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(54) Title: ORALLY DISINTEGRATING FORMULATIONS OF LACOSAMID

(57) Abstract: The present invention relates to a pharmaceutical formulation comprising a therapeutically effective amount of lacosamide or a pharmaceutically acceptable salt thereof in the form of orally disintegrating tablet.

Description

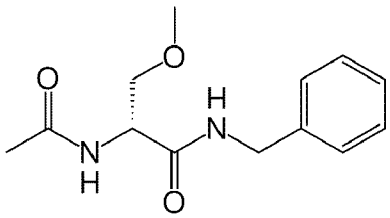
ORALLY DISINTEGRATING FORMULATIONS OF LACOSAMID

Field of Invention

The present invention relates to a pharmaceutical formulation comprising a therapeutically effective amount of lacosamide or a pharmaceutically acceptable salt thereof in the form of orally disintegrating tablet.

Background of Invention

Lacosamide is an aminoacid derivative with an anticonvulsant activity useful in the adjunctive treatment of partial-onset seizures with or without secondary generalization in adults with epilepsy. It is also called as erlosamide or harkoseride. Its chemical name is (2R)-2-(Acetylamino)-3-methoxy-N-(phenylmethyl) propanamide and its chemical structure is shown in the Formula I.



Formula 1

The precise mechanism of antiepileptic effects of lacosamide in humans remains to be fully elucidated. In vitro electrophysiological studies have shown that lacosamide selectively enhances slow inactivation of voltage-gated sodium channels, resulting in stabilization of hyperexcitable neuronal membranes and inhibition of repetitive neuronal firing. Inactivation of sodium channels is important to control of abnormal neuronal activity in the brain of epilepsy patient, and it can occur via fast or slow mechanism. While tranditional sodium channel blocking antiepileptics (e.g., Lamotrigine, Carbamazepine, Oxcarbazepine or Phenytoin) act primarly via fast inactivation, lacosamide acts by selectively enhancing slow inactivation of voltage-gated sodium channels to control and stabilise the neural network in the brain.

Lacosamide is sparingly soluble in water and it has low flowability, which makes the tableting process difficult at the high amount of active substance in tablets.

There is lacosamide immediate release formulation licensed in the US and Europe in the form of immediate release tablets, oral solutions and intravenous injection solutions under the brand name Vimpat® by UCB. Vimpat® IR tablet has crospovidone as disintegrant agent, microcrystalline cellulose, HPC (low substituted) and HPC as filler and binder, silicified microcrystalline cellulose as glidant, colloidal silicon dioxide as filler, magnesium stearate as lubricant and a non-functional coating.It may be taken with or without food. The initial dose should be 50 mg twice daily (100 mg per day). Vimpat® IR tablet is prepared by wet granulation. To overcome poor flowability of lacosamide, wet granulation comprising HPC (including low substituted HPC) is selected.

Lacosamide can be increased at weekly intervals by 100 mg/day given as two divided doses up to the recommended maintenance dose of 200 to 400 mg/day, based on individual patient response and tolerability. The currently commercially available tablets are available in strengths of 50, 100, 150 and 200 mg of lacosamide.

In prior art, there are several patents which disclose orally disintegrating compositions but none of them includes lacosamide or a pharmaceutically acceptable salt thereof.

Over the past decades, orally disintegrating tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance. ODTs are solid dosage forms containing active ingredients which disintegrate rapidly through buccal mucosa. It is desirable in the treatment of a number of diseases. Particularly, in epilepsy treatment in which it is very crucial to use drug on time and properly as described by the doctor. They are also advantageous for administrations of medicaments to patients who are traveling or have little access to water are similarly affected or patients who are mentally retarded, uncooperative, nauseated, or patients who have difficulties swallowing other dosage forms.

It is difficult to develop orally disintegrating compositions because of several different reasons and requirements such as disintegration, stability and taste masking properties. Dosage form must disintegrate in the oral cavity with the existence of saliva in a short period of time. So those compositions should have a porous structure. However, these porous characteristic tend to be very sensitive to humidity and may be lead to stability problems.

Moreover, effective taste masking technologies should also be adopted for bitter taste of active ingredients.

To fulfill all these requirements, the formulation for lacosamide needs to be adapted in particular by a careful selection of the excipients which give a high porous structure with high stability and suitable disintegration time. Additionally, to overcome bitter taste problem, taste masking have to be taken into consideration during the process.

