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(54) **Progestagen-only contraceptive**

Progestogen als einziges Kontrazeptivum

Progestogène comme seul contraceptif

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Description

Technical Field. The invention relates generally to contraceptive preparations, and more specifically to a contraceptive regimen involving only the administration of desogestrel, 3-ketodesogestrel or mixtures thereof.

Background Art. It has been known for some time that contraception can be achieved by the oral administration of sufficient quantities of a progestogen to a female of child-bearing age.

For example in French Patent Application No. 2,223,018 to Ortho Pharmaceutical, a progestogen is administered from at least the fifth day to the twenty-fifth day of the menstrual cycle, the dosage of the progestogen being greater during the last seven days of administration than it is in the first seven days.

U.S. Patent No. 4,018,919 to Eli Lilly & Co. describes a sequential oral contraceptive method using two different types of progestational agents. These different types of progestational agents are a Type A progestin (e.g. norethindrone) and Type B progestin (e.g. chlormadione acetate).

Another contraceptive regimen using these two types of progestational agents is described in Belgian Patent 773,064 to Ciba Geigy AG.

U.S. Patent 4,171,358 to Eli Lilly & Co. describes another contraceptive method in which a progestin (e.g. chlormadione acetate) is administered on days 6 to 16 of the menstrual cycle, followed by a period in which no hormone is administered.

DT 1,950,857 to Merck Patent GmbH describes a progestogen-only contraceptive pack containing 28 dosage units, 14 to 18 of which are "blanks", containing no contraceptive steroid. Disclosed progestogens include chlormadione acetate, megestrol acetate, melengestrol acetate and medroxyprogesterone acetate. A similar regimen is disclosed in DT 1,965,881, also to Merck Patent GmbH.

U.S. Patent No. 3,822,355 to Biological Concepts Inc. describes a method of controlling the ovulatory cycle in women involving administering placebo tablets daily for 12 to 16 days; followed administering daily tablets containing 2 to 20 mg progestogen (e.g. norethindrone) for four days; finally followed by administering tablets containing 10 to 40 % of the previous progestogen dosage for the remainder of the cycle.

"Progestogen-only pills" are a preferred method of contraception for breast-feeding mothers, older women, women for whom estrogen is contraindicated, women who are hypertensive, and women who develop migraine headaches when taking a combined pill (i.e. one containing an estrogen and progestogen component). See, e.g. "Contraception for women over the age of 35", IPPF Medical Bulletin, 22: 3-4 (1988) and Howie, PW "The progestogen-only pill", Brit. J. Obstet. Gynaecol., 92: 1001-2 (1985).

While different progestogen-only regimens have been described, they are still associated with incomplete ovulation inhibition, and relatively high failure rates. Vessey et al "Progestogen-only oral contraception. Findings in a large prospective study with special reference to effectiveness", Brit. J. Family Planning, 292: 526-30 (1986). It has been suggested to increase the daily dosage of progestogen in order to induce complete ovulation inhibition, however such an increase in dosage also increases the frequency of intermenstrual bleeding (i.e. "spotting"), which is clearly not desired. E. Diczfalusy et al, Progestogens in Therapy, p. 150 (Raven Press, NY 1983).

Moreover, a high prevalence of functional ovarian cysts have been reported with progestogen only contraceptive regimens, which resolve after discontinuation of the progestogen-only contraceptive. Fotherby, K. "The Progestogen-pill", in: Filshie et al eds. Contraception: Science and Practice, pp. 94-108 (1989), and Howie, supra.

A need exists for a progestogen-only contraceptive regimen which more effectively inhibits ovulation, while still not increasing the frequency of intermenstrual bleeding, or leading to persistent functional ovarian cysts.

Disclosure of the Invention

Surprisingly it has been found that by selecting desogestrel or 3-ketodesogestrel as the progestogen at certain specified dosages for use in an oral contraceptive regimen administered over an entire menstrual cycle (e.g. 28 days), complete ovulation inhibition is achieved, while retaining acceptable cycle control. Moreover, this regimen also seems to prevent the formation of ovarian cysts, and decreases the amount of spotting.

