Edition: BP 2025 (Ph. Eur. 11.6 update)

Medroxyprogesterone Tablets

General Notices

Action and use

Progestogen.

DEFINITION

Medroxyprogesterone Tablets contain Medroxyprogesterone Acetate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of medroxyprogesterone acetate, $C_{24}H_{34}O_4$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Disperse a quantity of the powdered tablets containing 50 mg of Medroxyprogesterone Acetate in 8 mL of *petroleum spirit* (*boiling range, 40° to 60°*) and extract with three 8-mL quantities of a mixture of 7 volumes of *glacial acetic acid* and 3 volumes of *water*. Wash the combined extracts with 10 mL of *petroleum spirit* (*boiling range, 40° to 60°*), dilute with *water* until the solution becomes turbid, allow to stand in ice for 2 hours and filter. Wash the precipitate with water and dry at 105°. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of medroxyprogesterone acetate *(RS 421)*.

TESTS

Dissolution

Comply with the dissolution test for tablets and capsules, Appendix XII B1, using apparatus 2. Use as the medium 900 mL of 0.5% w/v *sodium lauryl sulfate* and rotate the paddle at 50 revolutions per minute. Withdraw a sample of the medium and filter.

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) To a quantity of the filtrate add sufficient of a solution of 0.5% w/v *sodium lauryl sulfate* to produce a solution expected to contain 0.0028% w/v of Medroxyprogesterone Acetate.
(2) 0.0028% w/v of *medroxyprogesterone acetate BPCRS* in a solution of 0.5% w/v *sodium lauryl sulfate*.

CHROMATOGRAPHIC CONDITIONS

(a) Stainless steel column (8 cm × 4 mm) packed with *octylsilyl silica gel for chromatography R1* (10 µm) (Zorbax C8 is suitable)
(b) Isocratic elution using the mobile phase described below.
(c) Flow rate of 1.5 mL per minute.
(d) Ambient column temperature.

(e) Detection wavelength of 254 nm.
(f) Injection volume of 20 µL for each solution.

MOBILE PHASE

40 volumes of *water* and 60 volumes of *acetonitrile*.

DETERMINATION OF CONTENT

Calculate the content of medroxyprogesterone acetate, $C_{24}H_{34}O_4$, in the medium using the declared content of $C_{24}H_{34}O_4$ in *medroxyprogesterone acetate BPCRS*.

Impurity F (6a-methyl-3,20-dioxo-5b-pregnan-17-yl acetate)

Carry out the method for *thin-layer chromatography*, Appendix III A using the following solutions.

(1) Shake a quantity of powdered tablets containing 0.2 g of Medroxyprogesterone Acetate with *dichloromethane*, add sufficient *dichloromethane* to produce 10 mL, centrifuge and use the supernatant liquid.
(2) 2.0% w/v of *medroxyprogesterone acetate for performance test EPCRS* (containing 0.5% of impurity F) in *dichloromethane*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as coating *silica gel* (Merck silica gel 60 plates are suitable).
(b) 10 volumes of *tetrahydrofuran*, 45 volumes of *1,1-dimethylethyl methyl ether* and 45 volumes of *hexane* as the mobile phase.
(c) Apply to the plate 10 µL of each of solutions (1) and (2).
(d) After removal of the plate, allow the plate to dry in air and carry out a second development in the same direction using a freshly prepared mobile phase.
(e) Dry the plate at 100° to 105° and allow to cool, spray with a 200 g/L solution of *toluenesulfonic acid* in *ethanol (96 %)*. Heat at 120 °C for 10 min, allow to cool and examine the plate in *ultraviolet light 365 nm*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (2) shows two clearly separated spots.

LIMITS

In the chromatogram obtained with solution (1) any blue fluorescent spot with an Rf value higher than that of the principal spot is not more intense than the corresponding blue fluorescent spot due to impurity F in the chromatogram obtained with solution (2) (0.5%).

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of the powdered tablets containing 40 mg of Medroxyprogesterone Acetate with 50 mL of the mobile phase for 15 minutes, add sufficient of the mobile phase to produce 100 mL, mix, filter and use the filtrate.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) 0.002% w/v of *medroxyprogesterone acetate BPCRS* and 0.005% w/v of *megestrol acetate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Phenomenex Prodigy ODS3 is suitable).
(b) Isocratic elution using the mobile phase described below.
(c) Flow rate of 2 mL per minute.
(d) Maintain the temperature of the column at 40°.
(e) Detection wavelength of 241 nm.
(f) Injection volume of 20 µL for each solution.

MOBILE PHASE

A mixture of 100 volumes of *tetrahydrofuran*, 350 volumes of *acetonitrile*, 500 volumes of *water* and allowed to equilibrate and the volume adjusted to 1000 volumes with *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3):

the *resolution factor* between the two principal peaks is at least 3.3;

the *symmetry factor* of the peak due to medroxyprogesterone acetate is not more than 1.3.

LIMITS

In the chromatogram obtained with solution (1):

the area of any secondary peak is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of any such peaks is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%).

Disregard any peaks with an area not greater than 0.05 times the area of the principal peak in solution (2) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of the powdered tablets containing 40 mg of Medroxyprogesterone Acetate with 50 mL of the mobile phase for 15 minutes, add sufficient of the mobile phase to produce 100 mL, mix and filter. To 5mL of the filtrate add sufficient of the mobile phase to produce 50 mL.
(2) 0.004% w/v of *medroxyprogesterone acetate BPCRS* in the mobile phase.
(3) 0.002% w/v of *medroxyprogesterone acetate BPCRS* and 0.005% w/v of *megestrol acetate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3):

the *resolution factor* between the two principal peaks is at least 3.3;

the *symmetry factor* of the peak due to medroxyprogesterone acetate is not more than 1.3.

DETERMINATION OF CONTENT

Calculate the content of medroxyprogesterone acetate, $C_{24}H_{34}O_4$, in the tablets using the declared content of $C_{24}H_{34}O_4$ in *medroxyprogesterone acetate BPCRS*.

IMPURITIES

A. 6-hydroxy-6-methyl-3,20-dioxopregn-4-en-17-yl acetate (6-hydroxymedroxyprogesterone acetate),
B. 17-hydroxy-6-methylpregn-4-ene-3,20-dione (medroxyprogesterone),
C. 6,17a-dimethyl-3,17-dioxo-*D*-homoandrost-4-en-17a-yl acetate,
D. 6-methyl-3,20-dioxopregn-4-en-17-yl acetate (6-epimedroxyprogesterone acetate),
E. 6-methylidene-3,20-dioxopregn-4-en-17-yl acetate (6-methylenehydroxyprogesterone acetate),
F. 6-methyl-3,20-dioxo-5-pregnan-17-yl acetate (4,5-dihydromedroxyprogesterone acetate),
G. 6-methyl-3,20-dioxopregna-4,6-dien-17-yl acetate (megestrol acetate).