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Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO  
DIVISION DE NUEVAS CREACIONES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-055545- -00003-0000

Fecha: 2008-07-15 16:24:52 Dep. 2020 NUECREACIONE  
Tra. 11 PATENTEIYII Eve: 379 FASENACIONALII  
Act. 538 PETICION Folios: 5

E. \_\_\_\_\_ S. \_\_\_\_\_ D. \_\_\_\_\_

Ref.: Expediente N°. 07-055.545

**Solicitud de Patente de Invención titulada: "FORMAS DE DOSIFICACION ORAL  
SÓLIDSA QUE CONTIENEN UNA DOSIS BAJA DE ESTRADIOL".**

**Solicitante: BAYER SCHERING PHARMA AKTIENSELLSCHAFT**

**Nuestra Ref.: P2007/000075**

**SOLICITUD DE EXAMEN DE PATENTABILIDAD SEGÚN**  
**EL ARTÍCULO 44 DE LA DECISION 486, GACETA No. 587**

J. IAN RAISBECK, mayor de edad y vecino de Bogotá, D.C., identificado tal como aparece al pie de mi firma, en mi carácter de apoderado de la sociedad solicitante, respetuosamente me permito solicitar que se examine si la invención reúne los requisitos de patentabilidad previstos en la misma, dando cumplimiento a lo establecido en el artículo 44 de la Decisión 486 de la comisión de la Comunidad Andina. Adjunto recibo por el monto de \$210.000 pesos para cubrir la tasa correspondiente, según la Resolución No. 44372 del 26 de Diciembre de 2007.

Atentamente,

J. IAN RAISBECK  
C.C. 79.376.996 de Bogotá  
T.P. 135.799

Anexo: Recibo por \$210.000 pesos

LMB/P2007/000075 080619 Sol Exam

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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FECHA : JULIO 11 DE 2008

\*\*\*\*\* CONSIGNACION \*\*\*\*\*

| DEPOSITANTE    | TIPO PAGO    | BANCO           | CUENTA    | No. PAGO | FECHA PGO  | Vr. PAGO     |
|----------------|--------------|-----------------|-----------|----------|------------|--------------|
| CLARTE RAISBEK | CONSIGNACION | BANCO DE BOGOTA | 062754387 | 4801882  | 11/07/2008 | 8,352,000.00 |

\*\*\*\*\* CONCEPTO \*\*\*\*\*

| CANT. | RENTISTICO  | CONCEPTO                              | TOTAL CONCEPTO |
|-------|-------------|---------------------------------------|----------------|
| 1     | 50005-01-01 | SOLICITUDES                           |                |
|       |             | 114 PTC CAP-II EXAMEN DE PATENTIBILID | 210,000.00     |
|       |             | TOTAL :                               | \$ 210,000.00  |

SP" DOSCIENTOS DIEZ MIL PESOS

RESPONSABLE : \_\_\_\_\_

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. \_\_\_\_\_



**DIVISIÓN DE NUEVAS CREACIONES**

RADICACIÓN EXPEDIENTE No. 07-55545

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **587** DE

FECHA **18 DE ENERO DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR LA LEY

EXPIRA EL **16 DE ABRIL DE 2008**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI \_\_\_\_\_

NO   X

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PA 2000 01892 15 December 2000 (15.12.2000) DK(71) Applicant: **NOVO NORDISK A/S** [DK/DK]; Novo Allé,  
DK-2880 Bagsvaerd (DK).(72) Inventors: **KVORNING, Ingelise**; Akacievej 1, DK-3650  
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(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
NE, SN, TD, TG).**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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.

**WO 02/47692 A1**

(54) Title: USE OF AN OESTROGEN IN THE MANUFACTURE OF A COMPOSITION CONTAINING OESTROGEN FOR THE TREATMENT OF ATROPHIC VAGINITIS

(57) Abstract: Use of an oestrogen in the manufacture of a composition containing oestrogen for the treatment of atrophic vaginitis in woman by administering weekly an amount of about 10- to 30 ug estradiol to a woman.

Table 8. Mean and mean change from baseline in percentage of superficial urethral cells

| Treatment Group |          |      |                     |          |      |                   |         |      |        |
|-----------------|----------|------|---------------------|----------|------|-------------------|---------|------|--------|
| Time Point      | 25 µg E2 |      |                     | 10 µg E2 |      |                   | Placebo |      |        |
|                 | N        | Mean | Change              | N        | Mean | Change            | N       | Mean | Change |
| Week 0          | 86       | 3.2  |                     | 83       | 2.5  |                   | 42      | 3.0  |        |
| Week 2          | 83       | 21.9 | 19.2 <sup>a,b</sup> | 79       | 16.7 | 14.1 <sup>c</sup> | 34      | 6.5  | 3.3    |
| Week 7          | 77       | 17.6 | 14.2 <sup>d</sup>   | 70       | 13.5 | 10.7              | 38      | 8.6  | 5.5    |
| Week 12         | 70       | 11.2 | 7.5                 | 64       | 9.5  | 6.8               | 34      | 7.0  | 3.6    |

5 A two-tailed linear model analysis was used to compare treatment groups at each time point.

a Comparison with placebo, statistically significant;  $P \leq .001$

b Comparison with 10 µg E2, statistically significant;  $P \leq .05$

c Comparison with placebo, statistically significant;  $P \leq .01$

10 d Comparison with placebo, statistically significant;  $P \leq .05$

#### Example 4

15 Manufacture of 10 µg tablets

##### Suspension of estradiol

10.3 g estradiol hemihydrate (equivalent to 10.0 g estradiol, anhydrous) is suspended in a solution of hypromellose (14.8 g) in purified water 15.6 L) while stirring.

