(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 September 2007 (27.09.2007)

PCT

(10) International Publication Number
WO 2007/107878 A2

(51) International Patent Classification: Not classified

(21) International Application Number:
PCT/IB2007/000809

(22) International Filing Date: 19 March 2007 (19.03.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
488/CHE/2006 17 March 2006 (17.03.2006) IN

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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) **Title:** SOLID DOSAGE FORMS OF HYPNOTIC AGENT

(57) **Abstract:** The present invention relates to solid dosage forms of nonbenzodiazepine hypnotic agent. More particularly, the present invention relates to solid dosage forms of Zaleplon. The present invention also relates to a process for preparing solid dosage forms of Zaleplon.

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SOLID DOSAGE FORMS OF HYPNOTIC AGENT

Filed of the invention

The present invention relates to solid dosage forms of nonbenzodiazepine hypnotic agent. More particularly, the present invention relates to solid dosage forms of Zaleplon.

The present invention also relates to process for preparing solid dosage forms of Zaleplon.

Background of the invention

Zaleplon is a nonbenzodiazepine hypnotic from the pyrazolopyrimidine class. Chemically Zaleplon is N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylacetamide. Zaleplon is disclosed and claimed in US patent No 4,626,538. It is commercially available in capsule dosage form under the trademark of SONATA® for the treatment of Insomnia. The inactive ingredients of the commercial capsule dosage form of Zaleplon are: microcrystalline cellulose, pregelatinized starch, silicon dioxide, sodium lauryl sulfate, magnesium stearate, and lactose.

Magnesium stearate is the most commonly used lubricant in pharmaceutical tablets. Pregelatinized starch is incompatible with magnesium stearate and effects the disintegration and dissolution rate of the formulation. Incompatibility between magnesium stearate and pregelatinised starch is well known in the prior art as described in technical data sheet published by Colorcon for Hydrochlorothiazide formulations. During long-term capsule filling operation, formulations containing magnesium stearate become over lubricated and show increased disintegration time and thereby reduce the dissolution rate of capsules containing insoluble actives like hydrochlorothiazide, zaleplon etc. These formulations, which contain magnesium stearate, show slow dissolution profile. Hence, there is a need for selection of proper lubricant in the dosage form, which doesn't impair dissolution rate and is devoid of compatibility

problems. Hence, the focus of present invention was to evaluate and select compatible lubricant for formulating Zaleplon dosage forms.

Objective of the invention

Accordingly, the main objective of the present invention is to provide solid dosage forms of Zaleplon.

Yet, another objective of the present invention is to provide simple, cost effective and efficient process for preparing solid dosage forms of Zaleplon.

Yet, another objective of the present invention is to provide solid dosage forms of Zalelpon in such a way that it will comply with the reference product in terms of *in vitro* parameters like dissolution, disintegration, etc and *in vivo* parameters for bioequivalence such as C_{max}, AUC, T_{max}.etc.

Summary of the invention

Accordingly, the present invention provides solid dosage forms comprising Zaleplon and stearic acid as lubricant.

The present invention also provides process for preparing solid dosage forms of Zaleplon wherein the composition is prepared by blending Zaleplon with one or more pharmaceutically acceptable excipients lubricating the blend with stearic acid and finally filling into capsules or compressing into tablets.

Detailed description of the invention

In an embodiment the solid dosage form of the present invention, is in the form of tablet or capsule.

In yet another embodiment of the present invention, solid dosage forms of Zaleplon further comprise one or more pharmaceutical acceptable excipients such as diluents, binders, disintegrants, surfactants and glidants.

Suitable diluents used according to the present invention are selected from calcium phosphate-dibasic, calcium carbonate, sucrose, lactose, cellulose-microcrystalline, cellulose powdered, calcium silicate, kaolin, starch, starch pregelatinized, polyols such as mannitol, sorbitol, lactitol, xylitol, maltitol or combinations thereof.

Suitable binders used according to the present invention are selected from hydroxy propyl cellulose, hydroxypropyl methylcellulose, gelatin, hydroxy ethyl cellulose, povidone, polyvinyl alcohol, copovidone, ethylcellulose, starch and methylcellulose or a combination thereof.

Suitable disintegrants used according to the present invention are selected from croscarmellose sodium, crospovidone, sodium starch glycolate, starch, sodium carboxymethylcellulose, pregelatinised starch, hydroxypropylcellulose or combination thereof.

Suitable surfactants used according to present invention are selected from sodium lauryl sulfate, polysorbates, sorbitan esters or combination thereof.

Suitable glidants used according to the present invention are selected from magnesium trisilicate, talc, tribasic calcium phosphate, glyceryl monostearate, glyceryl stearate and colloidal silica or a combination thereof.

In yet another embodiment of the present invention, when the solid dosage forms of Zaleplon is tablet, may be prepared by dry granulation (slugging or compaction), wet granulation, and direct compression. Preferably, the pharmaceutical composition of the present invention is prepared by direct compression or direct filling into capsules.

Suitable solvents used for preparing solid dosage forms by wet granulation are selected from water, ethanol, methanol, and isopropanol or a combination thereof.

In yet another embodiment of the present invention, there is provided process for the preparation of solid dosage forms comprising Zaleplon and stearic acid as lubricant as follows:

i) blending Zaleplon with one or more diluents, binder, disintegrants, surfactants, glidants,

ii) lubricating the blend of step (i) with stearic acid and

iii) filling the blend into capsules or compressing into tablets.