The invention thus includes a drug delivery system containing daily oral dosage units, each unit containing from 70 to 80 micrograms of desogestrel, 3-ketodesogestrel, or mixtures thereof.

The invention also includes a pharmaceutical product (i.e. the dosage units or the package containing the dosage units), a method of using the product, and a process of manufacturing the pharmaceutical product.

The invention also includes a method of providing contraception for a pre-menopausal woman involving orally administering to the woman, on a daily basis, 70 to 80 micrograms of desogestrel, 3-ketodesogestrel, or mixtures thereof.

Best Mode of the Invention

Progestogens for use with the invention are 3-ketodesogestrel ("etonogestrel") and desogestrel. Desogestrel has the chemical name 13-ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17-ol. Desogestrel is believed to be metabolized in the body into 3-ketodesogestrel. In the dosage units, 75 μg of desogestrel or 3-ketodesogestrel are preferably used. Both compounds are available from Organon International, bv of Oss, The Netherlands.

The progestogen ("contraceptive steroid"), is incorporated into dosage units for oral administration. The

term "dosage unit" generally refers to physically discrete units suitable as unitary dosages for humans, each containing a predetermined quantity of active material calculated to produce the desired effect.

Methods and compositions for making such dosage units are well-known to those skilled in the art. For example, conventional techniques for making tablets and pills, containing active ingredients, are described in the standard reference, Chase et al., Remington's Pharmaceutical Sciences, (16th ed., Mack Publishing Co., Easton. PA, U.S.A., 1980) ("Remington's"), at pages 1553 through 1584. Conventional techniques for making powders, and their composition are described at pages 1535 through 1552 of the reference. Conventional techniques for coating pharmaceutical dosage forms are described at pages 1585 to 1593 of Remington's.

For making dosage units, e.g. tablets, the use of conventional additives, e.g. fillers, colorants, polymeric binders and the like is contemplated. In general any pharmaceutically acceptable additive which does not interfere with the function of the active compounds can be used in the one or more of the compositions.

Suitable carriers with which the compositions can be administered include lactose, starch, cellulose derivatives and the like used in suitable amounts. Lactose is a preferred carrier. Mixtures of carriers can also be used.

A process of manufacturing the combination and contraceptive kit of the invention comprises mixing predetermined quantities of desogestrel, 3-ketodesogestrel, or mixtures thereof with predetermined quantities of excipients and converting the mixture into dosage units containing 70 to 80 µg of desogestrel or 3-ketodesogestrel.

Converting the mixture into dosage units generally involves molding the mixture into a tablet, filling a capsule with a dried mixture, or filling a capsule with a wet mixture.

A preferred process of manufacturing the pharmaceutical product according to the invention involves incorporating the desired dosages of contraceptive steroid (i.e. desogestrel, 3-ketodesogestrel, or mixtures thereof) into tablets by techniques such as wet granulation tableting techniques. The package containing the dosage units will contain between 7 and 180, preferably 28, dosage units.

A preferred method of contraception using the invention comprises administering, orally, to a female of childbearing age, 70 to 80 µg of desogestrel, 3-ketodesogestrel, or mixtures thereof daily. After the completion of one cycle of the regimen, the regimen may be repeated for as long as contraception is desired.

Desogestrel and 3-ketodesogestrel are 70 to 80 % bioavailable after oral administration in comparison with non-enteral forms of administration (e.g. via an implant).

The invention is further explained by the following illustrative EXAMPLES.

EXAMPLE I

The following coated tablets intended for once daily administration were made:

Composition (per tablet):		
Compound	Amount (mg/tablet)	
desogestrel		0.075
corn starch		6.500
povidone		1.950
stearic acid		0.650
colloidal silicone dioxide		0.650
dl-α-tocopherol		0.080
lactose	qsad	65.000

Coating layer: (filmcoat-dry)	
Compound	Amount (mg/tablet)
hydroxypropylmethylcellulose	0.75
polyethylene glycol 400	0.15
titanium dioxide	0.1125
talc	0.1875

The tablets were packed in push-through packs. The push through packs are placed in folding cartons, which are additionally sealed in aluminum sachets.

