(12) PATENT APPLICATION PUBLICATION
(19) INDIA
(22) Date of filing of Application :26/03/2018

(21) Application No.201841011100 A
(43) Publication Date : 27/09/2019

(54) Title of the invention : STABLE BILAYER TABLET COMPOSITIONS

(51) International classification	:A61K31/00; A61K45/06
(31) Priority Document No	:NA
(32) Priority Date	:NA
(33) Name of priority country	:NA
(86) International Application No	:NA
Filing Date	:NA
(87) International Publication No	: NA
(61) Patent of Addition to Application Number	:NA
Filing Date	:NA
(62) Divisional to Application Number	:NA
Filing Date	:NA

(71)**Name of Applicant :**
1)HETERO LABS LIMITED
Address of Applicant :Plot No: 22-110,Unit-III, IDA, Jeedimetla, Hyderabad,Telangana,India-500 055. Telangana India
(72)**Name of Inventor :**
1)PARTHASARADHI REDDY,Bandi
2)KHADGAPATHI, Podile
3)TIWARI, Sunil, Deviprasad
4)SRINIVASA RAO, Gella

(57) Abstract :
STABLE BILAYER TABLET COMPOSITIONS ABSTRACT: The invention relates to stable bilayer tablet compositions comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients which show no incompatibilities and the compositions having good stability and superior dissolution profile.

No. of Pages : 17 No. of Claims : 10

WE CLAIM:

1. A stable bilayer tablet composition comprising 10mg to 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 1-20% (w/w) and linagliptin is present in an amount of 1-10 % (w/w) based on total weight of the composition.

2. A stable bilayer tablet composition comprising 10mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 3-10 % (w/w) and linagliptin is present in an amount of 1-6 % (w/w) based on total weight of the composition.

3. A stable bilayer tablet composition comprising 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 8-16 % (w/w) and linagliptin is present in an amount of 1-6 % (w/w) based on total weight of the composition.

4. The composition according to claims 1-3 comprises pharmaceutically acceptable excipients such as microcrystalline cellulose, lactose monohydrate and croscarmellose sodium.

5. A stable bilayer tablet composition comprising empagliflozin, linagliptin, 5-30% (w/w) of microcrystalline cellulose, 10-40% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

6. The composition according to claim 5 comprises empagliflozin, linagliptin, 10-25% (w/w) of microcrystalline cellulose, 20-30% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 26/03/2018 15:27

7. The stable bilayer tablet composition according to any of the claims, wherein the composition exhibits dissolution of more than 85 % of empagliflozin and linagliptin within 15 minutes in a dissolution test using USP paddle type dissolution apparatus.

8. The composition according to any of the claims is in the form of an immediate release tablet.

9. The composition according to any of the claims is prepared by wet granulation method.

10. A stable bilayer tablet composition comprising 10mg to 25mg of empagliflozin, 5mg of linagliptin with not more than 0.2% of any single impurity and not more than 1 % of total impurities.

Dated this twenty first (21st) day of March, 2018

For:

Signature: ----------

Name: **Dr. KHADGAPATHI PODILE**
EXECUTIVE DIRECTOR
HETERO LABS LIMITED

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 26/03/2018 15:27

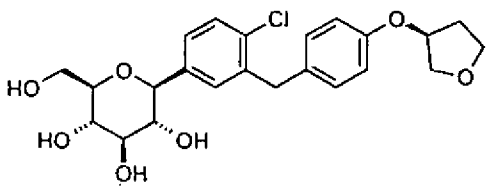
26-Mar-2018/23241/201841011100/Form 2(Title Page)

FIELD OF THE INVENTION

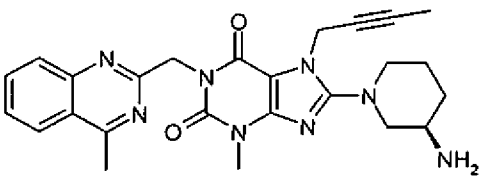
The invention relates to stable bilayer tablet compositions comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients and process for the preparation of such compositions.