20 Granulation

Blending, granulation, and drying are performed in a fluid bed.

Hypromellose (53.69 kg), lactose monohydrate (17.90 kg), and maize starch (8.00 kg) are sucked into the fluid bed through a sieve and then blended.

The granulation takes place by spraying the suspension of estradiol on the mixture of excipients. After spraying the granulate is dried.

##### Blending

Sieving is performed and magnesium stearate (400 g) is blended into the granulate

### Compression

The tablets are compressed using a rotary tablet press.

### Preparation of film-coating solution

- 5 Hypromellose (400 g) and macrogol 6000 (50 g) are dissolved in purified water (9.55 kg)

### Film-coating

- 10 In a coating pan, the tablets are coated with the coating solution (0.576 mg dried substance /tablet), using an air atomizing spray system. After coating sampling of tablets to release testing takes place.

### EXPLANATION TO THE FIGURES

- 15 Figure 1. Serum concentrations of estradiol at week 0.

---□--- 25 µg E2      —●— 10 µg E2

Figure 2. Serum concentrations of estradiol at week 12.

---□--- 25 µg E2      —●— 10 µg E2

20

Figure 3. Area under the serum estradiol curve at weeks 0 and 12.

□ 25 µg E2      ● 10 µg E2

Figure 4. Area under the serum estradiol curve and serum FSH concentration at week 12.

15

□ 25 µg E2      ● 10 µg E2

Figure 5. Area under the serum estradiol curve and maturation value at week 12. Maturation values at baseline were 52.4 in the 25-µg E2 group and 51.0 in the 10-µg E2 group.

0

□ 25 µg E2      ● 10 µg E2

# CLAIMS

1. The use of an oestrogen in the manufacture of a composition containing oestrogen for the treatment of atrophic vaginitis in woman, by administering weekly an amount of about  
5 10 to about 30  $\mu\text{g}$  estradiol to a woman.
2. The use according to claim 1, wherein the women treated is menopausal or post-menopausal women.
- 10 3. The use according to any one of the preceding claims, wherein weekly an amount of about 15 to about 25  $\mu\text{g}$  estradiol is administered.
4. The use according to any one of the preceding claims, wherein daily about 1.5 to about 4  
15  $\mu\text{g}$  estradiol is administered.
5. The use according to any one of the preceding claims, wherein daily about 2 to about 3  
15  $\mu\text{g}$  estradiol is administered.
6. The use according to any one of the preceding claims, wherein twice weekly about 5 to  
20 about 15  $\mu\text{g}$  estradiol is administered.
7. The use according to any one of the preceding claims, wherein twice weekly about 7 to  
about 13  $\mu\text{g}$  estradiol is administered.
- 25 8. The use according to the preceding claim, wherein twice weekly about 9 to about 11  $\mu\text{g}$   
estradiol is administered.
9. The use according to any one of the preceding claims, wherein no progestogen is  
administered.
- 30 10. The use according to any one of the preceding claims, wherein the composition is to be  
administered vaginally.

11. The use according to any one of the preceding claims, wherein it is used for a period of time of more than 2 weeks, preferably more than 1 month, more preferred more than 2 months, and even more preferred more than 3 months.
- 5 12. The use according to any one of the preceding claims, wherein administration is performed using a tablet.
13. The use according to any one of the preceding claims, wherein each tablet contains, in addition to the active material, about 53.7 mg hypromellose, about 17.9 mg lactose  
10 monohydrate, about 8 mg maize starch, about 0.4 mg magnesium stearate.
14. The use according to any one of the preceding claims, wherein each tablet is coated with a film consisting of about 0.5 mg hypromellose and about 0.06 mg macrogel 6000 (poly-ethylene glycol 6000 NF).  
15
15. The use according to any one of the preceding claims, furnishing no or only inferior systemic absorption.
16. The use according to any one of the preceding claims, furnishing significant improvement  
20 in the vaginal mucosa.
17. The use according to any one of the preceding claims, furnishing no or only inferior systemic effect.
- 25 18. The use according to any one of the preceding claims, furnishing low absorption of estrogen.
19. The use according to any one of the preceding claims, furnishing low serum concentration of estradiol.  
30
20. The use according to any one of the preceding claims, furnishing no or only inferior accumulation of circulating estradiol.
21. The use according to any one of the preceding claims, furnishing positive effects on an  
5 atrophic vaginal epithelium.