EXAMPLE II

The following tablets intended for once daily administration are made:

Compositions of tablets:		
Compound	Amount (mg/tablet)	
3-ketodesogestrel		0.075
corn starch		6.500
povidone		1.950
stearic acid		0.650
colloidal silicone dioxide		0.650
dl-α-tocopherol		0.080
lactose	qsad	65.000

Coating layer:	
Compound	Amount (mg/tablet)
hydroxypropylmethylcellulose	0.75
polyethylene glycol 400	0.15
titanium dioxide	0.1125
talc	0.1875

EXAMPLE III

The tablets of EXAMPLE I, along with similar tablets containing 0.030 and 0.050 mg of desogestrel were tested in 44 healthy female volunteers in a non-public, double-blind randomized study. Ovulation was completely inhibited with the tablets of EXAMPLE I (i.e. those containing 0.075 mg desogestrel), whereas incomplete inhibition of ovulation occurred at the other lower doses. Furthermore, the use of the tablets of EXAMPLE I also had the lowest percentage of bleeding and spotting days (mean of 22%) in comparison to 0.030 mg desogestrel (mean of 32%) and 0.050 mg (mean of 33%). Amenorrhea occurred only once in the group administered the tablets of EXAMPLE I. No luteinized follicles were observed with the group administered the tablets of EXAMPLE I, while the group administered 0.030 mg daily had three cycles, and the group administered 0.050 mg daily had one cycle of luteinized follicles. Non-luteinized small follicular cysts (15-40 mm diameter) were observed in all dose groups during 50 to 75 % of the cycles investigated. Persistent cysts occurred in the 0.050 mg group (10 out of 32 cycles). Follicles regressed spontaneously in women administered 0.075 mg desogestrel daily, and persistent cyst formation was not observed in this group.

Reference herein to specific embodiments or examples should not be interpreted as limitations to the scope of the invention, which is defined by the appended claims.

Claims

Claims for the following Contracting States : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, MC, NL, SE

1. A combination and contraceptive kit comprising sequential daily dosage units for oral administration each containing as the sole contraceptively effective ingredient from 70 to 80 micrograms of desogestrel, 3-ketodesogestrel, or mixtures thereof.

2. The combination and contraceptive kit of claim 1 wherein said kit contains 21 to 35 of said daily sequential dosage units.

3. The combination and contraceptive kit of claim 2 wherein said progestogen is 3-ketodesogestrel present in a quantity of 75 micrograms per dosage unit.

4. The combination and contraceptive kit of claim 2 wherein said progestogen is desogestrel present in a quantity of 75 micrograms per dosage unit.

5. The use of an oral daily dosage unit consisting essentially of 70 to 80 micrograms of a progestogen selected from the group of progestogens consisting of desogestrel, 3-ketodesogestrel, or mixtures thereof, in the preparation of a drug delivery system, said drug delivery system characterized by consisting of daily dosage units containing only a progestogenic compound as sole therapeutically effective ingredient.

6. A drug delivery system comprising a package containing 26 to 30 daily sequential dosage units consisting essentially of from 70 to 80 micrograms of a compound selected from the group consisting of desogestrel, 3-ketodesogestrel, and mixtures thereof.

7. A contraceptive kit of the type containing progestogen-only daily dosage units, wherein the improvement comprises using from 70 to 80 micrograms of 3-ketodesogestrel, desogestrel, or mixtures thereof as the progestogen in said daily dosage units.

8. A process of manufacturing a drug delivery system comprising:
mixing predetermined quantities of a progestogen selected from the group consisting of desogestrel, 3-ketodesogestrel, and mixtures thereof, with predetermined quantities of excipients and converting the mixture into dosage units each containing 70 to 80 µg of desogestrel, 3-ketodesogestrel, or mixtures thereof, and packaging a plurality of said dosage units into a kit.

9. The process of claim 8 wherein said mixture is converted into dosage units selected from the group consisting of capsules and tablets.