BACKGROUND OF THE INVENTION

Empagliflozin is an orally-active inhibitor of the sodium-glucose co-transporter 2 (SGLT2) known from U.S Patent No. 7,579,449. It is chemically D-Glucitol,1,5-anhydro-1-C-[4-chloro-3-[[4-[[(3S)-tetrahydro-3-furanyl]oxy]phenyl]methyl]phenyl]-, (1S) having structure as below:



Linagliptin is an orally-active inhibitor of the dipeptidyl peptidase-4 (DPP-4) enzyme known from U.S Patent No. 7,407,955. It is chemically 1H-Purine-2,6-dione, 8-[(3R)-3-amino-1-piperidinyl]-7-(2-butyn-1-yl)-3,7-dihydro-3-methyl-1-[(4-methyl-2-quinazolinyl) methyl] having structure as below:



Tablets of empagliflozin in combination with linagliptin for oral administration are currently being marketed in United States under the name Glyxambi® by Boehringer Ingelheim indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus and are available as single layer tablets in two dosage strengths i.e. 10mg/5mg and 25mg/5mg respectively.

PATENT OFFICE CHENNAI 27/03/2018 15:27

U.S Patent publication No. 20110014284 describes pharmaceutical compositions comprising empagliflozin, process for the preparation of such compositions and their use in the treatment of various conditions including type 1 diabetes mellitus and type 2 diabetes mellitus.

U.S Patent publication No. 20170312287 (hereinafter '287) describes pharmaceutical compositions of linagliptin, their preparation and their use in the treatment of type 1 diabetes mellitus and type 2 diabetes mellitus.

U.S Patent publication No. 20100209506 (hereinafter '506) claims single layered pharmaceutical compositions comprising combination of empagliflozin and linagliptin.

According to '287 and '506, in attempts to prepare pharmaceutical compositions of linagliptin, it has been observed that linagliptin with a primary or secondary amino group show incompatibilities, degradation problems, or extraction problems with a number of customary excipients. Though the compounds themselves are very stable, they react with many excipients used in solid dosage forms. The amino group appears to react with reducing sugars and with other reactive carbonyl groups and with carboxylic acid functional groups formed for example at the surface of microcrystalline cellulose by oxidation. These unforeseen difficulties are primarily observed in low dosage ranges which are required due to the surprising potency of the selected inhibitors. Thus, pharmaceutical compositions are required to solve these technical problems associated with the unexpected potency of linagliptin.

Hence, there exists a need to develop formulations without compromising on the formulation properties, dissolution profile as well as stability of the formulation.

Inventors of the present invention have prepared stable bilayer tablet compositions comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients. The compositions according to the invention having good stability and superior dissolution profile.

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27

SUMMARY OF THE INVENTION

One aspect of the present invention relates to stable bilayer tablet compositions comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients.

Another aspect of the present invention is a stable bilayer tablet composition comprising 10mg to 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 1-20% (w/w) and linagliptin is present in an amount of 1-10 % (w/w) based on total weight of the composition.

Another aspect of the present invention is a stable bilayer tablet composition comprising 10mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 3-10 % (w/w) and linagliptin is present in an amount of 1-6 % (w/w) based on total weight of the composition.

Another aspect of the present invention is a stable bilayer tablet composition comprising 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 8-16 % (w/w) and linagliptin is present in an amount of 1-6 % (w/w) based on total weight of the composition.

Another aspect of the present invention is a stable bilayer tablet composition comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients such as microcrystalline cellulose, lactose monohydrate and croscarmellose sodium which shows no incompatibilities and the composition having good stability and superior dissolution profile.

Another aspect of the present invention is a stable bilayer tablet composition comprising empagliflozin, linagliptin, 5-30% (w/w) of microcrystalline cellulose, 10-40% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

PATENT OFFICE CHENNAI 27/03/2018 15:27

26-Mar-2018/23241/201841011100/Form 2(Title Page)

Another aspect of the present invention is a stable bilayer tablet composition comprising empagliflozin, linagliptin, 10-25% (w/w) of microcrystalline cellulose, 20-30% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

Another aspect of the present invention is a stable bilayer tablet composition comprising 1-20% (w/w) of empagliflozin, 1-10 % (w/w) of linagliptin, 5-30% (w/w) of microcrystalline cellulose, 10-40% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

Yet another aspect of the present invention is a stable bilayer tablet composition comprising 10mg to 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients which shows no incompatibilities and having good stability, superior dissolution profile and the composition having not more than 0.2% of any single impurity and not more than 1 % of total impurities.

The details of one or more embodiments of the present invention are set forth in the description below. Other features, objects and advantages of the invention will be apparent from the description.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to stable bilayer tablet compositions comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients.

The term "composition" as used herein refers to a dosage form suitable for oral administration, such as tablets, granules, powder, spheroids, pellets, pills, capsule, solution, suspension, emulsion and the like.

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27

The term "bilayer tablet" as used herein refers to a coated or uncoated tablet with two layers of different materials compressed together wherein each layer having same or different release profiles.

