

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

**BAYER SCHERING PHARMA AG AND BAYER
HEALTHCARE PHARMACEUTICALS INC.**

Plaintiffs,

v.

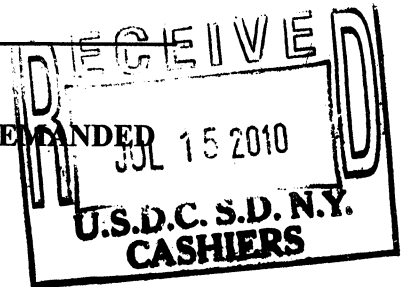
**LUPIN LTD. AND LUPIN PHARMACEUTICALS,
INC.**

Defendants,

10 CV 5423

Case No. _____

JURY TRIAL DEMANDED JUL 15 2010



COMPLAINT

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Paul J. Skiermont
Sundeep K. Addy
Matthew R. Ford
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*Attorneys for Bayer Schering Pharma AG and
Bayer HealthCare Pharmaceuticals Inc.*

Plaintiffs Bayer Schering Pharma AG and Bayer HealthCare Pharmaceuticals Inc. (collectively “Bayer”) bring this Complaint for patent infringement against Defendants Lupin Ltd. and Lupin Pharmaceuticals, Inc. (collectively “Lupin”) and allege as follows:

PARTIES

1. Plaintiff Bayer Schering Pharma AG (“Bayer Schering”), formerly known as Schering AG, is a corporation organized and existing under the laws of the Federal Republic of Germany, having a principal place of business in Müllerstrasse 178, 13353 Berlin, Germany.
2. Plaintiff Bayer HealthCare Pharmaceuticals Inc. (“Bayer HealthCare”), formerly known as Berlex, Inc., is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 6 West Belt, Wayne, New Jersey 07470.
3. On information and belief, Lupin Ltd. is an Indian corporation having a place of business at B/4 Laxmi Towers, Bandra-Kurla Complex, Bandra (A), Mumbai 400 051, India, and having a registered office at 159 CST Road, Kalina, Santacruz (E), Mumbai 400 098, India. On information and belief, Lupin Ltd. is in the business of, among other things, manufacturing and selling generic copies of branded pharmaceutical products through various operating subsidiaries, including Lupin Pharmaceuticals, Inc.
4. On information and belief, Lupin Pharmaceuticals, Inc. is a corporation organized and existing under the laws of the Commonwealth of Virginia, having a place of business at Harborplace Tower, 111 South Calvert Street, Baltimore, Maryland 21202. On information and belief, Lupin Pharmaceuticals, Inc. is in the business of, among other things, manufacturing and selling generic copies of branded pharmaceutical products for the U.S. market. Lupin Pharmaceuticals, Inc. is a wholly owned subsidiary and alter ego of Lupin Ltd.
5. On information and belief and consistent with their practice with respect to other generic products, following any FDA approval of an Abbreviated New Drug Application (“ANDA”), Lupin Ltd. and Lupin Pharmaceuticals, Inc. will act in concert to distribute and sell Lupin’s oral-contraceptive product for ANDA No. 20-1663 throughout the United States, including

within New York. On information and belief, Lupin Ltd. and Lupin Pharmaceuticals, Inc. know and intend that Lupin's ANDA product for ANDA No. 20-1663 will be distributed and sold in the United States, including within New York.

6. On information and belief, and consistent with their practice with respect to other generic products, Lupin Ltd. and Lupin Pharmaceuticals, Inc. acted in concert to prepare and submit ANDA No. 20-1663. On information and belief, Lupin Ltd. and Lupin Pharmaceuticals, Inc. actively participated in the preparation of ANDA No. 20-1663 and both entities submitted this ANDA to the FDA. On information and belief, Lupin Pharmaceuticals, Inc. acted as the agent of Lupin Ltd. in submitting ANDA No. 20-1663 to the FDA.