Claims for the following Contracting States : ES, GR

1. A method of manufacturing of a combination and contraceptive kit comprising sequential daily dosage units for oral administration each containing as the sole contraceptively effective ingredient from 70 to 80 micrograms of desogestrel, 3-ketodesogestrel,

or mixtures thereof, by mixing predetermined quantities of a progestogen selected from the group consisting of desogestrel, 3-ketodesogestrel, and mixtures thereof, with predetermined quantities of excipients and converting the mixture into dosage units each containing 70 to 80 µg of desogestrel, 3-ketodesogestrel, or mixtures thereof, and packaging a plurality of said dosage units into the kit.

2. The method of manufacturing of the combination and contraceptive kit according to claim 1 wherein said kit contains 21 to 35 of said daily sequential dosage units.

3. The method of manufacturing of the combination and contraceptive kit according to claim 2 wherein said progestogen is 3-ketodesogestrel present in a quantity of 75 micrograms per dosage unit.

4. The method of manufacturing of the combination and contraceptive kit according to claim 2 wherein said progestogen is desogestrel present in a quantity of 75 micrograms per dosage unit.

5. The use of an oral daily dosage unit consisting essentially of 70 to 80 micrograms of a progestogen selected from the group of progestogens consisting of desogestrel, 3-ketodesogestrel, or mixtures thereof, in the preparation of a drug delivery system, said drug delivery system characterized by consisting of daily dosage units containing only a progestogenic compound as sole therapeutically effective ingredient.

6. A method of manufacturing of a drug delivery system comprising a package containing 26 to 30 daily sequential dosage units consisting essentially of from 70 to 80 micrograms of a compound selected from the group consisting of desogestrel, 3-ketodesogestrel, and mixtures thereof, by mixing predetermined quantities of a progestogen selected from the group consisting of desogestrel, 3-ketodesogestrel, and mixtures thereof, with predetermined quantities of excipients and converting the mixture into dosage units each containing 70 to 80 µg of desogestrel, 3-ketodesogestrel, or mixtures thereof, and packaging 26 to 30 of said dosage units into a kit.

7. A method of manufacturing of a contraceptive kit of the type containing progestogen-only daily dosage units, wherein the improvement comprises using from 70 to 80 micrograms of 3-ketodesogestrel, desogestrel, or mixtures thereof as the progestogen in said daily dosage units, by mixing predetermined quantities of a progestogen selected from the group consisting of desogestrel, 3-ketodesogestrel, and mixtures thereof, with predetermined quantities of excipients and converting the mixture into dosage units each containing 70 to 80 µg of desogestrel, 3-ketodesogestrel, or mixtures thereof, and packaging a plurality of said dosage units into the kit.

8. The method of manufacturing according to claim 6 or 7 wherein said mixture is converted into dosage units selected from the group consisting of capsules and tablets.

Patentansprüche

Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, MC, NL, SE

1. Kombination und Empfängnisverhütungspackung umfassend sequentielle tägliche Dosiseinheiten zur oralen Verabreichung, von denen jede als einzigen empfängnisverhütend wirksamen Bestandteil 70 bis 80 Mikrogramm Desogestrel, 3-Ketodesogestrel oder Mischungen davon enthält.

2. Kombination und Empfängnisverhütungspackung nach Anspruch 1, worin diese Packung 21 bis 35 dieser täglichen sequentiellen Dosiseinheiten enthält.

3. Kombination und Empfängnisverhütungspackung nach Anspruch 2, worin dieses Gestoden 3-Ketodesogestrel ist, das in einer Menge von 75 Mikrogramm pro Dosiseinheit vorhanden ist.

4. Kombination und Empfängnisverhütungspackung nach Anspruch 2, worin dieses Gestoden Desogestrel ist, das in einer Menge von 75 Mikrogramm pro Dosiseinheit vorhanden ist.

5. Anwendung einer täglichen oralen Dosiseinheit, bestehend im wesentlichen aus 70 bis 80 Mikrogramm eines Gestodens, das aus der Gruppe von Gestodenen bestehend aus Desogestrel, 3-Ketodesogestrel oder Mischungen davon ausgewählt wird, bei der Herstellung eines Arzneiabgabesystems, wobei dieses Arzneiabgabesystem dadurch gekennzeichnet ist, dass es aus täglichen Dosiseinheiten besteht, die nur eine Gestodenverbindung als einzigen therapeutisch wirksamen Bestandteil enthält.

