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(54) **Title:** PHARMACEUTICAL COMPOSITION OF VILAZODONE AND PROCESSES OF PREPARATION THEREOF

(57) **Abstract:** The present invention relates to pharmaceutical compositions comprising vilazodone and one or more non-ionic surfactants. It also relates to processes for the preparation of said pharmaceutical compositions, and a method of treating and/or preventing a central nervous system disorder by administering said pharmaceutical compositions.



PHARMACEUTICAL COMPOSITION OF VILAZODONE AND PROCESSES OF PREPARATION THEREOF

Field of the Invention

5 The present invention relates to pharmaceutical compositions comprising vilazodone and one or more non-ionic surfactants. It also relates to processes for the preparation of said pharmaceutical compositions and methods of treating and/or preventing central nervous system disorders by administering said pharmaceutical compositions.

10 Background of the Invention

Vilazodone hydrochloride, disclosed in U.S. Patent No. 5,532,241, is chemically designated as 2-benzofurancarboxamide, 5-[4-[4-(5-cyano-1*H*-indol-3-yl)butyl]-1-piperazinyl]-, hydrochloride (1:1). Vilazodone hydrochloride is a selective serotonin reuptake inhibitor and a 5HT_{1A} receptor partial agonist. It is indicated for the treatment of major depressive disorder.

A review of the art shows that U.S. Patent No. 7,834,020 discloses fifteen crystalline modifications of vilazodone hydrochloride designated as Form I through Form XV. It also discloses conventional forms of administration such as tablets and capsules. PCT Publication No. WO 2012/131706 discloses the amorphous form of vilazodone hydrochloride. Further, PCT Publication No. WO 2013/078361 discloses several other polymorphic forms of vilazodone hydrochloride.

There still remains a need in the art to provide alternative pharmaceutical compositions of vilazodone which are bioequivalent to commercially available Viibryd® tablets. The present inventors have discovered that the use of a non-ionic surfactant in the pharmaceutical composition helps to achieve the desired release profile of the drug.

Summary of the Invention

The present invention relates to pharmaceutical compositions of vilazodone which are bioequivalent to commercially available Viibryd® tablets. The present invention includes pharmaceutical compositions of vilazodone and one or more non-ionic

surfactants. It further includes pharmaceutical compositions of vilazodone and one or more non-ionic surfactants encapsulated within an inert carrier.

The present invention includes processes for the preparation of said pharmaceutical compositions. It further includes a method of treating and/or preventing central nervous system disorders by administering said pharmaceutical compositions.

Detailed Description of the Invention

The desired dissolution profile is a prerequisite for the development of a regulatory compliant drug product. Although the use of a surfactant for enhancing the dissolution of the drugs in compositions is known, the choice of a particular surfactant is critical. The scientists of the present invention have found that the use of a particular non-ionic surfactant in vilazodone compositions enhances the rate and extent of dissolution and provides the desired dissolution profile. Further, it has been found that the non-ionic surfactant encapsulated within an inert carrier provides a free-flowing powder which can be easily formulated into the pharmaceutical compositions. Also, because particle size plays a key role in the solubility and dissolution profile of a drug, the present invention uses micronized vilazodone particles to achieve the desired release profile.

A first aspect of the present invention provides a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants.

According to one embodiment of the present invention, there is provided a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the non-ionic surfactant is encapsulated within an inert carrier.

According to another embodiment of the present invention, there is provided a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the vilazodone particles have a D_{50} range of about 0.1 μm to about 20 μm .

According to another embodiment of the present invention, there is provided a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the vilazodone particles have a D_{90} range of about 0.5 μm to about 40 μm .

According to another embodiment of the present invention, there is provided a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the vilazodone particles have D_{10} range of about 0.05 μm to about 10 μm .

According to another embodiment of the present invention, there is provided a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein more than 40% w/w of vilazodone dissolves within 30 minutes in 0.1N HCl, in a USP type II apparatus.

5 According to another embodiment of the present invention, there is provided a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the pharmaceutical composition is a stable composition.

 According to another embodiment of the present invention, there is provided a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants,
10 wherein the composition is bioequivalent to Viibryd[®] tablets when bioavailability studies are conducted in humans.

A second aspect of the present invention provides a process for the preparation of a pharmaceutical composition of vilazodone, wherein the process comprises the steps of:

- 15 (a) blending vilazodone and one or more non-ionic surfactants with one or more pharmaceutically acceptable excipients;
- (b) directly compressing the blend of step (a) to form tablets; and
- (c) film coating the tablets obtained from step (b).

