Claims

1. Use of a composition comprising from 10 to 25 mg estetrol and from 1 to 4 mg drospirenone in the manufacture of a medicament for oral contraception, wherein said composition is to be administered to a subject, and wherein said composition does not result in haemostatic changes exceeding the boundaries of the normal haemostatic range in said subject.

2. The use according to claim 1, for reducing cardiovascular effects in said subject.

3. The use according to claim 1, for preventing risk increase of developing venous thromboembolism (VTE) and/or of developing aortic thromboembolism (ATE) in a subject compared to other combined oral contraceptives (COCs).

4. Use of a combined oral contraceptive in the manufacture of a medicament for avoiding haemostatic changes exceeding the boundaries of the normal haemostatic range in subjects using said combined oral contraceptive, wherein the combined oral contraceptive comprises from 10 to 25 mg estetrol and from 1 to 4 mg drospirenone.

5. The use according to claim 4, for preventing risk increase of developing venous thromboembolism (VTE) and/or of developing aortic thromboembolism (ATE) associated with the use of COC's in subjects using the combined oral contraceptive.

6. The use according to claim 4, for preventing risk increase of developing VTE in subjects using the combined oral contraceptive.

7. The use according to any one of claims 1 to 6, wherein the normal haemostatic range is defined as the prediction interval that 95% of the population fall into.

8. The use according to any one of claims 1 to 7, wherein said haemostatic change is determined based on any one or more of the following markers: SHBG, free TFPI, free and total Protein-S, Protein-S activity, CBG, Ceruloplasmin, antithrombin III, APC resistance, protein-C activity, D-dimer, Prothrombin, Prothrombin fragment

1+2, Factor VII, Factor VIII, von Willebrand factor, Factor II, PAI-I, t-PA, plasminogen, E-selectin and fibrinogen.

9. The use according to any one of claims 1 to 8, wherein said haemostatic change is determined based on a change in level of Protein-S or TFPI when compared to the normal haemostatic range.

10. The use according to any one of claims 1 to 9, wherein said haemostatic change is measured after one cycle of treatment, after two cycles of treatment or after three cycles of treatment.

11. The use according to any one of claims 1 to 10, wherein said oral contraceptive comprises from 15 to 20 mg estetrol.

12. The use according to any one of claims 1 to 11, wherein said oral contraceptive comprises about 15 mg estetrol.

13. The use according to any one of claims 1 to 11, wherein said oral contraceptive comprises about 20 mg estetrol.

14. The use according to any one of claims 1 to 13, wherein said oral contraceptive comprises from about 3 mg drospirenone.

15. The use according to any one of claims 1 to 14, wherein said estetrol is estetrol monohydrate.

16. The use according to any one of claims 1 to 15, wherein said composition is to be administered orally.

17. The use according to any one of claims 1 to 16, wherein said composition is to be administered during at least 21 days, or during 24 days, respectively followed by an administration-free period of about 7 to 4 days.

1. An effective amount of an estetrol component for use as the estrogenic component in a combined oral contraceptive comprising an effective amount of drospirenone as the progestogenic component, to reduce the risk of thromboembolism associated with the use of drospirenone.

2. The effective amount of an estetrol component for use of claim 1, wherein said risk of thromboembolism is reduced to less than 8, preferably less than 7, more preferably less than 6, even more preferably less than 5, yet even more preferably less than 4 per 10,000 women using said contraceptive during one year.

3. The effective amount of an estetrol component for use of claims 1 or 2, wherein the estetrol component is used at a daily dose of from 1 mg to 40 mg, preferably at a daily dose of from 5 mg to 25 mg.

4. The effective amount of an estetrol component for use of any of claims 1-3 wherein drospirenone is used at a daily dose of from 0.5 mg to 10 mg, preferably at a daily dose of from 1 mg to 4 mg.

5. The effective amount of an estetrol component for use of any one of claims 1-4 wherein the administration method is a combined method with an administration-free interval of about 7 days, preferably with an administration-free interval of about 4 days.

6. The effective amount of an estetrol component for use of any one of claims 1-5 wherein the estetrol component is estetrol, preferably estetrol monohydrate.r

7. The effective amount of an estetrol component for use of claim 6 wherein estetrol is used at a daily dose of about 15 mg of estetrol.

8. The effective amount of an estetrol component for use of claim 7 wherein drospirenone is used at a daily dose of about 3 mg.

9. The effective amount of an estetrol component for use of any of the preceding claims wherein the contraceptive is formulated as an oral dosage unit.

10. The effective amount of an estetrol component for use according to claim 9 wherein the oral dosage unit is formulated to correspond to a daily dosage unit.

11. The effective amount of an estetrol component for use according to any one of the preceding claims wherein the VTE risk is lower than the VTE risk associated with a 2nd generation COC.

12. The effective amount of an estetrol component for use according to claims 10 or 11 wherein the profile of side effects other than VTE is better than the profile of side effects associated with a 2nd generation COC.

13. The effective amount of an estetrol component for use according to any one of the preceding claims wherein the relative venous thrombosis risk, by comparison to a woman not using COCs, is lower than 3.5, preferably lower than 3.2, more preferably lower than 3.0, even more preferably lower than 2.5, yet even more preferably lower than 2.0.

14. The effective amount of an estetrol component for use according to any one of the preceding claims wherein the percentage of subjects in the high risk category for thrombosis, defined as subjects having an odds ratio of 2 or above for thrombosis risk compared to subjects not using COCs, represents less than 40%, preferably less than 35%, more preferably less than 30%, even more preferably less than 25%, yet even more preferably less than 20%, of the total population using said composition.

15. The effective amount of an estetrol component for use according to any one of the preceding claims wherein the composition is administered to a woman who is a first-ever user, or a woman who is a switcher or a re-starter with a break of greater than 4 weeks, or a woman with increased baseline risk for VTE due to

~~one or more major risk factors selected from BMI greater than 30, older age, and positive personal and/or family history.~~

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