JURISDICTION AND VENUE

7. This action arises under the patent laws of the United States of America. This Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331 and 1338(a).

8. On information and belief, Lupin Ltd. is subject to personal jurisdiction in New York because, among other things, Lupin Ltd., itself and through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc., has purposely availed itself of the benefits and protections of New York's laws such that it should reasonably anticipate being haled into court here. On information and belief, Lupin Ltd., itself and through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc. markets and sells generic drugs throughout the United States and within the State of New York and therefore transacts business within the State of New York, and/or has engaged in systematic and continuous business contacts within the State of New York, including through relationships with New York-based banks and other financial institutions. In addition, Lupin Ltd. is subject to personal jurisdiction in New York because, on information and belief, it controls and dominates Lupin Pharmaceuticals, Inc. and therefore the activities of Lupin Pharmaceuticals, Inc. in this jurisdiction are attributed to Lupin Ltd.

9. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) markets its branded and generic drug products to residents of the State of New York through its website.

10. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) offers its branded and generic drug products for sale to residents of the State of New York on third-party websites that New York residents can use to purchase Lupin products for shipment to and within the State of New York.
11. On information and belief, residents of the State of New York purchase branded and generic drug products from Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) in the State of New York.
12. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) receives revenue from the sales and marketing of its branded and generic drug products in the State of New York.
13. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) conducts business with banks or other financial institutions located in New York.
14. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) uses sales representatives in the State of New York to promote the sales of Lupin's branded and generic drugs throughout the State of New York.
15. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) has attended trade shows in the State of New York for the purpose of promoting and selling Lupin's branded and generic drug products.
16. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) has several authorized distributors in the State of New York to distribute Lupin's branded and generic drug products throughout the State of New York.
17. On information and belief, Lupin Ltd. (itself or through its wholly-owned subsidiary Lupin Pharmaceuticals, Inc.) plans to market and sell the product that is the subject of Lupin's ANDA No. 20-1663, if approved, in the State of New York as an alternative to Bayer's Yasmin® product currently being sold in the State of New York.
18. On information and belief, Lupin Pharmaceuticals, Inc. is subject to personal

jurisdiction in the State of New York because, among other things, it has purposely availed itself of the benefits and protections of New York's laws such that it should reasonably anticipate being haled into court here. On information and belief, Lupin Pharmaceuticals, Inc. markets and sells branded and generic drugs throughout the United States and in particular within the State of New York, and therefore Lupin Pharmaceuticals, Inc. transacts business within the State of New York such that it has engaged in systematic and continuous business contacts within the State of New York, including through relationships with New York banks and other New York financial institutions.

19. On information and belief, Lupin Pharmaceuticals, Inc. markets its branded and generic drug products to residents of the State of New York through its website.

20. On information and belief, Lupin Pharmaceuticals, Inc. offers its branded and generic drug products for sale to residents of the State of New York on third-party websites that New York residents can use to purchase Lupin products for shipment to and within the State of New York.

21. On information and belief, residents of the State of New York purchase branded and generic drug products from Lupin Pharmaceuticals, Inc. in the State of New York.

22. On information and belief, Lupin Pharmaceuticals, Inc. receives revenue from the sales and marketing of its branded and generic drug products in the State of New York.

23. On information and belief, Lupin Pharmaceuticals, Inc. conducts business with banks or other financial institutions located in New York.

24. On information and belief, Lupin Pharmaceuticals, Inc. uses sales representatives in the State of New York to promote the sales of Lupin's branded and generic drugs throughout the State of New York.

25. On information and belief, Lupin Pharmaceuticals, Inc. has attended trade shows in the State of New York for the purpose of promoting and selling Lupin's branded and generic drug products.

26. On information and belief, Lupin Pharmaceuticals, Inc. has several authorized distributors in the State of New York to distribute Lupin's branded and generic drug products

throughout the State of New York.

