.0 mm anti-scatter slit, Soller slits 0.02 rad, detector X'Celerator with maximal active length.

Physical stability testing

Storage stability of amorphous products (saxagliptin dispersed within a polymer selected from PVP K30, Klucel EF, Methocel E5 and PVP K25) were carried out at 75% RH and at controlled temperature (40°C) for 7 days, then further for 4

weeks. The samples were evaluated by XRPD. The results are shown in the Tables 1 and 2.

Spray drying

- 5 Saxagliptin and polymer were spray dried using Buchi B-290 spray-drier. The following conditions were used for all experiments; aspirator flow: 100%, gas flow rate: 577 l/min, solution flowrate: 1.0–2.0 ml/min, inlet temperature: 50°C.

Hot melt-extruder

- 10 Saxagliptin and polymer blends were extruded using Three-Tec Extruder ZE 12 ZD 5 FB a twin-screw extruder with a temperature cascade rising to 165 °C.

Examples

Example 1- Spray drying

- 15 Saxagliptin free base (1 g), which was acidified with aq. HCl, and polymer (2 g) (selected from PVP K30, Klucel EF, Methocel E5 and PVP K25) was dissolved in dichloromethane and ethanol solvent mixture (150 ml). The resulting solution was then spray dried using a Buchi B-290 spray drier. Obtained amorphous products were dried in a vacuum oven over desiccant at 40 °C for 12 h.

Example 2- Spray drying

- 20 Saxagliptin hydrochloride (1 g) and polymer (2 g) (selected from PVP K30, Klucel EF, Methocel E5 and PVP K25) were dissolved in mixture of dichloromethane and ethanol (150 ml) then spray dried using a Buchi B-290 spray drier. The spray dried amorphous products were dried in a vacuum oven over desiccant at 40 °C
25 for 12 h.

Example 3 - Hot Melt Extrusion

Saxagliptin hydrochloride (1 g) was mixed with polymer (2 g) (selected from PVP K30, Klucel EF and Methocel E5). The mixture was then fed continuously to a

temperature-controlled extruder. The resulting extrudate was cooled to room temperature yielding in amorphous product.

Claims

1. Glass solution or glass suspension of saxagliptin base, or pharmaceutically acceptable salt thereof, dispersed within a polymer matrix, wherein the polymer is selected from polyvinylpyrrolidone, hydroxypropyl methylcellulose and hydroxypropylcellulose.
2. Glass solution according to claim 1 wherein said polymer is polyvinylpyrrolidone polymer, type PVP K30 with molecular weight about 50,000 Da (g/mol).
3. Glass solution according to claim 2 that exhibits a powder x-ray diffraction pattern having characteristic of amorphous halo (Figure 1).
4. Glass solution according to claim 1, where said polymer is hydroxypropyl methylcellulose, type Methocel E5 with molecular weight about 22,000 Da (g/mol).
5. Glass solution according to claim 4 that exhibits a powder x-ray diffraction pattern having characteristic of amorphous halo.
6. Glass solution according to claim 1, wherein said polymer is hydroxypropylcellulose, type Klucel EF with molecular weight about 80,000 Da (g/mol).
7. Glass solution according to claim 6 that exhibits a powder x-ray diffraction pattern having characteristic of amorphous halo.
8. Glass solution according to any of the preceding claims characterised in that it is a single-phase with a glass transition temperature (T_g) of more than 100°C.
9. Glass suspension according to claim 1 wherein the polymer is polyvinylpyrrolidone, type PVP K25 with molecular weight about 30,000 Da (g/mol).
10. Glass suspension according to claim 9 that exhibits a powder x-ray diffraction pattern having characteristic of amorphous halo (Figure 4).
11. Glass suspension according to claim 9 characterised in that it is two glass transition temperatures (T_g) (Figure 3).
12. A process for the preparation of glass solution or glass suspension of saxagliptin, defined in any of claims 1-11, wherein saxagliptin base, or pharmaceutically acceptable salt thereof, and the polymer are dissolved in a solvent selected from organic solvents and water or mixture thereof and then spray dried.
13. The process according to claim 12 wherein the organic solvent is methanol, ethanol, ethyl acetate, isopropanol, acetone, dichloromethane, tetrahydrofuran or mixture thereof.
14. The process according to claim 13 wherein the solvent is mixture of DCM and ethanol.