Description of the invention

The present invention provides a pharmaceutical formulation comprising a therapeutically effective amount of lacosamide or a pharmaceutically acceptable salt thereof in the form of orally disintegrating tablet.

The main object of the present invention is to obtain rapidly disintegrating, stable and taste masked formulation that comprise lacosamide.

According to another embodiment, the formulation of lacosamide is disintegrated in less than 1 min.

According to another object of the present invention is to provide the orally disintegrating composition wherein lacosamide or a pharmaceutically acceptable salt thereof is present in an amount of about 5 to 80 % by weight of total composition, preferably it is about 20 to 60 % by weight of total composition.

The main embodiment of the present invention is to provide an orally disintegrating composition comprising lacosamide or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.

The orally disintegrating compositions of this invention comprising at least one pharmaceutically acceptable excipient selected from the group comprising super disintegrants, taste masking coating, diluents, binders, lubricants, glidants, sweeteners and flavouring agents.

Another object of the present invention is to provide a formulation comprising crospovidone as a super-disintegrant which avoids the humidity, stability and bitter taste problems.

As used herein, the term "super-disintegrant" is defined as the pharmaceutical ingredient that provides improved compressibility and compatibility and achieves disintegration substantially faster than the conventional disintegrants. According to this embodiment, the term "super-disintegrant" is selected from the group comprising crospovidone, croscarmellose sodium, sodium carboxymethyl starch, sodium starch glycolate, soy polysaccharide, cross-linked alginic acid, crospovidone, gellan gum, xanthan gum, calcium silicate or ion exchange resins, preferably crospovidone.

It has been suprisingly found that in this orally disintegrating composition having a weight ratio of lacosamide to super disintegrants, particularly crospovidone, in the range of between 1 and 15 (w/w), preferably 2 and 6 (w/w).

The amount of crospovidone is present in an amount of 5 to 25 % by weight of total composition, preferably it is 8 to 15% by weight of total composition.

In one embodiment, granules are coated during the process, to overcome bitter taste of lacosamide. The taste-masking coating comprising aminoalkyl metacrylate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, carnauba wax, cellulose acetate, cellulose acetate phthalate, ceresin, cetyl alcohol, chitosan, ethylcellulose, fructose, gelatin, glycerin, glyceryl behenate, glyceryl palmitostearate, hydroxyethyl cellulose, hydroxyethylmethyl cellulose, hydroxypropyl cellulose, hypromellose, hypromellose phthalate, isomalt, liquid glucose, maltitol, maltodextrin, methylcellulose, microcrystalline wax, paraffin, poloxamer, polydextrose, polyethylene glycol, polyethylene oxide, poly-DL-(lactic acid), polyvinyl acetate phthalate, polyvinyl alcohol, potassium chloride, povidone, shellac, shellac with stearic acid, sucrose, surface color agents, titanium oxide, tributyl citrate, triethyl citrate, vanillin, white wax, xylitol, yellow wax, zein or their copolymers or their mixtures.

The taste-masking coating preferably comprises dimethylaminoethyl methacrylate, butyl methacrylate and methyl methacrylate (Eudragit E 100) (Poly(butyl methacrylate-co-(2-demethylaminoeethyl)methacrylate-co-methyl methacrylate)) or mixture of polyethylene glycol and polyvinyl alcohol (Kollicoat IR).

The taste-masking coating is in the range of 1.0 to 50.0% by weight of total composition, preferably it is 2 to 30.0% by weight of total composition.

The diluents are selected from the group comprising microcrystalline cellulose, mannitol, spray-dried mannitol, lactose, starch, sodium carbonate, sodium bicarbonate, calcium carbonate and the like and mixtures thereof; preferably the diluents is mannitol.

The amount of mannitol is in the range of 1.0 to 60.0% by weight of total composition, preferably it is 10.0 to 40.0% by weight of total composition.