27. On information and belief, Lupin Pharmaceuticals, Inc. plans to market and sell the product that is the subject of ANDA No. 20-1663, if approved, in the State of New York as an alternative to Bayer's Yasmin® product currently being sold in the State of New York.

28. Venue is proper under 28 U.S.C. §§ 1391(b) and (c), and § 1400(b).

BACKGROUND

29. Bayer HealthCare is the holder of approved New Drug Application ("NDA") No. 21-098 for Yasmin® tablets, which contain as active ingredients micronized drospirenone and micronized 17 α -ethinylestradiol. The United States Food and Drug Administration ("FDA") has approved Yasmin® tablets.

30. Bayer HealthCare sells Yasmin® tablets in the United States as a 28-day oral contraceptive regimen that contains 21 tablets comprising 3 mg of drospirenone and 0.03 mg of ethinylestradiol plus 7 placebo tablets.

31. On information and belief, Lupin submitted to the FDA ANDA No. 20-1663 under the provisions of 21 U.S.C. § 355(j) seeking approval to engage in the commercial manufacture, use, offer for sale, sale and/or importation of a generic version of Bayer's Yasmin® tablets.

32. On information and belief, the composition of the product that is the subject of ANDA No. 20-1663 contains 3 mg of drospirenone and 0.03 mg of ethinylestradiol in tablet form for oral contraception in a human female (hereinafter "Lupin's Yasmin® ANDA product").

33. On information and belief, on June 2, 2010, Lupin sent a Notice Letter regarding ANDA No. 20-1663 to Plaintiffs Bayer Schering and Bayer HealthCare, purporting to comply with the provisions of 21 U.S.C. § 355(j)(2)(B) and the FDA regulations relating thereto.

PATENT-IN-SUIT

34. The patent-in-suit is United States Patent No. 5,569,652.

35. United States Patent No. 5,569,652 ("the '652 patent") issued on October 29, 1996. Inventors Sybille Beier, Walter Elger, Yukishige Nishino and Rudolf Wiechert filed their application

for this patent on December 7, 1993. Bayer Schering is the current owner of the '652 patent. Bayer attaches a true and correct copy of the '652 patent as Exhibit 1.

**COUNT ONE: CLAIM FOR PATENT INFRINGEMENT OF U.S. PATENT NO. 5,569,652
UNDER 35 U.S.C. § 271(E)(2)(A)**

36. Bayer incorporates paragraphs 1-35 of this Complaint as if fully set forth herein.

37. Lupin's filing of ANDA 20-1663 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, importation, offer for sale and/or sale, or inducement thereof, of Lupin's Yasmin® ANDA product before the expiration of the '652 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

38. The '652 patent covers Bayer HealthCare's Yasmin® tablets, and Bayer has listed the '652 patent for Yasmin® in the FDA *Approved Drug Products and Therapeutic Equivalence Evaluations* ("the Orange Book").

39. Lupin's manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of Lupin's Yasmin® ANDA product will infringe or induce infringement of at least one claim of the '652 patent under 35 U.S.C. § 271 (e)(2)(A).

40. On information and belief, Lupin is aware, or reasonably should be aware, of the widespread use of Yasmin® (drospirenone and ethinylestradiol) to produce simultaneously a gestagenic, anti-androgenic, and anti-aldosterone effect in premenopausal or menopausal female patients. This use of drospirenone and ethinylestradiol to produce simultaneously these three effects would be readily apparent to customers of Lupin (*e.g.*, including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients). Further, by filing ANDA No. 20-1663, Lupin has indicated that its Yasmin® ANDA product will be bioequivalent to Bayer's Yasmin® product.