The following examples further exemplify the invention and are not intended to limit the scope of the invention. It is obvious to those skilled in the art to find out the composition for other dosage forms and substitute the equivalent excipients as described in this specification or with the one known to the industry.

Example 1

S. No.	Ingredients	Qty (mg)
1.	Zaleplon	10.0
2.	Microcrystalline Cellulose	30.0
3.	Lactose monohydrate	38.0
4.	Pregelatinized starch	20.0
5.	Sodium lauryl sulfate	0.50
6.	Colloidal silicon dioxide	1.00
7.	Stearic acid	0.10

The processing steps involved are:

i) sifted and blended Zaleplon, microcrystalline cellulose, lactose monohydrate, pregelatinized starch, sodium lauryl sulfate and colloidal silicon dioxide,

ii) lubricated the blend of step (i) with stearic acid and finally

iii) the lubricated blend was filled into capsules or compressed into tablets.

The solid dosage forms of Zaleplon disclosed in example 2-6 were prepared by a similar procedure described in example 1.

Example 2

S. No.	Ingredients	Qty (mg)
1.	Zaleplon	10.0
2.	Microcrystalline Cellulose	30.0
3.	Lactose monohydrate	36.5
4.	Pregelatinized starch	20.0
5.	Sodium lauryl sulfate	0.50
6.	Colloidal silicon dioxide	1.00
7.	Stearic acid	2.00

Example 3

S. No.	Ingredients	Qty (mg)
1.	Zaleplon	10.0
2.	Microcrystalline Cellulose	30.0
3.	Lactose monohydrate	54.4
4.	Pregelatinized starch	4.00
5.	Sodium lauryl sulfate	0.50
6.	Colloidal silicon dioxide	1.00
7.	Stearic acid	0.10

Example 4

S. No.	Ingredients	Qty (mg)
1.	Zaleplon	10.0
2.	Microcrystalline Cellulose	30.0
3.	Lactose monohydrate	52.4
4.	Pregelatinized starch	4.00
5.	Sodium lauryl sulfate	0.50
6.	Colloidal silicon dioxide	1.00
7.	Stearic acid	2.00

Example 5

S. No.	Ingredients	Qty (mg)
1.	Zaleplon	10.0
2.	Microcrystalline Cellulose	30.0
3.	Lactose monohydrate	38.0
4.	Pregelatinized starch	20.00
5.	Sodium lauryl sulfate	0.50
6.	Colloidal silicon dioxide	1.00
7.	Stearic acid	0.50

Example 6

S. No.	Ingredients	Qty (mg)
1.	Zaleplon	10.0
2.	Microcrystalline Cellulose	20.0
3.	Lactose monohydrate	48.8
4.	Pregelatinized starch	20.00
5.	Sodium lauryl sulfate	0.50
6.	Colloidal silicon dioxide	0.20
7.	Stearic acid	0.50

Dissolution profile:

The Zaleplon capsules prepared according to the present invention were tested for drug release in water using USP apparatus 2 with paddle speed at 75 rpm. The samples of the media were periodically withdrawn and spectrophotometrically analyzed for Zaleplon content. The dissolution profile data is given in Table 1.

Table 1

	Cumulative % Zaleplon release in min					
	5 min	10 min	15 min	20 min	30 min	45min
Sonata®	78	96	98	99	100	100
Example 5	89	97	98	98	98	98
Example 6	82	97	98	98	98	98

We claim:

1. A solid dosage form comprising Zaleplon and stearic acid as lubricant.

2. The solid dosage form as claimed in claim 1, further comprises one or more pharmaceutically acceptable excipients comprising diluents, binders, disintegrants, surfactants and glidants.

3. The solid dosage form as claimed in claim 2, wherein the diluent is selected from the group consisting of calcium phosphate-dibasic, calcium carbonate, lactose, sucrose, cellulose-microcrystalline, cellulose powdered, calcium silicate, kaolin, starch, starch pregelatinized, polyols such as mannitol, sorbitol, lactitol, xylitol, maltitol or combinations thereof.

4. The solid dosage form as claimed in claim 2, wherein the binder is selected from the group consisting of hydroxy propyl cellulose, hydroxypropyl methylcellulose, gelatin, hydroxy ethyl cellulose, povidone, polyvinyl alcohol, copovidone, ethylcellulose, starch and methylcellulose or a combination thereof.

5. The solid dosage form as claimed in claim 2, wherein the disintegrant is selected from the group consisting of croscarmellose sodium, crospovidone, sodium starch glycolate, starch, sodium carboxymethylcellulose, pregelatinised starch, hydroxypropylcellulose or combination thereof.

6. The solid dosage form as claimed in claim 2, wherein the surfactant is selected from the group consisting of sodium lauryl sulfate, polysorbates, sorbitan esters or combination thereof.

7. The solid dosage form as claimed in claim 2, wherein the glidant is selected from the group consisting of magnesium trisilicate, talc, tribasic calcium phosphate, glyceryl monostearate, glyceryl stearate and colloidal silica or a combination thereof.

8. A process for the preparation of solid dosage form comprising Zaleplon and stearic acid as lubricant, which comprises the steps of

i) blending Zaleplon with one or more diluents, binder, disintegrants, surfactants, glidants,

ii) lubricating the blend of step (i) with stearic acid and

iii) filling the blend into capsules or compressing into tablets.

9. The solid dosage form as claimed in claim 1, in the form of tablets or capsules.