The binders are selected from the group comprising carbomers, carboxymethylcellulose sodium, cellulose acetate phthalate, chitosan, copovidone, corn starch and pregelatinized starch, dextrates, dextrin, dextrose, ethylcellulose, gelatin, glyceryl behenate, guar gum, hydrogenated vegetable oil type I, hydroxyethyl cellulose, hydroxyethylmethyl cellulose, hydroxypropyl cellulose, hydroxypropyl starch, hypromellose, liquid glucose, magnesium aluminum silicate, maltodextrin, maltose, methylcellulose, pectin, poloxamer, polycarbophil, polydextrose, polyethylene oxide, polymethacrylates, povidone, sodium alginate, starch, pregelatinized starch, stearic acid, sucrose or mixtures thereof.

The lubricants are selected from the group comprising magnesium strearate, calcium stearate, sodium stearyl fumarate, sodium lauryl sulphate, stearic acid and the like and mixtures thereof; preferably sodium stearyl fumarate.

The glidants selected from the group comprising colloidal silicon dioxide, colloidal anhydrous silica, talc, aluminium silicate and the like or mixtures thereof; preferably colloidal anhydrous silica.

The sweetners are selected from the group comprising aspartame, sucralose, saccharin, sugars such as glucose, lactose, fructose and sugar alcohols such as mannitol, sorbitol, xylitol, erythritol and the like or mixtures thereof; preferably sucralose.

The flavouring agents are selected from the group comprising menthol, peppermint, cinnamon, chocolate, vanillin and fruit essences such as cherry, orange, strawberry, grape etc. and the like or mixtures thereof; preferably strawberry.

In this present invention, to improve tablet compressibility and achieve faster disintegration, this orally disintegrating tablet composition has been designed, made up of the following:

- 5 to 80% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 1 to 60 % by weight of mannitol powder,

- 5 to 25 % by weight of crospovidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.01 to 5 % by weight of colloidal anhydrous silica,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- Preferably, taste masking coating,

- 5 to 80% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 1 to 60 % by weight of mannitol powder,
- 5 to 25 % by weight of crospovidone,
- 1 to 5 % by weight of povidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.01 to 5 % by weight of colloidal anhydrous silica,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- Preferably, taste masking coating

- 5 to 80% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 10 to 40 % by weight of granulated mannitol,
- 5 to 25 % by weight of crospovidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- 1 to 50 % taste masking coating.

- 20 to 60% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 10 to 40 % by weight of mannitol powder,
- 8 to 15 % by weight of crospovidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.01 to 5 % by weight of colloidal anhydrous silica,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- Preferably, taste masking coating,

- 20 to 60% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 10 to 40 % by weight of mannitol powder,

- 8 to 15 % by weight of crospovidone,
- 1 to 5 % by weight of povidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.01 to 5 % by weight of colloidal anhydrous silica,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- Preferably, taste masking coating

and

- 20 to 60% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 10 to 40 % by weight of granulated mannitol,
- 8 to 15 % by weight of crospovidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- 1 to 50 % taste masking coating.

The invention is further defined by reference of the following examples. Although the examples are not intended to limit the scope of the present invention, it should be considered in the light of the description detailed above.

Example 1: Orally Disintegrating Tablet (wet granulation)

ingredients	amount (%)
lacosamide	50.00
mannitol powder	33.1 6
crospovidone	14.00
flavor	1.00
sucralose	0.24
colloidal anhydrous silica	0.10
sodyum stearil fumarat	1.50

The production of the formulation is carried out as follows: lacosamide, mannitol powder and 50% of crospovidone are taken into granulator and mixed for 5 min. Granulation is achieved in suitable amount of water and granules are dried in fluid bed dryer or oven. Dried granules are sieved and strawberry flavor, sucralose, colloidal anhydrous silica and 50% of crospovidone are added. Mixed for 5 min. Sodium stearyl fumarate was added and mixed for 3 min. and pressed.

Example 2: Orally Disintegrating Tablet (wet granulation)

ingredients	amount (%)
lacosamide	40.00
mannitol powder	43.16
crospovidone	14.00
flavor	1.00
sucralose	0.24
colloidal anhydrous silica	0.10
sodyum stearil fumarat	1.50

The production of the formulation is carried out as follows: lacosamide, mannitol powder and 50% of crospovidone are taken into granulator and mixed for 5 min. Granulation is achieved in suitable amount of water and granules are dried in fluid bed dryer or oven. Dried granules are sieved and strawberry flavor, sucralose, colloidal anhydrous silica and 50% of crospovidone are added. Mixed for 5 min. Sodium stearyl fumarate was added and mixed for 3 min. and pressed.