41. On information and belief, Lupin's proposed label for its Yasmin® ANDA product does not restrict the intended use of its product to the creation of a gestagenic effect in patients. As is well known to Lupin, a significant proportion of drospirenone and ethinylestradiol prescriptions are written with the intent of producing three pharmacological effects -- gestagenic, anti-aldosterone,

and anti-androgenic. The beneficial effects of simultaneously and intentionally producing these three effects are well known to Lupin and customers of Lupin. On information and belief, Lupin will be marketing its Yasmin® ANDA product with specific intent, and/or with the desire to actively induce, aid, and abet infringement of the '652 patent. Lupin knows or reasonably should know that its proposed conduct will induce infringement.

42. On information and belief, Lupin's proposed label for its Yasmin® ANDA product provides or will be required by the FDA to provide, information for patients regarding the anti-aldosterone and antiandrogenic properties of drospirenone. By including this information in its proposed label, Lupin will be marketing its Yasmin® ANDA product with specific intent, and/or with the desire to actively induce, aid, and abet infringement of the '652 patent. Lupin knows or reasonably should know that its proposed conduct will induce infringement.

43. Drospirenone's pharmacological profile -- *i.e.*, its three mechanisms of action (gestagenic, anti-androgenic, and anti-mineralocorticoid) -- is disclosed in the approved product insert for Yasmin®. The use of drospirenone under conditions where drospirenone will exhibit this pharmacological profile is thus within the scope of the approved product insert.

44. On information and belief, Lupin's generic marketing practices include listing generic products on its website and referring customers (*e.g.*, including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients) to a corresponding brand name product. On information and belief, Lupin intends to do the same for its Yasmin® ANDA product with respect to Bayer HealthCare's Yasmin® tablets.

45. On information and belief, Lupin's generic marketing practices include representing to its customers (*e.g.*, including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients) that its generic products are bioequivalent to a corresponding brand name product and therefore representing (implicitly or explicitly or both) that Lupin's generic products are suitable for the same pharmacological uses as the corresponding branded product. On information and belief,

Lupin intends to do the same for its Yasmin® ANDA product with respect to Bayer HealthCare's Yasmin® tablets.

46. On information and belief, Lupin has planned and intended to actively induce others to infringe the '652 patent when ANDA No. 20-1663 is approved and plans and intends to do so on approval.

47. Unless Lupin is enjoined from infringing and inducing the infringement of the '652 patent, Bayer will suffer substantial and irreparable injury. Bayer has no adequate remedy at law.

COUNT TWO: CLAIM FOR PATENT INFRINGEMENT OF U.S. PATENT NO. 5,569,652 UNDER 35 U.S.C. § 271(B)

48. Bayer incorporates paragraphs 1-47 of this Complaint as if fully set forth herein.

49. On information and belief, approval of Lupin's ANDA 20-1663 is substantially likely to result in the commercial manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a method claimed in one or more claims of the '652 patent, immediately or imminently upon approval of ANDA No. 20-1663.

50. Unless Lupin is enjoined from infringing and inducing the infringement of the '652 patent, Bayer will suffer substantial and irreparable injury. Bayer has no adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE Bayer respectfully requests the following relief:

A. Judgment that Lupin has infringed one or more claims of the '652 patent by filing ANDA No. 20-1663 relating to Lupin's Yasmin® ANDA product containing drospirenone and ethinylestradiol;

B. Judgment pursuant to 28 U.S.C § 2201 et seq. that inducing the making, using, offering for sale, selling and/or importing of Lupin's Yasmin® ANDA product will infringe at least one claim of the '652 patent;

C. A permanent injunction restraining and enjoining Lupin and its officers, agents, attorneys and employees, and those acting in privity or concert with it, from engaging in the

commercial manufacture, use, offer to sell, or sale within the United States or its territories, or importation into the United States or its territories, of Lupin's Yasmin® ANDA product;

D. An order that the effective date of any approval of Lupin's ANDA No. 20-1663 relating to Lupin's Yasmin® ANDA product containing drospirenone and ethinylestradiol be a date which is not earlier than the expiration date of the '652 patent or any later date of exclusivity to which Bayer becomes entitled;


E. Damages and treble damages from Lupin for any commercial activity constituting infringement of the '652 patent; and

F. Such other and further relief as the Court may deem just and proper.

JURY DEMAND

Bayer hereby demands a jury trial on all issues so triable.