A third aspect of the present invention provides a process for the preparation of a pharmaceutical composition of vilazodone, wherein the process comprises the steps of:

- 20 (a) blending vilazodone and one or more non-ionic surfactants with one or more pharmaceutically acceptable excipients;
- (b) granulating the blend of step (a);
- (c) blending the granules of step (b) with one or more pharmaceutically acceptable excipients;
- 25 (d) compressing the blend of step (c) to form tablets; and
- (e) film coating the tablets obtained from step (d).

A fourth aspect of the present invention provides a method of treating and/or preventing a central nervous system disorder by administering a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants.

30 According to one embodiment of the present invention, there is provided a method of treating and/or preventing a central nervous system disorder by administering a

pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the central nervous system disorder is selected from major depressive disorder, anxiety disorders, bipolar disorders, mania, dementia, eating disorders, sleeping disorders, psychiatric disorders, cerebral infarct, tension, and any combination thereof.

5 According to another embodiment of the present invention, there is provided a method of treating and/or preventing central nervous system disorder by administering a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the central nervous system disorder is major depressive disorder.

10 According to another embodiment of the present invention, there is provided a method of treating and/or preventing central nervous system disorders by administering a pharmaceutical composition comprising vilazodone and one or more non-ionic surfactants, wherein the method comprises co-administration of additional drugs acting on the central nervous system.

15 The term “vilazodone”, as used herein, refers to 2-benzofurancarboxamide, 5-[4-[4-(5-cyano-1*H*-indol-3-yl)butyl]-1-piperazinyl]. It further includes salts, polymorphs, hydrates, solvates, prodrugs, chelates, and complexes thereof. The preferred salt of vilazodone is vilazodone hydrochloride. The pharmaceutical compositions of the present invention comprise vilazodone in an amount of from about 1% w/w to about 30% w/w, preferably from about 5% w/w to about 20% w/w of the total composition. Vilazodone
20 hydrochloride may be used in the pharmaceutical composition in strengths of 10 mg, 20 mg, and 40 mg of vilazodone. The vilazodone hydrochloride used in the pharmaceutical composition may encompass any known polymorphs at the time of the invention. It may also encompass the amorphous form of vilazodone hydrochloride. Preferably, the pharmaceutical composition of the present invention comprises vilazodone hydrochloride
25 Form IV.

 The term “D₅₀”, as used herein, refers to a particle diameter at which 50% of the particles have diameters which are greater or smaller than the given value. The present invention includes vilazodone particles having a D₅₀ range of about 0.1 μm to about 20 μm, in particular from about 1 μm to about 10 μm.

30 The term “D₉₀”, as used herein, refers to a particle diameter at which 90% of the particles have diameters which are smaller than the given value. The present invention

includes vilazodone particles having a D_{90} range of about 0.5 μm to about 40 μm , in particular, about 5 μm to about 20 μm .

The term " D_{10} ", as used herein, refers to a particle diameter at which 10% of the particles have diameters which are smaller than the given value. The present invention
5 includes vilazodone particles having a D_{10} range of about 0.05 μm to about 10 μm , in particular from about 0.1 μm to about 5 μm .

It should be understood that the D_{10} , D_{50} and D_{90} values given above refer to a discrete number, e.g., 1 μm . Therefore, by providing a range for D_{10} it should be understood that the D_{10} particle diameter is a discrete value within that range.

10 The size reduction or micronization of vilazodone may be carried out by using any of the conventional mills such as air jet mills, ball mills, colloid mills, grinding mills, roller mills, or impact mills. Preferably, the particle size is reduced by a ball mill. Further, the particle size may be determined by any known technique such as a sieve analyzer, electrical conductance instruments such as a coulter counter, and laser diffraction
15 particle size analyzer such as a Malvern[®] instrument. Preferably, the particle size is determined by a Malvern[®] instrument.

The term "stable", as used herein, refers to chemical as well as physical stability. Chemical stability means maintaining the original formulation specifications, and physical stability means that there is no change in the polymorphic form determined by X-ray
20 powder diffraction after exposure to a relative humidity of 75% at 40°C or relative humidity of 60% at 25°C, for a period of at least about three months to the extent necessary for sale and use of the composition.

Further, in the present invention, unmiconized and micronized vilazodone hydrochloride particles show polymorphic stability, as there is no conversion of
25 polymorphic forms during micronization.