The term "stable bilayer tablet" as used herein refers to a bilayer tablet with not more than 0.2% of any single impurity and not more than 1 % of total impurities.

The term "pharmaceutically acceptable" as used herein means that which is useful in preparing a pharmaceutical composition that is generally safe and non-toxic.

The term "excipients" as used herein means a component of a pharmaceutical product that is not an active ingredient such as, for example, diluents, binders, carriers and the like. The excipients that are useful in preparing a pharmaceutical composition are generally safe and non-toxic.

One embodiment of the present invention is a stable bilayer tablet composition comprising 10mg to 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 1-20% (w/w) and linagliptin is present in an amount of 1-10 % (w/w) based on total weight of the composition.

Another embodiment of the present invention is a stable bilayer tablet composition comprising 10mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 3-10 % (w/w) and linagliptin is present in an amount of 1-6 % (w/w) based on total weight of the composition.

Another embodiment of the present invention is a stable bilayer tablet composition comprising 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients thereof, wherein empagliflozin is present in an amount of 8-16 % (w/w) and linagliptin is present in an amount of 1-6 % (w/w) based on total weight of the composition.

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27

The present invention provides a stable bilayer tablet composition comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients comprising one or more of fillers, binders, disintegrants, lubricants, glidants and the like.

Suitable fillers include, but are not limited to starch, dibasic calcium phosphate, tribasic calcium phosphate, microcrystalline cellulose, calcium carbonate, dextrose, kaolin, magnesium carbonate, magnesium oxide, lactose monohydrate, sugar alcohols such as mannitol, sorbitol, erythritol and the like and combinations thereof. Preferred fillers are microcrystalline cellulose, lactose monohydrate, mannitol and combinations thereof.

Suitable binders include, but are not limited to carbomers, dextrin, ethyl cellulose, hydroxypropyl cellulose, povidone, copovidone, gelatin, polymethacrylates, pregelatinized starch, sodium alginate, gums, synthetic resins, silicic acid and the like and combinations thereof. Preferred binders are hydroxypropyl cellulose, copovidone and combinations thereof.

Suitable disintegrants include, but are not limited to croscarmellose sodium, sodium starch glycolate, crospovidone, polacrillin potassium, microcrystalline cellulose, carboxymethyl cellulose calcium, starches such as corn starch, potato starch, pre-gelatinized starch and modified starches, clays, bentonite, and the like and combinations thereof. Preferred disintegrants are croscarmellose sodium, corn starch and combinations thereof.

Suitable lubricants include, but are not limited to calcium stearate, glyceryl monostearate, glyceryl palmitostearate, hydrogenated castor oil, hydrogenated vegetable oil, light mineral oil, magnesium stearate, mineral oil, polyethylene glycol, sodium benzoate, sodium lauryl sulfate, sodium stearyl fumarate, stearic acid, talc, zinc stearate, and the like and combinations thereof. Preferred lubricant is magnesium stearate.

Suitable glidants include, but are not limited to colloidal silicon dioxide, talc, starch, starch derivatives, and the like and combinations thereof. Preferred glidant is colloidal silicon dioxide.

26-Mar-2018/23241/2018411011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27

Another embodiment of the present invention is a stable bilayer tablet composition comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients such as microcrystalline cellulose, lactose monohydrate and croscarmellose sodium which shows no incompatibilities and the composition having good stability and superior dissolution profile.

Another embodiment of the present invention is a stable bilayer tablet composition comprising empagliflozin, linagliptin, 5-30% by weight of microcrystalline cellulose, 10-40% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

Another embodiment of the present invention is a stable bilayer tablet composition comprising empagliflozin, linagliptin, 10-25% by weight of microcrystalline cellulose, 20-30% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

Another embodiment of the present invention is a stable bilayer tablet composition comprising 1-20% (w/w) of empagliflozin, 1-10 % (w/w) of linagliptin, 5-30% (w/w) of microcrystalline cellulose, 10-40% (w/w) of lactose monohydrate and 0.5-5% (w/w) of croscarmellose sodium based on total weight of the composition.

Another embodiment of the present invention is a stable bilayer tablet composition comprising empagliflozin and linagliptin exhibits dissolution of more than 85 % of empagliflozin and linagliptin within 15 minutes in a dissolution test using USP paddle type dissolution apparatus.

Another embodiment of the present invention is a stable bilayer tablet composition comprising 10mg to 25mg of empagliflozin, 5mg of linagliptin and pharmaceutically acceptable excipients which shows no incompatibilities and having good stability, superior dissolution profile and the composition having not more than 0.2% of any single impurity and not more than 1 % of total impurities.