15. A process for the preparation of glass solution or glass suspension of saxagliptin, defined in any of claims 1-11, wherein saxagliptin base, or pharmaceutically acceptable salt thereof, is mixed with polymer and the mixture is extruded by use of temperature-controlled extruder.
16. Glass solution or glass suspension according to any of the preceding claims, wherein the ratio of the amount by weight of saxagliptin within the glass solution to the amount by weight of the polymer therein is 1:2.
17. Use of the glass solution or glass suspension of saxagliptin within a polymer matrix according to any of the preceding claims for the preparation of a pharmaceutical composition.

Figure 1 XRPD pattern of the amorphous glass solution of saxagliptin with PVP K30 polymer

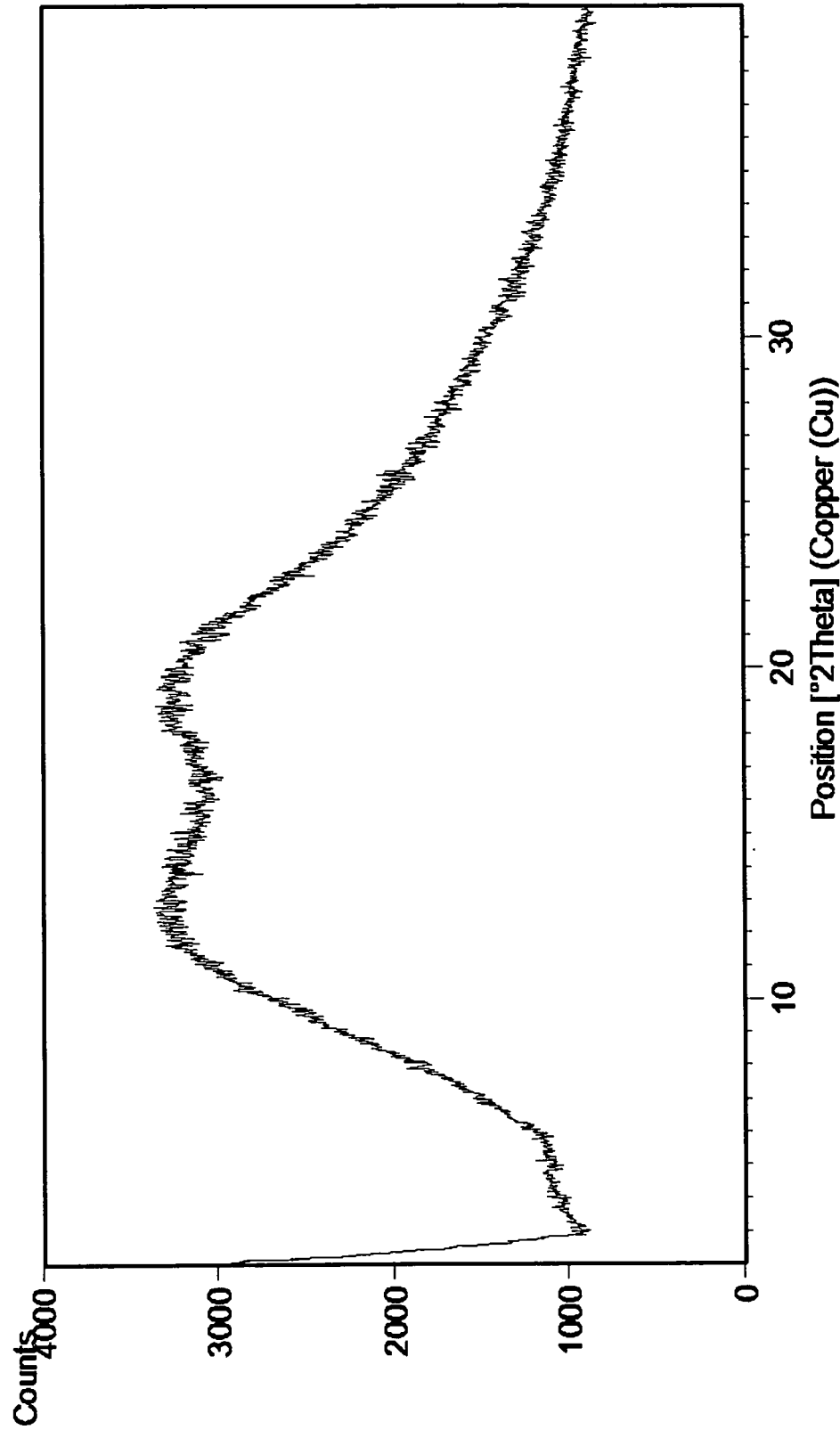


Figure 2 DSC curve of the amorphous glass solution of saxagliptin with PVP K30 polymer