Example 3: Orally Disintegrating Tablet (dry granulation)

ingredients	amount (%)
lacosamide	50.00
mannitol powder	30.1 6
crospovidone	14.00
Povidone K25	3.00
flavor	1.00
sucralose	0.24
colloidal anhydrous silica	0.10
sodyum stearil fumarat	1.50

The production of the formulation is carried out as follows: lacosamide, mannitol powder, povidone K25 and 50% of crospovidone passed through the compactor or pressed in slug briquettes. Then sieved. Strawberry flavor, sucralose, colloidal anhydrous silica and 50% of crospovidone are added and mixed for 5 min. Sodium stearyl fumarate was added and mixed for 3 min. and pressed.

Example 4: Orally Disintegrating Tablet (wet granulation)

ingredients	amount (%)
lacosamide	50.00
mannitol powder	30.16
crospovidone	14.00
Povidone K25	3.00
flavor	1.00
sucralose	0.24
colloidal anhydrous silica	0.10
sodyum stearil fumarat	1.50

The production of the formulation is carried out as follows: lacosamide, mannitol powder and 50% of crospovidone are taken into granulator and mixed for 5 min. Granulation is achieved in povidone solution prepared with suitable amount of water. Granules are dried in fluid bed dryer or oven. Dried granules are sieved and strawberry flavor, sucralose, colloidal anhydrous silica and 50% of crospovidone are added. Mixed for 5 min. Sodium stearyl fumarate was added and mixed for 3 min. and pressed.

Example 5: Orally Disintegrating Tablet (wet granulation)

ingredients	amount (%)
lacosamide	60.00
mannitol powder	20.1 6
crospovidone	14.00
Povidone K25	3.00
flavor	1.00
sucralose	0.24
colloidal anhydrous silica	0.10
sodyum stearil fumarat	1.50

The production of the formulation is carried out as follows: lacosamide, mannitol powder and 50% of crospovidone are taken into granulator and mixed for 5 min. Granulation is achieved in povidone K25 solution prepared with suitable amount of water. Granules are dried in fluid bed dryer or oven. Dried granules are sieved and strawberry flavor, sucralose, colloidal anhydrous silica and 50% of crospovidone are added. Mixed for 5 min. Sodium stearyl fumarate was added and mixed for 3 min. and pressed.

Example 6: Orally Disintegrating Tablet (granulation and granule coating)

ingredients	amount (%)
lacosamide	50.00
mannitol powder	28.16
crospovidone	14.00
Povidone K25	2.00
Eudragit E 100	3.00
flavor	1.00
sucralose	0.24
colloidal anhydrous silica	0.10
sodyum stearil fumarat	1.50

The production of the formulation is carried out as follows: lacosamide, mannitol powder and 50% of crospovidone are taken into granulator and mixed for 5 min. Granulation is achieved in povidone K25 solution prepared with suitable amount of water. Granules are dried in fluid bed dryer or oven. Dried granules are sieved and sieved granules are coated in fluid bed dryer with Eudragit E 100 solution prepared with suitable amount of water. Strawberry flavor, sucralose, colloidal anhydrous silica and 50% of crospovidone are added. Mixed for 5 min. Sodium stearyl fumarate was added and mixed for 3 min. and pressed.

Example 7: Orally Disintegrating Tablet (powder granule coating)

ingredients	amount (%)
lacosamide	50.00
mannitol powder	30.1 6
crospovidone	14.00
Kollicoat IR	3.00

flavor	1.00
sucralose	0.24
colloidal anhydrous silica	0.10
sodyum stearil fumarat	1.50

The production of the formulation is carried out as follows: lacosamide, mannitol powder and 50% of crospovidone are taken into fluid bed dryer. Powder mixture is coated - granulated with Kollicoat IR solution prepared with suitable amount of water and dried. Dried granules was sieved. Strawberry flavor, sucralose, colloidal anhydrous silica and 50% of crospovidone are added. Mixed for 5 min. Sodium stearyl fumarate was added and mixed for 3 min. and pressed.