6. Arzneiabgabesystem umfassend eine Packung, die 26 bis 30 sequentielle tägliche Dosiseinheiten enthält, die im wesentlichen aus 70 bis 80 Mikrogramm einer Verbindung bestehen, die aus der Gruppe bestehend aus Desogestrel, 3-Ketodesogestrel und Mischungen davon ausgewählt wird.

7. Empfängnisverhütungspackung vom Typus, der tägliche Nur-Gestoden-Dosiseinheiten enthält, worin die Verbesserung die Anwendung von 70 bis 80 Mikrogramm 3-Ketodesogestrel, Desogestrel

oder Mischungen davon als das Gestoden in diesen täglichen Dosiseinheiten umfasst.

8. Verfahren zur Herstellung eines Arzneiabgabesystems, umfassend:
Mischen vorbestimmter Mengen eines Gestodens, das aus der Gruppe bestehend aus Desogestrel, 3-Ketodesogestrel und Mischungen davon ausgewählt wird, mit vorbestimmten Mengen Arzneiträgern und Umwandeln der Mischung in Dosiseinheiten, von denen jede 70 bis 80 µg Desogestrel, 3-Ketodesogestrel oder Mischungen davon enthält, und Abpacken einer Mehrzahl dieser Dosiseinheiten in eine Packung.

9. Verfahren nach Anspruch 9, worin diese Mischung in Dosiseinheiten umgewandelt wird, die aus der Gruppe bestehend aus Kapseln und Tabletten ausgewählt werden.

Patentansprüche für folgenden Vertragsstaaten : ES, GR

1. Verfahren zur Herstellung einer Kombination und Empfängnisverhütungspackung umfassend sequentielle tägliche Dosiseinheiten zur oralen Verabreichung, von denen jede als einzigen empfängnisverhütend wirksamen Bestandteil 70 bis 80 Mikrogramm Desogestrel, 3-Ketodesogestrel oder Mischungen davon enthält, indem vorbestimmte Mengen eines Gestodens, das aus der Gruppe bestehend aus Desogestrel, 3-Ketodesogestrel und Mischungen davon ausgewählt wird, mit vorbestimmten Mengen Arzneiträgern gemischt wird, und Umwandeln der Mischung in Dosiseinheiten, von denen jede 70 bis 80 µg Desogestrel, 3-Ketodesogestrel oder Mischungen davon enthält, und Abpakken einer Mehrzahl dieser Dosiseinheiten in die Packung.

2. Verfahren zur Herstellung der Kombination und Empfängnisverhütungspackung nach Anspruch 1, worin diese Packung 21 bis 35 dieser täglichen sequentiellen Dosiseinheiten enthält.

3. Verfahren zur Herstellung der Kombination und Empfängnisverhütungspackung nach Anspruch 2, worin dieses Gestoden 3-Ketodesogestrel ist, das in einer Menge von 75 Mikrogramm pro Dosiseinheit vorhanden ist.

4. Verfahren zur Herstellung der Kombination und Empfängnisverhütungspackung nach Anspruch 2, worin dieses Gestoden Desogestrel ist, das in einer Menge von 75 Mikrogramm pro Dosiseinheit vorhanden ist.

5. Anwendung einer täglichen oralen Dosiseinheit bestehend im wesentlichen aus 70 bis 80 Mikrogramm eines Gestodens, das aus der Gruppe von Gestodenen bestehend aus Desogestrel, 3-Ketodesogestrel oder Mischungen davon ausgewählt wird, bei der Herstellung eines Arzneiabgabesystems, wobei dieses Arzneiabgabesystem dadurch gekennzeichnet ist, dass es aus täglichen Dosiseinheiten besteht, die nur eine Gestodenverbindung als therapeutisch wirksamer Bestandteil enthält.