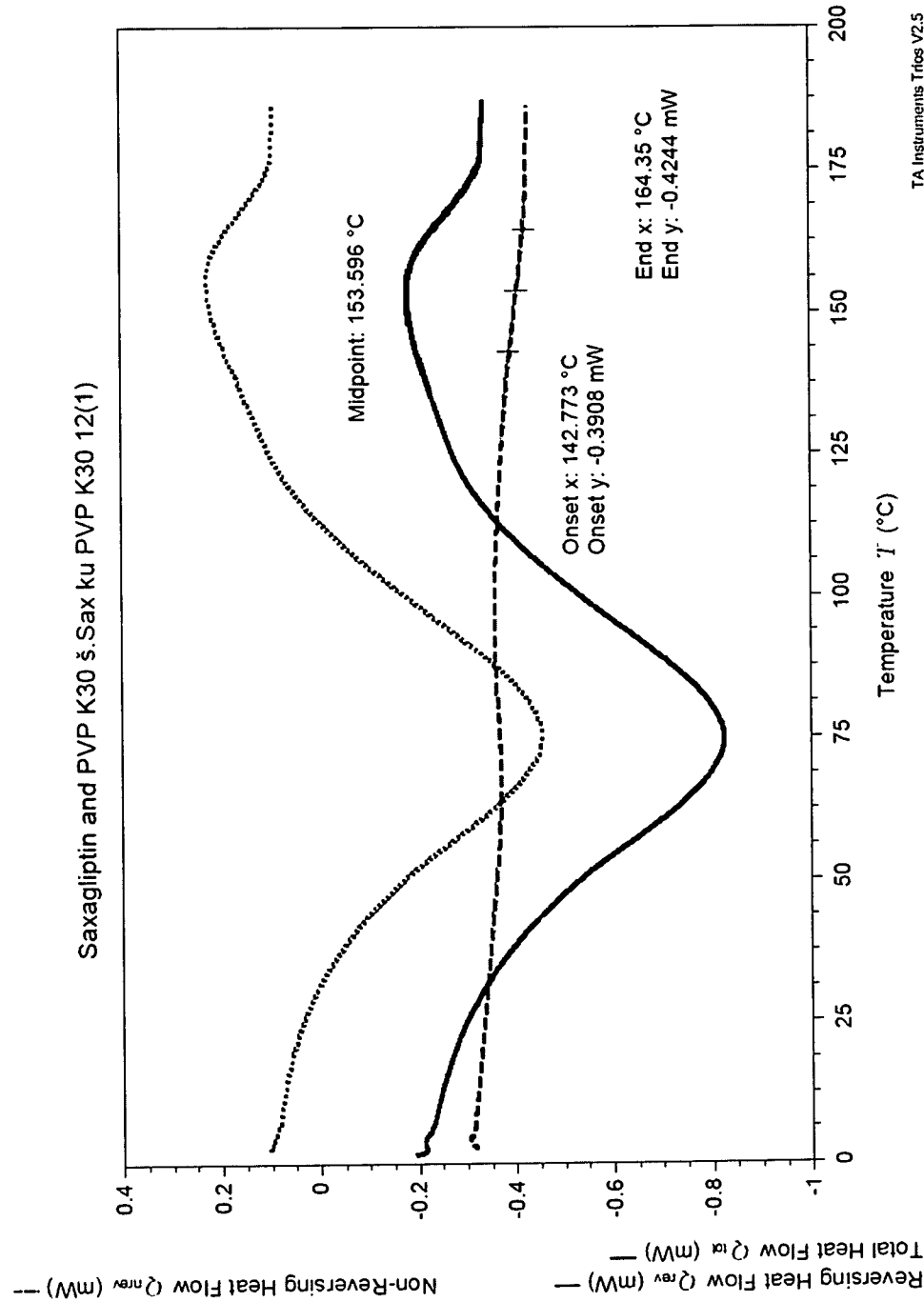


Figure 3 DSC curve of amorphous glass suspension of saxagliptin with PVP K25 polymer