Example 8: Orally Disintegrating Tablet (hot - melt extrusion)

ingredients	amount (%)
lacosamide	33.33
granulated mannitol	22.17
crospovidone	9.34
Eudragit E 100	33.33
flavor	0.67
sucralose	0.16
sodyum stearil fumarat	1.00

The production of the formulation is carried out as follows: lacosamide and Eudragit E 100 are taken into an extruder. Extrudes are obtained via hot-melt extrusion technique. Extrudes are cut and pellets are obtained. Mannitol powder, crospovidone, flavor, sucralose are added to pellets and mixed for 5 min. Sodium stearyl fumarate was added to mixed granules and mixed for 3 min. and pressed.

CLAIMS

1. An orally disintegrating composition comprising lacosamide or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.

2. The orally disintegrating composition according to claim 1, wherein the formulation of lacosamide is disintegrated in less than 1 min.

3. The orally disintegrating composition according to claim 1, wherein lacosamide or a pharmaceutically acceptable salt thereof is present in an amount of about 5 to 80 % by weight of total composition, preferably it is about 20 to 60 % by weight of total composition.

4. The orally disintegrating composition according to claims 1 and 2, wherein the one or more pharmaceutically acceptable excipients are selected from the group comprising super disintegrants, taste masking coating, diluents, binders, lubricants, glidants, sweeteners and flavouring agents.

5. The orally disintegrating composition according to claim 3, wherein the super disintegrants are selected from the group comprising crospovidone, croscarmellose sodium, sodium carboxymethyl starch, sodium starch glycolate, soy polysaccharide, cross-linked alginic acid, crospovidone, gellan gum, xanthan gum, calcium silicate or ion exchange resins, low-substituted hydroxypropylcellulose, sodium starch glycollate and mixtures thereof.

6. The orally disintegrating composition according to claims 1 to 4, wherein the weight ratio of lacosamide to super disintegrants is in the range of between 1 and 15 (w/w), preferably 2 and 6 (w/w).

7. The orally disintegrating composition according to claim 4 and 5, wherein the super disintegrant is preferably crospovidone.

8. The orally disintegrating composition according to claim 6, wherein the amount of crospovidone is present in an amount of 5 to 25 % by weight of total composition, preferably it is 8 to 15% by weight of total composition.

9. The orally disintegrating composition according to claim 3, wherein taste-masking coating comprising aminoalkyl metacrylate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, carnauba wax, cellulose acetate, cellulose acetate phthalate, ceresin, cetyl alcohol, chitosan, ethylcellulose, fructose, gelatin, glycerin, glyceryl behenate, glyceryl palmitostearate, hydroxyethyl cellulose, hydroxyethylmethyl cellulose, hydroxypropyl cellulose, hypromellose, hypromellose phthalate, isomalt, liquid glucose, maltitol, maltodextrin, methylcellulose, microcrystalline wax, paraffin, poloxamer, polydextrose, polyethylene glycol, polyethylene oxide, poly-DL-(lactic acid), polyvinyl acetate phthalate, polyvinyl alcohol, potassium chloride, povidone, shellac, shellac with stearic acid, sucrose, surface color agents, titanium oxide, tributyl citrate, triethyl citrate, dimethylaminoethyl methacrylate, butyl methacrylate, methyl methacrylate, vanillin, white wax, xylitol, yellow wax, zein and their copolymers or their mixtures thereof.

10. The orally disintegrating composition according to claim 8, wherein the taste-masking coating is copolymer of dimethylaminoethyl methacrylate, butyl methacrylate and methyl methacrylate or mixture of polyethylene glycol and polyvinyl alcohol.

11. The orally disintegrating composition according to claim 8 and 9, wherein the amount of taste-masking coating is in the range of 1.0 to 50.0% by weight of total composition, preferably it is 2 to 30.0% by weight of total composition.

12. The orally disintegrating composition according to claim 3, wherein the diluents are selected from the group comprising microcrystalline cellulose, mannitol, spray-dried mannitol, lactose, starch, sodium carbonate, sodium bicarbonate, calcium carbonate or mixtures thereof; preferably the diluents is mannitol.

13. The orally disintegrating composition according to claim 11, wherein the amount of mannitol is in an amount of 1.0 to 60.0% by weight of total composition, preferably it is 10.0 to 40.0% by weight of total composition.