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27

The stable bilayer tablet compositions mentioned herein are in the form of immediate release tablets and are prepared by dry granulation, wet granulation or direct compression, preferably, wet granulation.

The stable bilayer tablet compositions were prepared by making two separate granulations containing empagliflozin in one granulation and linagliptin in other granulation, Empagliflozin and/or linagliptin and other excipients, in particular one or more diluents, one or more disintegrants are premixed and granulated with the binder solution, for example using a high shear granulator. The wet granulation step is usually followed by one or more drying and sieving steps. Glidants and lubricants are blended with the dried granules. Suitable bilayer compression machine was used to compress the empagliflozin layer followed by linagliptin layer with suitable tooling and finally the bilayer tablets were film coated.

The stable bilayer tablet compositions of empagliflozin and linagliptin of the present invention can be used as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

EXAMPLES

Certain specific aspects and embodiments of this invention are described in further detail by the examples below, which are provided only for purposes of illustration and are not intended to limit the scope of the invention in any manner.

Example 1:

Bilayer tablet composition comprising empagliflozin and linagliptin:

Table 1

Ingredients	mg/unit	mg/unit
First layer:		
Empagliflozin	10.00	25.00

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27

Ingredients	mg/ unit	mg/ unit
Microcrystalline cellulose	25.00	25.00
Lactose monohydrate	60.50	45.50
Croscarmellose sodium	4.50	4.50
Hydroxypropyl cellulose	1.00	1.00
Purified water	Qs	Qs
Extra granular		
Colloidal silicon dioxide	1.00	1.00
Magnesium stearate	1.00	1.00
Second layer:		
Linagliptin	5.00	5.00
Mannitol	72.50	72.50
Corn starch	6.00	6.00
Croscarmellose sodium	2.00	2.00
Copovidone	10.00	10.00
Purified water	Qs	Qs
Extra granular		
Magnesium stearate	1.50	1.50
Core tablet weight (First layer + Second layer)	200.00	200.00
Film coating material weight	5.00	5.00
Total weight of coated tablet	**205**	**205**

Brief manufacturing process:

Empagliflozin Layer:

1. Empagliflozin, lactose monohydrate, croscarmellose sodium and microcrystalline cellulose were sifted through mesh #40.

2. Materials of step no.1 were blended for 15 minutes using a suitable blender.

3. Binder solution was prepared by slowly adding hydroxypropyl cellulose to purified water under continuous stirring until clear solution was obtained.

4. Granulate the blend of step no.2 with binder solution of step no.3 to obtain suitable granules.

5. Wet granules of step no.4 were dried in a suitable dryer at 60 ±5°C, drying continued to get desired LOD range.

6. Dried granules of step no.5 were passed through mesh #24.

7. Colloidal silicon dioxide was sifted through mesh #40,

8. Dried granules of step no.6 were loaded in to suitable blender and colloidal silicon dioxide of step no.7 was added and blended for 15 minutes,

26-Mar-2018/23241/201841011100/Form 2(Title Page)

9. Magnesium stearate was sifted through suitable mesh,

10. Magnesium stearate of step no.9 was added to the blend of step no.8 and blended for 5 minutes.

Linagliptin layer:

1. Linagliptin, corn starch, croscarmellose sodium and mannitol were sifted through suitable mesh,

2. Materials of step no.1 were blended for 15 minutes using a suitable blender.

3. Binder solution was prepared by slowly adding copovidone to purified water under continuous stirring until clear solution was obtained.

4. Granulate the blend of step no.2 with binder solution of step no.3 to obtain suitable granules.

5. Wet granules of step no.4 were dried in a suitable dryer at 60 ±5°C, drying continued to get desired LOD range.

6. Dried granules of step no.5 were passed through mesh #24.

7. Materials of step no.6 was loaded into suitable blender and blended for 15 minutes.

8. Magnesium stearate was sifted through suitable mesh.

9. Magnesium stearate of step no.8 was added to the materials of step no.7 and blended for 5 minutes.

Compression:

Suitable bilayer compression machine was used to compress the empagliflozin layer followed by linagliptin layer with suitable tooling and finally the bilayer tablets were film coated.