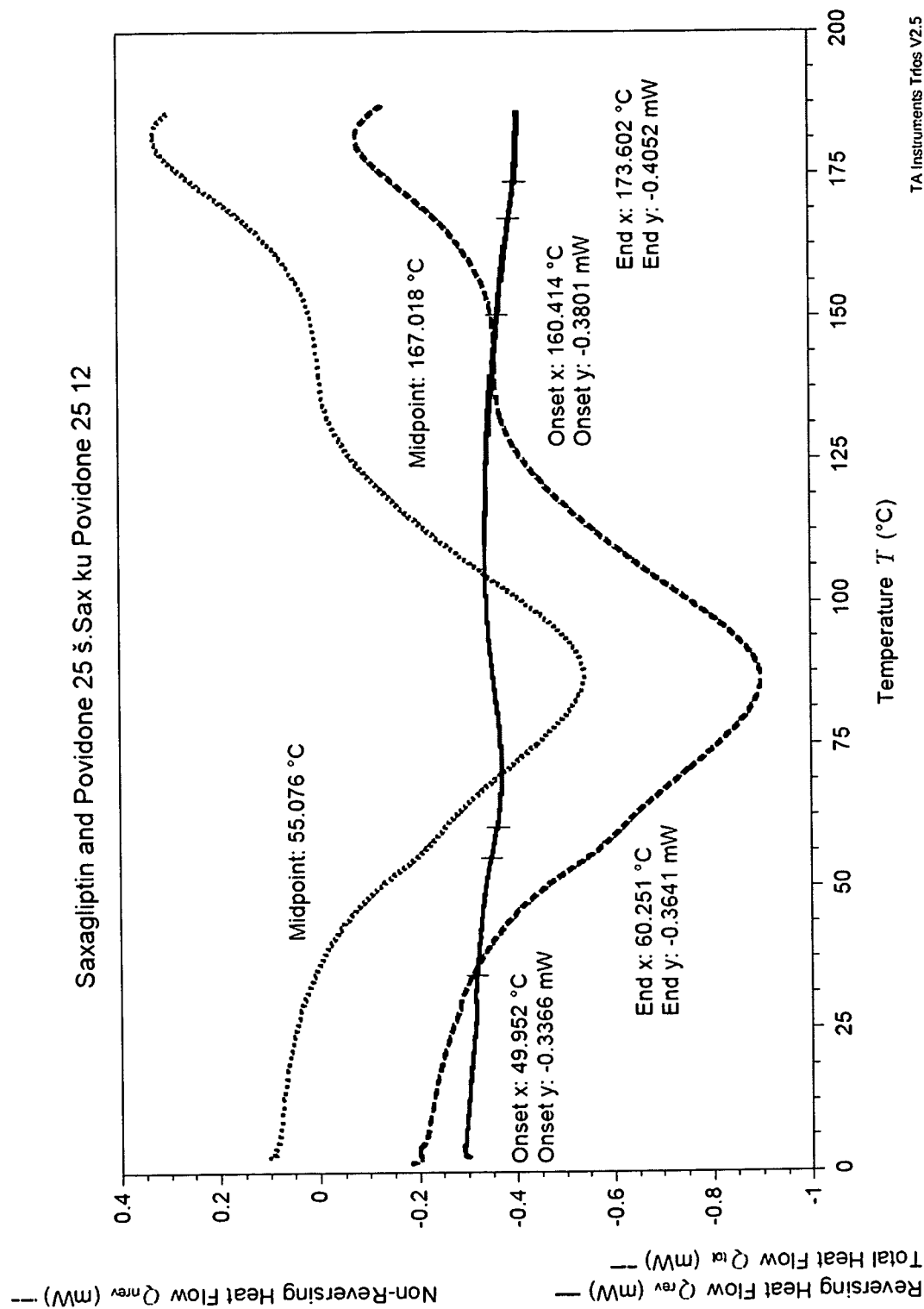