Dated: July 15, 2010



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EXHIBIT 1



US005569652A

United States Patent [19]

[11] **Patent Number:** 5,569,652

Beier et al.

[45] **Date of Patent:** Oct. 29, 1996

[54] **DIHYDROSPIRORENONE AS AN ANTIANDROGEN**

2652 761 5/1978 Germany .

OTHER PUBLICATIONS

[75] Inventors: **Sybille Beier; Walter Elger; Yukishige Nishino; Rudolf Wiechert**, all of Berlin, Germany

Breiner et al., "Inhibition of Androgen Receptor Binding by Natural and Synthetic Steroids in Cultured Human Genital Skin Fibroblasts," *Klin. Wochenschr.*, 64:732-737 (1986).

[73] Assignee: **Schering Aktiengesellschaft**, Berlin, Germany

Nishino et al., *Arch Pharmacol.*, vol. 316, R49 (1981).

Nishino et al., *Acta Endocrinologica, Suppl.* 246, vol. 99, p. 93, Abstract 105 (1982).

[21] Appl. No.: **162,387**

Primary Examiner—Theodore J. Criares

[22] Filed: **Dec. 7, 1993**

Attorney, Agent, or Firm—Millen, White, Zelano, & Branigan, P.C.

Related U.S. Application Data

[63] Continuation of Ser. No. 835,000, Feb. 14, 1992, abandoned, which is a continuation of Ser. No. 524,396, May 16, 1990.

[57] **ABSTRACT**

[30] **Foreign Application Priority Data**

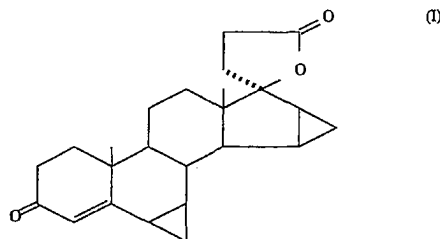
Dihydrospirorenone,

May 16, 1989 [DE] Germany 39 16 112.9

[51] **Int. Cl.⁶** **A61K 31/585**

[52] **U.S. Cl.** **514/173; 514/172**

[58] **Field of Search** **514/173, 172; 540/11, 8**



[56] **References Cited**

preferably together with an estrogen, can be used for the production of a pharmaceutical agent suitable for treatment of hormonal irregularities during premenopause (menstruation stabilization), for hormonal substitution therapy during menopause, for treatment of androgen-induced disorders and/or for contraception.

U.S. PATENT DOCUMENTS

4,347,245	8/1982	Shapiro	424/241
4,502,989	3/1985	Kamata et al.	552/615
4,584,288	4/1986	Nickish et al.	514/172
4,729,999	3/1988	Young	514/227
4,855,289	8/1989	Wester et al.	514/171
4,868,166	9/1989	Bitler et al.	514/173

FOREIGN PATENT DOCUMENTS

0 253 607 7/1987 European Pat. Off. .

27 Claims, No Drawings

5,569,652

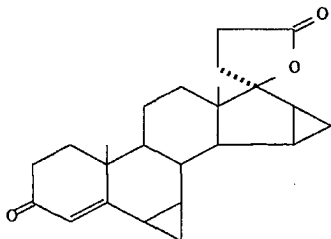
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DIHYDROSPIRORENONE AS AN ANTIANDROGEN

This application is a continuation of application Ser. No. 07/835,000, filed Feb. 14, 1992, ABN, which is a continuation of Ser. No. 07/524,396, filed May 16, 1990.

BACKGROUND OF THE INVENTION

This invention relates to the use of the compound of formula I



for the production of a pharmaceutical agent.

Compound I (dihydrospirorenone) is described in DE A-26 52 761, among others, as a diuretic of the aldosterone-antagonist type.