The term "non-ionic surfactant", as used herein, refers to a water-soluble surfactant which is liquid or semi-solid at 25°C. Suitable non-ionic surfactants are selected from the group consisting of polyoxyethyl-sorbitan-fatty acid esters such as polysorbates; ethers of sugars such as ethers of lactose, sucrose, xylose, mannitol, or xylitol; ethoxylated fatty
30 alcohols; fatty acids and their salts; ethoxylated fatty acids; polyglyceryl esters; copolymers of propylene oxide and of ethylene oxide; phospholipids or lecithins; amino acid fatty chain acrylates; triglycerides of plant or synthetic origin and their ethoxylated

derivatives such as polyoxyl 35 castor oil and polyoxyl 40 hydrogenated castor oil; acetylated monoglycerides; sodium lauryl sulphate and its derivatives; taurocholic acid; or mixtures thereof. The preferred non-ionic surfactant is a polysorbate.

The term “carrier”, as used herein, refers to the particulate or porous material having an appropriate surface area on which the drug may be encapsulated, microencapsulated, or adsorbed, preferably encapsulated. Suitable carriers are selected from the group consisting of magnesium aluminum silicate, aluminum silicate, calcium silicate, magnesium silicate, magnesium trisilicate, sodium magnesium silicate, lithium magnesium silicate, zirconium silicate, attapulgite, bentonite, fuller's earth, hectorite, kaolin, montmorillonite, pyrophyllite, zeolite, calcium carbonate, calcium phosphate, calcium gluconate, magnesium gluconate, manganese gluconate, calcium diphosphate, silicon dioxide, microcrystalline celluloses, sugars such as lactose, sorbitol, mannitol, xylitol, or maltitol, or mixtures thereof.

The term “encapsulated”, as used herein, refers to a non-ionic surfactant homogeneously distributed within the inert carrier particles. The term “microencapsulated”, as used herein, refers to very tiny droplets of liquid or semi-solid particles of a non-ionic surfactant surrounded or coated with inert carrier particles.

The term “adsorbed”, as used herein, refers to adherence of a non-ionic surfactant onto the surface of the inert carrier particles without penetrating inside the inert carrier particles.

Bioequivalence is established by comparing pharmacokinetic parameters, for example AUC and $C_{\max}$, of the present invention with Viibryd[®] tablets in healthy human subjects. The term “AUC” refers to the area under the time/plasma concentration curve after the administration of the vilazodone dosage form to healthy human subjects. The term “ $C_{\max}$ ” refers to the maximum concentration of vilazodone in the blood following the administration of the vilazodone dosage form to healthy human subjects.

Bioequivalence is defined to mean the term used by the drug approval agencies, such as the US Food and Drug Administration: “the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.” This is typically understood to mean that the test drug product is within

+25% and -20% of the reference drug product for AUC and $C_{\max}$, for example as explained in the US FDA's various bioequivalence guidance documents for oral tablets and capsules, which are incorporated herein by reference.

5 In the present invention, the non-ionic surfactant is encapsulated within an inert carrier using any suitable conventional processes such as dissolving the non-ionic surfactant in a suitable solvent, combining the inert carrier, and removing the solvent by filtration and/or evaporation. Alternatively, mechanical homogenization or spray drying processes can also be used for preparing the encapsulated non-ionic surfactant.

10 Commercially available SEPITRAP[®] 80 or SEPITRAP[®] 4000 may also be used as the non-ionic surfactant. SEPITRAP[®] 80 comprises from about 35% w/w to about 55% w/w of polysorbate 80 and from about 45% w/w to about 65% w/w of magnesium aluminum silicate. The pharmaceutical composition of the present invention comprises SEPITRAP[®] 80 in an amount of from about 0.1% w/w to about 10% w/w of the total composition.

15 The term "about", as used herein, refers to any value which lies within the range defined by a variation of up to $\pm 10\%$ of the value.

The term "pharmaceutical composition", as used herein, means a composition which is selected from the group consisting of tablets, capsules, pellets, pills, caplets, and granules, in particular tablets.

20 The term "pharmaceutically acceptable excipient", as used herein, includes excipients that may be added intragranularly and/or extragranularly in the pharmaceutical compositions. The pharmaceutically acceptable excipients include fillers, binders, lubricants, disintegrants, coloring agents, plasticizers, and opacifiers.

25 Suitable fillers are selected from the group consisting of lactose monohydrate, lactose anhydrous, pregelatinized starch, calcium carbonate, calcium phosphate dibasic, calcium phosphate tribasic, calcium sulphate, kaolin, starch, or mixtures thereof.