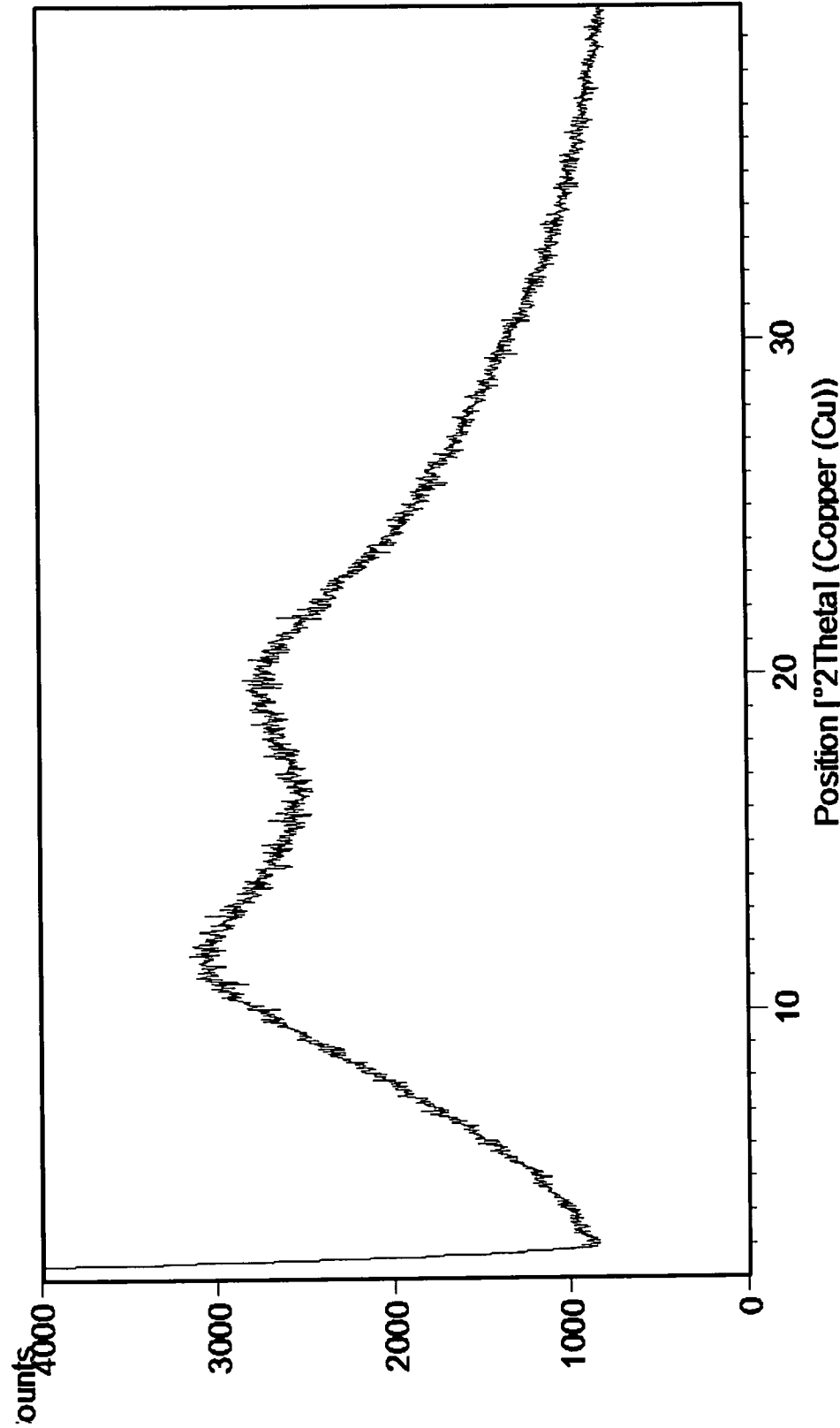