14. The orally disintegrating composition according to claim 3, wherein the binders are selected from the group comprising carbomers, carboxymethylcellulose sodium, cellulose acetate phthalate, chitosan, copovidone, corn starch and pregelatinized starch, dextrates, dextrin, dextrose, ethylcellulose, gelatin, glyceryl behenate, guar gum, hydrogenated vegetable oil type I, hydroxyethyl cellulose, hydroxyethylmethyl cellulose, hydroxypropyl cellulose, hydroxypropyl starch, hypromellose, liquid

glucose, magnesium aluminum silicate, maltodextrin, maltose, methylcellulose, pectin, poloxamer, polycarbophil, polydextrose, polyethylene oxide, polymethacrylates, povidone, sodium alginate, starch, pregelatinized starch, stearic acid, sucrose or mixtures thereof.

15. The orally disintegrating composition according to claim 3, wherein the lubricants are selected from the group comprising magnesium strearate, calcium stearate, sodium stearyl fumarate, sodium lauryl sulphate, stearic acid and mixtures thereof.

16. The orally disintegrating composition according to claim 3, wherein the glidants selected from the group comprising colloidal silicon dioxide, colloidal anhydrous silica, talc, aluminium silicate and mixtures thereof; preferably colloidal anhydrous silica.

17. The orally disintegrating composition according to claim 3, wherein the sweetners are selected from the group comprising aspartame, sucralose, saccharin, sugars such as glucose, lactose, fructose and sugar alcohols such as mannitol, sorbitol, xylitol, erythritol and mixtures thereof; preferably sucralose.

18. The orally disintegrating composition according to claim 3, wherein the flavouring agents are selected from the group comprising menthol, peppermint, cinnamon, chocolate, vanillin and fruit essences such as cherry, orange, strawberry, grape etc. and mixtures thereof; preferably strawberry.

19. The orally disintegrating composition according to any preceding claim comprising;

- 5 to 80% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 1 to 60 % by weight of mannitol powder,
- 5 to 25 % by weight of crospovidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.01 to 5 % by weight of colloidal anhydrous silica,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- Preferably, taste masking coating.

20. The orally disintegrating composition according to any preceding claim comprising;

- 5 to 80% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 1 to 60 % by weight of mannitol powder,

- 5 to 25 % by weight of crospovidone,
- 1 to 5 % by weight of povidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.01 to 5 % by weight of colloidal anhydrous silica,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- Preferably, taste masking coating.

21. The orally disintegrating composition according to any preceding claim comprising;

- 5 to 80% by weight of lacosamide or pharmaceutically acceptable salt thereof,
- 1 to 60 % by weight of granulated mannitol,
- 5 to 25 % by weight of crospovidone,
- 0.5 to 5 % by weight of flavor,
- 0.1 to 3 % by weight of sucralose,
- 0.1 to 5 % by weight of sodium stearyl fumarate,
- 1 to 50 % taste masking coating.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/059375

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/00 A61K9/20 A61K31/165
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, 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 2009/146325 A1 (PLIVA HRVATSKA D O O [HR] ; TEVA PHARMA [US] ; MUNDORFER TINA [HR] ; MARK) 3 December 2009 (2009-12-03) paragraph [0084] claim 1	1-21
X	WO 2011/055385 A1 (LUPIN LTD [IN] ; KULKARNI SHIRISHKUMAR [IN] ; DALAL SATISH KUMAR [IN] ; J) 12 May 2011 (2011-05-12) page 5, line 17 example 3 claim 1	1-21

-/- .

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 June 2014	17/06/2014

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Toulacis, C

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/059375

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/130615 A2 (REDDYS LAB LTD DR [IN] ; REDDYS LAB INC DR [US] ; ANUMULA RAGHUPATHI RED) 20 October 2011 (2011-10-20) page 18, line 5 page 18, lines 13-30 claim 1	1-21
X	WO 2010/060624 A2 (RATIOPHARM GMBH [DE] ; STRIEGEL HANS-GUENTER [DE] ; PAETZ JANA [DE] ; STE) 3 June 2010 (2010-06-03) page 17, lines 14-19 page 19, lines 21-27 examples 9a, 9b claim 1	1-21
A	EP 2 468 261 A1 (UCB PHARMA GMBH [DE]) 27 June 2012 (2012-06-27) example 6	1-21

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2014/059375

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009146325 A1	03-12-2009	EA 201170356 A1	30-08-2011
		EP 2297092 A1	23-03-2011
		US 2009298947 A1	03-12-2009
		WO 2009146325 A1	03-12-2009
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