It can be seen from DE-A 30 22 337 that compound I, at doses at which the antialdosterone effect already appears, also exhibits a marked gestagen effect. Therefore, compound I can be used alone or in combination with estrogens in contraceptive preparations.

According to DE-A 30 22 337, these preparations are to be used for women who desire contraception and suffer from high blood pressure or in whom blood pressure rises when they take oral contraceptives. Thus, also for women predisposed to increased blood pressure, hormonal contraception is possible.

A combined preparation for substitution therapy and contraception for women before menopause (starting at about age 40) is known from EP-A 0253 607. This combined preparation contains an estrogen from the group

17beta-estradiol,

ethynylestradiol and

mestranol

and a gestagen from the group

levonorgestrel,

gestodene,

desogestrel,

3 ketodesogestrel and

norethindrone.

A composition so selected should balance hormonal irregularities in the transition phase of premenopause and help to alleviate the discomfort caused by the hormonal change of the female organism during this phase. Simultaneously, such a composition guarantees the contraceptive protection still necessary at this age.

For various, known reasons and because of the increase in the incidence of contraindications with increasing age, the taking of the usual hormonal contraceptives is recommended for women only until about age 35, so that a hormonal treatment during premenopause and a substitution therapy during menopause using doses that simultaneously have a contraceptive effect can be considered problematic.

Besides these circumstances justifying contraindication, in women of such advanced age, symptoms of androgeni-

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zation such as, for example, beard growth, deepening of the voice and impure skin are often observed; further, a rise in blood pressure can often be noted.

Thus, there remains a need for good agents for hormonal therapy, especially for such woman, including achievement of one or more of such effects.

SUMMARY OF THE INVENTION

It has now been found that the compound of formula I, in addition to its gestagen and antialdosterone effect, surprisingly exhibits a strong antiandrogenic activity component, and specifically at doses that also make possible the formulation of this compound as an oral contraceptive. Dihydrospirorenone acts as an antiandrogen about as strongly as cyproterone acetate, considered the standard compound (same maximum effect). (Animal model: juvenile, castrated and testosterone-substituted male rat.)

This invention thus relates to the use of the compound of formula I for the production of a pharmaceutical agent suitable for treatment of hormonal irregularities during premenopause (e.g., menstruation stabilization) and/or for hormonal substitution therapy during menopause and/or for treatment of androgen-induced disorders and/or for contraception. Conventional protocols can be used to determine antiandrogenic activity, e.g., as disclosed in *Methods in Hormone Research*, Editor: R. I. Dorfman, Academic Press, New York, London, 1969, pp. 241; or *Androgens and Antiandrogens*, Editors: L. Martin and M. Motta, Raven Press, New York, 1977, pp. 163.

Thus, in various aspects, this invention relates to a method of achieving an antiandrogenic effect comprising administering I to a patient in need of antiandrogenic treatment; to a method of treating an androgen induced disorder in a female comprising administering I; to a method of achieving a contraceptive effect in a female during premenopause or menopause (both terms having their conventional meaning, e.g., as shown in "The Controversial Climacteric," P. A. van Keep et al., Ed., MTP Press (1981), e.g., page 9) comprising administering to the female an effective amount of I; to a method of treating gestagen-related hormonal irregularities in a female during premenopause comprising administering I; and/or to a method of achieving gestogen-related hormonal substitution therapy in a female in menopause comprising administering I. In preferred aspects, the females are suffering from and/or predisposed to high blood pressure disorders and/or to androgen-related disorders.

Preferably an estrogen is used together with the compound of formula I. Whether a synthetic or a natural estrogen is preferably used depends on whether the contraceptive effect or the substitutive effect is emphasized: in the first case, ethynylestradiol or another synthetic estrogen is preferred, in the second case, such a pharmaceutical agent should contain a natural estrogen.