Figure 4 XRPD pattern of the amorphous glass suspension of saxagliptin with PVP K25 polymer



INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/001887

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/001887

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D209/52 A61K9/10
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)
C07D 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, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2012/083517 A1 (MARINKOVIC MARINA [HR] ET AL) 5 April 2012 (2012-04-05) cited in the application paragraphs [0086] - [0087], [0108] - [0111]; claims 14,15; figure 17; examples 18-20	1-17
Y	----- BABAR IQBAL ET AL: "Recent Advances and Patents in Solid Dispersion Technology", RECENT PATENTS ON DRUG DELIVERY & FORMULATION, vol. 5, no. 3, 1 September 2011 (2011-09-01), pages 244-264, XP055023758, ISSN: 1872-2113, DOI: 10.2174/18722111797200551 the whole document ----- -/-	1-17



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

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"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

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"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

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Date of the actual completion of the international search

18 August 2014

Date of mailing of the international search report

01/09/2014

Name and mailing address of the ISA/

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Authorized officer

Grassi, Damian

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/001887

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 027 886 A2 (PFIZER PROD INC [US]) 16 August 2000 (2000-08-16) paragraphs [0002], [0003], [0024], [0050], [0065], [0069] - [0071], [0082]; claim 42 -----	1-17
Y	US 8 257 739 B2 (BABCOCK WALTER C [US] ET AL) 4 September 2012 (2012-09-04) columns 1-2 column 26, lines 25-31 column 52, lines 52-57; claim 12; example 1 column 49, line 64 column 17, lines 50-59 column 21, lines 34-66 -----	1-17
Y	EP 0 852 140 A1 (NISSAN CHEMICAL IND LTD [JP]) 8 July 1998 (1998-07-08) column 1 Comparative examples 1, 2; column 6, line 57 - column 7, line 4; claims 5-6; examples 2,3,7 -----	1-17
Y	EP 2 105 130 A1 (RATIOPHARM GMBH [DE]) 30 September 2009 (2009-09-30) paragraphs [0001] - [0003], [0007], [0010], [0011], [0014], [0016], [0038]; claim 4; example 1 -----	1-17
X,P	WO 2013/136343 A1 (MYLAN LAB LTD [IN]; JETTI RAMAKOTESWARA RAO; BHAGAVATULA NEELIMA; BEER) 19 September 2013 (2013-09-19) pages 4,5; claim 7; example 8 -----	1,2,8,17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/001887

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-17

Composition of claim 1 involving polyvinylpyrrolidone.

1.1. claims: 4, 5(completely); 1, 8, 12-17(partially)

Composition of claim 1 involving hydroxypropyl methylcellulose.

1.2. claims: 6, 7(completely); 1, 8, 12-17(partially)

Composition of claim 1 involving hydroxypropylcellulose.