30 Suitable binders are selected from the group consisting of methyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, gelatin, gum arabic, ethyl cellulose, polyvinyl alcohol, pullulan, pregelatinized starch, agar, tragacanth, sodium alginate, propylene glycol, or mixtures thereof.

Suitable lubricants are selected from the group consisting of colloidal silicon dioxide, stearic acid, magnesium stearate, calcium stearate, zinc stearate, sodium stearyl fumarate, talc, hydrogenated castor oil, sucrose esters of fatty acid, microcrystalline wax, yellow beeswax, white beeswax, or mixtures thereof.

- 5 Suitable disintegrants are selected from the group consisting of sodium starch glycolate, croscarmellose, pregelatinized starch, microcrystalline cellulose, calcium carboxymethyl cellulose, low substituted hydroxypropyl cellulose, magnesium silicate, aluminum silicate, or mixtures thereof.

Coloring agents include any FDA approved color for oral use.

- 10 Suitable plasticizers are selected from the group consisting of triethyl citrate, dibutyl sebacate, acetylated triacetin, tributyl citrate, glycerol tributyrate, monoglyceride, rapeseed oil, olive oil, sesame oil, acetyl tributyl citrate, acetyl triethyl citrate, glycerin sorbitol, diethyl oxalate, diethyl phthalate, diethyl malate, diethyl fumarate, dibutyl succinate, diethylmalonate, dioctyl phthalate, or mixtures thereof.

- 15 Suitable opacifiers are selected from the group consisting of titanium dioxide, manganese dioxide, iron oxide, silicon dioxide, or mixtures thereof.

The present invention provides a process for the preparation of a pharmaceutical composition, wherein the process comprises the steps of:

- 20 (a) blending vilazodone and one or more non-ionic surfactants with one or more pharmaceutically acceptable excipients;
- (b) directly compressing the blend of step (a) to form tablets; and
- (c) film coating the tablets obtained from step (b).

The present invention also provides a process for the preparation of a pharmaceutical composition, wherein the process comprises the steps of:

- 25 (a) blending vilazodone and one or more non-ionic surfactants with one or more pharmaceutically acceptable excipients;
- (b) granulating the blend of step (a);
- (c) blending the granules of step (b) with one or more pharmaceutically acceptable excipients;
- 30 (d) compressing the blend of step (c) to form tablets; and
- (e) film coating the tablets obtained from step (d).

In the present invention, the non-ionic surfactant may be encapsulated within an inert carrier and then the encapsulated surfactant may be used in the process for the preparation of a pharmaceutical composition. Further, the vilazodone used in the process for the preparation of the pharmaceutical composition may comprise micronized vilazodone hydrochloride particles.

The granulation may be carried out by using either a wet granulation or dry granulation process. Wet granulation may include rapid mixer granulation or fluid bed granulation. Dry granulation may involve the formation of slugs or the use of a chilsonator.

Examples of suitable solvents used for wet granulation include water, ethanol, methanol, isopropyl alcohol, dichloromethane, acetone, or mixtures thereof.

The pharmaceutical composition of the present invention is further coated with one or more functional or non-functional coatings. In particular, the pharmaceutical composition is coated with one or more non-functional coatings. The coating layers may comprise one or more film-forming polymers and coating additives.

Examples of film-forming polymers include ethylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, methylcellulose, carboxymethyl cellulose, hydroxymethyl cellulose, hydroxyethyl cellulose, cellulose acetate, hydroxypropyl methylcellulose phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, waxes, and methacrylic acid polymers such as Eudragit[®] and the like. Alternatively, commercially available coating compositions comprising film-forming polymers marketed under various trade names, such as Opadry[®], may also be used.

Coating additives may be selected from the group consisting of binders, plasticizers, coloring agents, and lubricants.

Specific examples of granulating fluid/solvents for coating include acetone, ethanol, isopropyl alcohol, methylene chloride, or combinations thereof.

Coating may be performed by applying the coating composition as a solution/suspension/blend using any conventional coating technique known in the art, such as spray coating in a conventional coating pan or fluidized bed processor, dip coating, or compression coating.

The invention may be further illustrated by the following example, which is for illustrative purposes only and should not be construed as limiting the scope of the invention in any way.

EXAMPLE

- 5 Vilazodone hydrochloride was micronized using an air-jet mill to give a powder having a D_{50} of 5.205 μm , a D_{90} of 14.77 μm , and a D_{10} of 1.02 μm .