But in any case, such a pharmaceutical agent guarantees a woman of middle age (about age 35-55) a stabilization of her menstruation cycle and the contraception still indispensable at this age, with simultaneous, favorable influence on androgen-induced disorders. Of course, this pharmaceutical agent is also suited for younger women, especially for those that have a particular predisposition toward high blood pressure and/or suffer from symptoms of androgenization or are predisposed to one or both of these, e.g., in view of their past medical history, family background, etc., in addition to age.

Here such a use is especially effective because the compound of formula I simultaneously combines a gestagen,

5,569,652

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antialdosterone effect as well as a strong antiandrogen effect. Previously no substance was known that simultaneously exhibited these three properties.

The dose of the compound of formula I can be 0.5 to 50 mg per day, preferably 1–10 mg per day for all uses of this invention.

Suitable as estrogens are all previously known estrogens. The estrogen used preferably for the various purposes of this invention should be administered in doses such that the estrogen amount used according to the invention is equal to that which corresponds to the administration of 0.02 to 0.04 mg of 17alpha-ethynylestradiol or 0.5 to 4.0 mg of estradiol valerate daily. Such amounts can be conventionally determined using fully conventional tests such as described in Dorfman, supra, page 62. As estrogenic components, among others the 17alpha-ethynyl-estradiol esters and others are suitable as well as, for example, esters of 17alpha-ethynyl-7alpha-methyl-1,3,5(10)-estratriene-1,3,17beta-triol (German patent 1 593 509 and German laid-open specification 2 818 164). Further, also the 14,17beta-ethano-14beta-estratrienes described in DE-A 36 28 189 as useful. The estrogenic and gestagenic active components are preferably administered together orally; but they can also be administered separately and/or parenterally or transdermally.

The agents of this invention can be used in the methods of this invention analogously to use of agents known for such purposes, e.g., those of EP 253607 but routinely taking into account the beneficial properties discussed herein.

The formulation of the preparations according to the invention based on 6beta, 7beta; 15beta, 16beta-dimethylene-3-oxo-4-androstene-[17(beta-1')-perhydrofuran-2'-one (I) is performed in a way known in the art by processing the active ingredient, optionally in combination with an estrogen, with the vehicles, diluents, optional flavorings, etc. common in galenicals, and converting it into the desired form of administration. For the preferred oral administration, tablets, coated tablets, capsules, pills, suspensions or solutions are especially suitable. For parenteral administration, in particular oily solutions, such as, for example, solutions in sesame oil, castor oil and cottonseed oil, are suitable. To increase solubility, solubilizers such as, for example, benzyl benzoate or benzyl alcohol, can be added.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

In the foregoing and in the following examples, all temperatures are set forth uncorrected in degrees Celsius and unless otherwise indicated, all parts and percentages are by weight.

The entire disclosures of all applications, patents and publications, if any, cited above and below, and of corresponding application Federal Republic of Germany P 39 16 112.9, filed May 16, 1989, are hereby incorporated by reference.

EXAMPLES

Example 1

20.0 mg of 6beta, 7beta; 15beta, 16beta-dimethylene-3-oxo-4-androstene-[17(beta-1')-spiro-5']-perhydrofuran-2'-one and 0.05 mg of 17alpha-ethynylestradiol are mixed homogeneously with 140.45 mg of lactose, 59.5 mg of

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cornstarch, 2.0 mg of aerosil, 2.5 mg of polyvinylpyrrolidone 25 and 0.5 mg of magnesium stearate and pressed without advance granulation into a tablet of 225 mg final weight.

Example 2

Analogous to example 1, 10 mg of 6beta, 7beta; 15beta, 16beta-dimethylene-3-oxo-4-androstene-[17(beta-1')-spiro-5']-perhydrofuran-2'-one and 0.05 mg of 17alpha-ethynylestradiol with 150.45 mg of 17alpha-ethynylestradiol with 150.45 mg of lactose, 59.5 mg of cornstarch, 2.0 mg of aerosil, 2.5 mg of polyvinylpyrrolidone 25 and 0.5 mg of magnesium stearate are pressed into tablets with a final weight of 225 mg.