6. Verfahren zur Herstellung eines Arzneiabgabesystems, umfassend eine Packung, die 26 bis 30 tägliche sequentielle Dosiseinheiten enthält, die im wesentlichen aus 70 bis 80 Mikrogramm einer Verbindung besteht, die aus der Gruppe bestehend aus Desogestrel, 3-Ketodesogestrel und Mischungen davon ausgewählt wird, indem vorbestimmte Mengen eines Gestodens, ausgewählt aus der Gruppe bestehend aus Desogestrel, 3-Ketogestrel und Mischungen davon, mit vorbestimmten Mengen Arzneiträgern gemischt werden, und Umwandeln der Mischung in Dosiseinheiten, von denen jede 70 bis 80 µg Desogestrel, 3-Ketodesogestrel oder Mischungen enthält, und Abpacken von 26 bis 30 dieser Dosiseinheiten in eine Packung.

7. Verfahren zur Herstellung einer Empfängnisverhütungspackung vom Typus, der tägliche Nur-Gestoden-Dosiseinheiten enthält, worin die Verbesserung die Anwendung von 70 bis 80 Mikrogramm 3-Ketodesogestrel, Desogestrel oder Mischungen davon als das Gestoden in diesen täglichen Dosiseinheiten umfasst, indem vorbestimmte Mengen eines Gestodens, ausgewählt aus der Gruppe bestehend aus Desogestrel, 3-Ketodesogestrel und Mischungen davon, mit vorbestimmten Mengen Arzneiträgern gemischt werden, und Umwandeln der Mischung in Dosiseinheiten, von denen jede 70 bis 80 µg Desogestrel, 3-Ketodesogestrel oder Mischungen davon enthält, und Abpacken einer Mehrzahl dieser Dosiseinheiten in die Packung.

8. Herstellungsverfahren nach Anspruch 6 oder 7, worin diese Mischung in Dosiseinheiten umgewandelt wird, die aus der Gruppe bestehend aus Kapseln und Tabletten ausgewählt werden.

Revendications

Revendications pour les Etats contractants suivants : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, MC, NL, SE

1. Combinaison et kit contraceptif comprenant des unités de dosage quotidiennes successives pour l'administration orale contenant chacune en tant qu'unique composant efficace du point de vue contraceptif de 70 à 80 µg de désogestrel, de 3-cétodésogestrel ou de leurs mélanges.

2. Combinaison et kit contraceptif suivant la revendication 1, dans lesquels ce kit contient 21 à 35 de ces unités de dosage successives quotidiennes.

3. Combinaison et kit contraceptif suivant la revendication 2, dans lesquels ce progestogène est du 3-cétodésogestrel présent en une quantité de 75 µg par unité de dosage.

4. Combinaison et kit contraceptif suivant la revendication 2, dans lesquels ce progestogène est du désogestrel présent en une quantité de 75 µg par unité de dosage.

5. Utilisation d'une unité de dosage quotidienne orale consistant essentiellement en 70 à 80 µg d'un progestogène choisi dans le groupe des progestogènes consistant en désogestrel, 3-cétodésogestrel ou leurs mélanges, dans la préparation d'un système de distribution de médicament, ce système de distribution de médicament étant caractérisé en ce qu'il consiste en unités de dosage quotidiennes ne contenant qu'un composé progestatif comme unique composant efficace du point de vue thérapeutique.

6. Système de distribution de médicament comprenant un conditionnement contenant 26 à 30 unités de dosage successives quotidiennes consistant essentiellement en 70 à 80 µg d'un composé choisi dans le groupe consistant en désogestrel, 3-cétodésogestrel ou leurs mélanges.

7. Kit contraceptif du type contenant des unités de dosage uniquement de progestogène, dans lequel l'amélioration comprend l'utilisation de 70 à 80 µg de désogestrel, 3-cétodésogestrel ou leurs mélanges, comme progestogène dans ces unités de dosage quotidiennes.