Ingredients	Quantity (% w/w)
Micronized vilazodone hydrochloride	9.71
Microcrystalline cellulose	36.89
Lactose monohydrate	47.86
SEPITRAP [®] 80	1.94
Colloidal silicon dioxide	0.19
Magnesium stearate	0.49
Core Tablet	100 mg
Film Coating	
Opadry [®] pink	2.91
Purified water	q.s.
Final Weight	103 mg

Procedure:

1. Microcrystalline cellulose and colloidal silicon dioxide were sifted and mixed together.
- 10 2. Micronized vilazodone hydrochloride was sifted and mixed with a portion of lactose monohydrate.
3. The remaining portion of lactose monohydrate was sifted and mixed with SEPITRAP[®] 80.
4. The mixtures from step 1, step 2, and step 3 were mixed together.
- 15 5. The mixture of step 4 was lubricated with sifted magnesium stearate.
6. The final blend of step 5 was compressed.
7. Opadry[®] pink was dispersed in water and stirred for 45 minutes.
8. The core tablets of step 6 were coated with the coating dispersion of step 7.

In-Vitro Studies

- 20 *In-vitro* drug release from the tablets prepared according to the above example was determined by dissolution using a USP type II apparatus at 60 rpm, in 1000 mL of 0.1N HCl. The results of the release studies of the tablets prepared as above along with the marketed formulation Viibryd[®] tablet are represented in the Table 1 below.

Table 1: Percentage (%) of *In-Vitro* Drug Release in USP Type II Apparatus (Media: 0.1N HCl, 1000 mL at 60 rpm)

Time (min)	Drug Dissolved (Percent w/w)	
	Example	Viibryd [®]
5	34	29
10	50	39
20	66	52
30	71	63
45	76	73
60	79	77

From the above table, it is clear that the pharmaceutical composition prepared according to the above example provides an *in-vitro* drug-release comparable to the innovator Viibryd[®] tablet.

In-vivo Studies

In-vivo performance of vilazodone hydrochloride tablets prepared as per the composition of Example 1 were evaluated with respect to the Viibryd[®] tablets in 24 healthy human volunteers under fasting and fed conditions with a wash out period of at least 14 days. The study protocol followed was an open label, balanced, randomized single-dose, crossover bioavailability study. Blood samples were collected at appropriate time intervals over a period of 144 hours and vilazodone content was quantified in plasma using validated chromatographic procedures. The 90% confidence intervals for the ratios of the log transformed mean values for C_{max} , AUC_{0-t} , and AUC_{0-inf} for the test and reference product (T/R ratio) were calculated. The results of the study are given in Table 2.

Table 2: Comparative Pharmacokinetic Data

	BE data	ln C_{max}	ln AUC_{0-t}	ln AUC_{0-inf}
Fasting	Ratio (T/R) (90% Confidence Interval)	98.06 (86.12 – 111.65)	100.91 (90.97 – 111.92)	99.19 (89.92 – 109.42)
	Intrasubject CV	24.78	19.67	18.60
Fed	Ratio (T/R) (90% Confidence Interval)	97.50 (89.71 – 105.97)	101.80 (95.82 – 108.15)	101.80 (95.99 – 107.95)
	Intrasubject CV	14.62	10.60	10.28

From the above table, it is clear that the 90% confidence intervals for the ratios of the log transformed mean values $C_{\max}$, AUC_{0-t} , and $AUC_{0-\infty}$ for the test and reference product (T/R ratio) were within the bioequivalence acceptance criteria. Therefore, vilazodone hydrochloride tablets prepared as per the composition of Example 1 were

5 bioequivalent to the Viibryd[®] tablets in 24 healthy human volunteers under both fasting and fed conditions.

We claim:

- 1 1. A pharmaceutical composition comprising vilazodone and one or more non-ionic
2 surfactants.
- 1 2. The pharmaceutical composition according to claim 1, wherein the non-ionic
2 surfactant is encapsulated within an inert carrier.
- 1 3. The pharmaceutical composition according to claim 1, wherein the non-ionic
2 surfactant is selected from the group consisting of polyoxyethyl-sorbitan-fatty acid esters;
3 ethers of sugars; ethoxylated fatty alcohols; fatty acids and their salts; ethoxylated fatty
4 acids; polyglyceryl esters; copolymers of propylene oxide and of ethylene oxide;
5 phospholipids or lecithins; amino acid fatty chain acrylates; triglycerides of plant or
6 synthetic origin and their ethoxylated derivatives; acetylated monoglycerides; sodium
7 lauryl sulphate and its derivatives; taurocholic acid; or mixtures thereof.
- 1 4. The pharmaceutical composition according to claim 3, wherein the non-ionic
2 surfactant is a polysorbate.
- 1 5. The pharmaceutical composition according to claim 2, wherein the inert carrier is
2 selected from the group consisting of magnesium aluminum silicate, aluminum silicate,
3 calcium silicate, magnesium silicate, magnesium trisilicate, sodium magnesium silicate,
4 lithium magnesium silicate, zirconium silicate, attapulgite, bentonite, fuller's earth,
5 hectorite, kaolin, montmorillonite, pyrophyllite, zeolite, calcium carbonate, calcium
6 phosphate, calcium gluconate, magnesium gluconate, manganese gluconate, calcium
7 diphosphate, silicon dioxide, microcrystalline celluloses, sugars such as lactose, sorbitol,
8 mannitol, xylitol, or maltitol, or mixtures thereof.
- 1 6. The pharmaceutical composition according to claim 1, wherein the vilazodone
2 particles have a D_{50} range from about 0.1 μm to about 20 μm .
- 1 7. The pharmaceutical composition according to claim 1, wherein the vilazodone
2 particles have a D_{90} range from about 0.5 μm to about 40 μm .
- 1 8. The pharmaceutical composition according to claim 1, wherein the vilazodone
2 particles have a D_{10} range from about 0.05 μm to about 10 μm .
- 1 9. The pharmaceutical composition according to any of the preceding claims,
2 wherein the composition further comprises fillers, binders, lubricants, disintegrants,
3 coloring agents, plasticizers, or opacifiers.

- 1 10. The pharmaceutical composition according to any of the proceeding claims,
2 wherein the composition is selected from the group consisting of tablets, capsules, pellets,
3 pills, caplets, and granules.
- 1 11. The pharmaceutical composition according to claim 10, wherein the composition is
2 a tablet.
- 1 12. The pharmaceutical composition of claim 11, wherein the tablet is further coated
2 with one or more non-functional coatings.
- 1 13. A process for the preparation of a pharmaceutical composition of vilazodone,
2 wherein the process comprises the steps of:
- 3 (a) blending vilazodone and one or more non-ionic surfactants with one or more
4 pharmaceutically acceptable excipients;
- 5 (b) directly compressing the blend of step (a) to form tablets; and
- 6 (c) film coating the tablets obtained from step (b).
- 1 14. A process for the preparation of a pharmaceutical composition of vilazodone,
2 wherein the process comprises the steps of:
- 3 (a) blending vilazodone and one or more non-ionic surfactants with one or more
4 pharmaceutically acceptable excipients;
- 5 (b) granulating the blend of step (a);
- 6 (c) blending the granules of step (b) with one or more pharmaceutically
7 acceptable excipients;
- 8 (d) compressing the blend of step (c) to form tablets; and
- 9 (e) film coating the tablets obtained from step (d).
- 1 15. A method of treating and/or preventing a central nervous system disorder by
2 administering a pharmaceutical composition comprising vilazodone and one or more non-
3 ionic surfactants.
- 1 16. The method of treating and/or preventing a central nervous system disorder
2 according to claim 15, wherein the central nervous system disorder is selected from major
3 depressive disorder, anxiety disorders, bipolar disorders, mania, dementia, eating

4 disorders, sleeping disorders, psychiatric disorders, cerebral infarct, tension, and any
5 combination thereof.

1 17. The method of treating and/or preventing a central nervous system disorder
2 according to claim 16, wherein the central nervous system disorder is major depressive
3 disorder.

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2014/063595

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K9/20 A61K31/496
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, CHEM ABS 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	WO 2012/131706 A1 (CADILA HEALTHCARE LTD [IN]; DWIVED SHRIPRAKASH DHAR [IN]; SINGH RAMESH) 4 October 2012 (2012-10-04) cited in the application page 1, line 6 - line 8 page 2, line 4 - line 13 page 10, line 20 - line 23 page 13, line 3 - line 5 -----	1-17
A	Anonymous: "VIIBRYD(TM) (vilazodone hydrochloride) Tablets", 2011, pages 1-13, XP055144766, Retrieved from the Internet: URL: http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022567s0001b1.pdf [retrieved on 2014-10-07] 11. Description; page 10 -----	1-17



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

7 October 2014

Date of mailing of the international search report

15/10/2014

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2014/063595

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
W0 2012131706 A1	04-10-2012	EP 2688884 A1	29-01-2014
		US 2014057925 A1	27-02-2014
		W0 2012131706 A1	04-10-2012