Example 3

Analogous to example 1, 20 mg of 6beta, 7beta; 15beta, 16beta-dimethylene-3-oxo-4-androstene-[17(beta-1')-spiro-5']-perhydrofuran-2'-one with 140.5 mg of lactose, 59.5 mg of cornstarch, 2.0 mg of aerosil, 2.5 mg of polyvinylpyrrolidone 25 and 0.5 mg of magnesium stearate are pressed into tablets with a final weight of 225 mg.

The preceding examples can be repeated with similar success by substituting the generically or specifically described reactants and/or operating conditions of this invention for those used in the preceding examples.

From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

What is claimed is:

1. A method of simultaneously achieving, during premenopause or menopause a gestagenic effect, antiandrogenic effect, and an antialdosterone effect in a female patient in need thereof comprising administering an amount of dihydrospirorenone to said female patient, wherein said amount of dihydrospirorenone is effective to simultaneously achieve a gestagenic effect, antiandrogenic effect and antialdosterone effect in said patient.

2. A method according to claim 1, wherein said patient is in premenopause.

3. A method of claim 2, wherein stabilization of menstruation is achieved.

4. A method according to claim 1, wherein said female is of age 35–55.

5. A method according to claim 1, wherein said patient is in menopause.

6. A method according to claim 1, wherein said effective amount of dihydrospirorenone is 0.5–50 mg per day.

7. A method according to claim 6, wherein said effective amount of dihydrospirorenone is 1–10 mg per day.

8. A method of claim 1, wherein said patient is predisposed to androgenization symptoms.

9. A method of claim 1, wherein said patient suffers from or is predisposed to high blood pressure.

10. A method of claim 2, wherein said patient suffers from or is predisposed to high blood pressure.

11. A method of simultaneously achieving, during premenopause or menopause, a contraceptive effect, an antiandrogenic effect, and an anti-aldosterone effect in a female patient in need thereof comprising administering an effective amount of dihydrospirorenone and an effective amount of an estrogenic compound, wherein said effective amount of dihydrospirorenone is effective to simultaneously achieve a

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gestagenic effect, anti-androgenic effect, and an anti-aldosterone effect in said female patient.

12. A method according to claim 11, wherein said effective amount of dihydrospirorenone is 0.5–50 mg per day and said effective amount of an estrogenic compound is an amount equivalent to 0.5–4.0 mg of estradiol valerate per day.

13. A method of claim 11, wherein said patient suffers from symptoms of androgenization.

14. A method of claim 11, wherein said patient suffers from or is predisposed to high blood pressure.

15. A method of claim 13, wherein said patient is in premenopause.

16. A method of claim 13, wherein said patient suffers from or is predisposed to high blood pressure.

17. A method of claim 11, wherein said estrogenic compound is a synthetic estrogen.

18. A method of claim 11, wherein said estrogenic compound is a natural estrogen.

19. A method according to claim 11, wherein said female is of age 35–55.

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20. A method of claim 11, wherein said estrogenic compound is a synthetic estrogen.

21. A method of claim 12, wherein said estrogenic compound is a natural estrogen.

22. A method of claim 11, wherein the estrogenic compound is 17 α -ethynylestradiol.

23. A method of claim 11, wherein said patient is in menopause.

24. A method according to claim 11, wherein said effective amount of dihydrospirorenone is 1–10 mg per day.

25. A method of claim 11, wherein said patient is predisposed to androgenization symptoms.

26. A method of claim 15, wherein stabilization of menstruation is achieved.

27. A method according to claim 11, wherein said effective amount of dihydrospirorenone is 0.5–50 mg per day and said effective amount of an estrogenic compound is an amount equivalent to 0.02–0.04 mg of 17 α -ethynylestradiol per day.

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