8. Procédé pour la fabrication d'un système de distribution de médicament comprenant le mélange de quantités prédéterminées d'un progestogène choisi dans le groupe consistant en désogestrel, 3-cétodésogestrel ou leurs mélanges, avec des quantités prédéterminées d'excipients et la conversion du mélange en unités de dosage contenant chacune 70 à 80 µg de désogestrel, de 3-cétodésogestrel ou de leurs mélanges, et le conditionnement d'un certain nombre de ces unités de dosage en un kit.

9. Procédé suivant la revendication 8, dans lequel ce mélange est converti en unités de dosage choisies dans le groupe consistant en gélules et comprimés.

Revendications pour les Etats contractants suivants : ES, GR

1. Procédé pour la fabrication d'une combinaison et d'un kit contraceptif comprenant des unités de dosage quotidiennes successives pour l'administration orale contenant chacune en tant qu'unique composant efficace du point de vue contraceptif de 70 à 80 µg de désogestrel, de 3-cétodésogestrel ou de leurs mélanges, par mélange de quantités prédéterminées d'un progestogène choisi dans le groupe consistant en désogestrel, 3-cétodésogestrel ou leurs mélanges, avec des quantités prédéterminées d'excipients et la conversion du mélange en unités de dosage contenant chacune 70 à 80 µg de désogestrel, de 3-cétodésogestrel ou de leurs mélanges, et le conditionnement d'un certain nombre de ces unités de dosage dans le kit.

2. Procédé pour la fabrication d'une combinaison et d'un kit contraceptif suivant la revendication 1, dans lequel ce kit contient 21 à 35 de ces unités de dosage successives quotidiennes.

3. Procédé pour la fabrication d'une combinaison et d'un kit contraceptif suivant la revendication 2, dans lequel ce progestogène est du 3-cétodésogestrel présent en une quantité de 75 µg par unité de dosage.

4. Procédé pour la fabrication d'une combinaison et d'un kit contraceptif suivant la revendication 2, dans lequel ce progestogène est du désogestrel présent en une quantité de 75 µg par unité de dosage.

5. Utilisation d'une unité de dosage quotidienne orale consistant essentiellement en 70 à 80 µg d'un progestogène choisi dans le groupe des progestogènes consistant en désogestrel, 3-cétodésogestrel ou leurs mélanges, dans la préparation d'un système de distribution de médicament, ce système de distribution de médicament étant caractérisé en ce qu'il consiste en unités de dosage quotidiennes ne contenant qu'un composé progestatif comme unique composant efficace du point de vue thérapeutique.

6. Procédé pour la fabrication d'un système de distribution de médicament comprenant un conditionnement contenant 26 à 30 unités de dosage successives quotidiennes consistant essentiellement en 70 à 80 µg d'un composé choisi dans le groupe consistant en désogestrel, 3-cétodésogestrel ou leurs mélanges, par mélange de quantités prédéterminées d'un progestogène choisi dans le groupe consistant en désogestrel, 3-cétodésogestrel ou de leurs mélanges, avec des quantités prédéterminées d'excipients et la conversion du mélange en unités de dosage contenant chacune 70 à 80 µg de désogestrel, de 3-cétodésogestrel ou de leurs mélanges, et le conditionnement de 26 à 30 de ces unités de dosage en un kit.

7. Procédé pour la fabrication d'un kit contraceptif du type contenant des unités de dosage quotidiennes

uniquement de progestogène, dans lequel l'amélioration comprend l'utilisation de 70 à 80 µg de désogestrel, de 3-céto-désogestrel ou de leurs mélanges, comme progestogène dans ces unités de dosage quotidiennes, par mélange de quantités prédéterminées d'un progestogène choisi dans le groupe consistant en désogestrel, 3-cétodésogestrel ou leurs mélanges, avec des quantités prédéterminées d'excipients et la conversion du mélange en unités de dosage contenant chacune 70 à 80 µg de désogestrel, de 3-cétodésogestrel ou de leurs mélanges, et le conditionnement d'un certain nombre de ces unités de dosage dans le kit.

8. Procédé pour la fabrication suivant les revendications 6 ou 7, dans lequel ce mélange est converti en unités de dosage choisies dans le groupe consistant en gélules et comprimés.