Example 2:

Table 2

Ingredients	mg/ unit	mg/ unit
First layer:		
Empagliflozin	10.00	25.00
Microcrystalline cellulose	34.00	34.00

26-Mar-2018/23241/201841011100/Form 2(Title Page)

Ingredients	mg/ unit	mg/ unit
Lactose monohydrate	40.50	35.50
Croscarmellose sodium	4.50	1.50
Hydroxypropyl cellulose	1.00	1.00
Extra granular		
Colloidal silicon dioxide	1.50	1.50
Magnesium stearate	1.50	1.50
Second layer:		
Linagliptin	5.00	5.00
Mannitol	40.50	33.50
Corn starch	6.00	6.00
Croscarmellose sodium	2.00	2.00
Copovidone	8.00	8.00
Extra granular		
Magnesium stearate	1.50	1.50
Core tablet weight (First layer + Second layer)	156	156
Film coating material weight	5.00	5.00
Total weight of coated tablet	**161**	**161**

Manufacturing process: Bilayer tablet composition of example 2 was prepared using standard dry granulation method (roller compaction).

Example 3:

Table 3

Ingredients	mg/ unit	mg/ unit
First layer:		
Empagliflozin	10.00	25.00
Microcrystalline cellulose	16.10	16.10
Lactose monohydrate	32.20	29.20
Croscarmellose sodium	3.22	3.22
Hydroxypropyl cellulose	1.00	1.00
Colloidal silicon dioxide	0.97	0.97
Magnesium stearate	1.61	1.61
Second layer:		
Linagliptin	5.00	5.00
Mannitol	32.40	32.40
Corn starch	2.00	2.00
Croscarmellose sodium	2.00	2.00
Copovidone	8.00	13.00

26-Mar-2018/23241/201841011100/Form 2(Title Page)

Ingredients	mg/ unit	mg/ unit
Magnesium stearate	1.50	1.50
Core tablet weight (empagliflozin layer + linagliptin layer)	116	133
Film coating material weight	5.00	5.00
Total weight of coated tablet	121	138

Manufacturing process: Bilayer tablet composition of example 3 was prepared using standard direct compression method.

Dissolution Test:

The standard dissolution test is described in USP31-NF26 S2, chapter 711 (dissolution). The paddle method (apparatus 2) with an agitation speed of 50 rpm was used. The dissolution media is 900 mL 0.05 M Potassium phosphate buffer pH 6.8 at a temperature of 37° C. Samples were taken after 10, 15, 20, 30 and 45 minutes. The samples were analyzed via HPLC method.

Table 4

Dissolution profile of bilayer tablets according to the example 1:

Time in Min	10mg/ 5mg		25mg/ 5mg	
	Empagliflozin	Linagliptin	Empagliflozin	Linagliptin
10	87	93	89	86
15	91	100	93	89
20	92	101	94	91
30	93	102	95	94
45	94	102	95	95

The stability can be tested in standard tests, for example after 3 months storage at 40° C and 75% relative humidity. The tablets were packed in HDPE container with 2gm silica gel.

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27

Table 5

Stability data:

Example 1				
Condition & Storage period	40 ^{0}C/75% RH			
	Initial		3 Months	
	Empagliflozin	Linagliptin	Empagliflozin	Linagliptin
Assay (% w/w)	96.6	96.8	98.7	102.3
Water content (% w/w)	4.05		3.25	
Impurities:				
(2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-hydroxybenzyl) phenyl)-6-(hydroxymethyl) tetrahydro-2H-pyran-3,4,5-triol	0.000		0.00	
(3R)-tetrahydro-3-furanyl-4-methylbenzenesulfonate	0.008		0.010	
(2S,3S,4R,5R,6R)-2-(3-(4-Acetoxybenzyl)-4-chlorophenyl)-6-(acetoxymethyl tetrahydro-2H-pyran-3,4,5-triyl triacetate	0.000		0.000	
8-Bromo-7-(but-2-ynyl)-3-methyl-1-((4-methylquinazolin-2-yl) methyl)-1H-purine-2,6(3H,7H)-dione	0.028		0.018	
(R)-7-(but-2-yn-1-yl)-3-methyl-1-((4-methylquinazolin-2-yl)methyl)-8-(piperidin-3-ylamino)-3,7-dihydro -1H-purine-2,6-dione	0.004		0.000	
MSUI (Maximum Single Unknown Impurity)	0.059		0.093	
TUI (Total Unknown Impurities)	0.059		0.160	
Total impurities	0.158		0.281	

26-Mar-2018/23241/201841011100/Form 2(Title Page)

"STABLE BILAYER TABLET COMPOSITIONS"

ABSTRACT:

The invention relates to stable bilayer tablet compositions comprising empagliflozin, linagliptin and pharmaceutically acceptable excipients which show no incompatibilities and the compositions having good stability and superior dissolution profile.

26-Mar-2018/23241/201841011100/Form 2(Title Page)

PATENT OFFICE CHENNAI 27/03/2018 15:27