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

Estradiol Transdermal Patches

General Notices

Action and use

Estrogen.

DEFINITION

Estradiol Transdermal Patches contain Estradiol Hemihydrate in a suitable matrix or reservoir presentation.

PRODUCTION

A suitable test is carried out to demonstrate the appropriate release of estradiol.

The transdermal patches comply with the requirements stated under Transdermal Patches and with the following requirements.

Content of estradiol, $C_{18}H_{24}O_2$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Remove the release liner from a patch, score the exposed surface and cover the sticky surface with a small piece of glass wool. Place the patch in a centrifuge tube and add sufficient *methanol* to produce a solution containing the equivalent of 2 mg of estradiol in 5 mL of solvent, mix with the aid of ultrasound, shake for 15 minutes and, if necessary, filter through a glass-fibre filter paper (Whatman GF/C is suitable) followed by a 0.45-µm membrane filter.
(2) 0.04% w/v of *estradiol hemihydrate BPCRS* in *absolute ethanol*, dissolved with the aid of ultrasound.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (100 mm × 100 mm) (Merck plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 7 cm.
(e) After removal of the plate, dry in a stream of warm air for 5 minutes, spray with *methanolic sulfuric acid (50%)* and heat at 110° for 10 minutes. Allow to cool and examine under *ultraviolet light (366 nm)*.

MOBILE PHASE

2 volumes of *acetone* and 8 volumes of *dichloromethane*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the test for Uniformity of content, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Remove the release liners from 10 patches, score the exposed surfaces and cover the sticky surfaces with small pieces of glass wool. Place the patches in a flask containing sufficient mobile phase to produce a solution containing the equivalent of 0.01% w/v of estradiol, mix with the aid of ultrasound for 10 minutes, shake mechanically for 1 hour and filter through a glass-fibre filter paper (Whatman GF/C is suitable). If the filtrate is not clear, filter it through a membrane filter with a pore size of 0.45 µm.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecysilyl silica gel for chromatography* (10 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 280 nm.
(f) Inject 50 µL of each solution.
(g) Allow the chromatography to proceed for twice the retention time of the principal peak.

MOBILE PHASE

35 volumes of *acetonitrile* and 65 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *signal to-noise ratio* for the peak due to Estradiol is at least 10.

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 twice the area of the principal peak in the chromatogram obtained with solution (2) (2%).

Disregard any peak due to diethyltoluamide.

Uniformity of content

Comply with the requirements stated under *uniformity of content*, Appendix XII C3, Test C, with respect to the individual content of each dosage unit and using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Remove the release liner from a patch, score the exposed surface and cover the sticky surface with a small piece of glass wool. Place the patch in a flask containing sufficient mobile phase to produce a solution containing the equivalent of 0.01% w/v of estradiol, mix with the aid of ultrasound for 10 minutes, shake mechanically for 1 hour and, if necessary, filter through a glass-fibre filter paper (Whatman GF/C is suitable). Using a disposable syringe, collect part of the supernatant liquid and filter through a membrane filter with a pore size of 0.45 µm.

(2) Dilute 1 volume of a 0.1% w/v solution of *estradiol hemihydrate BPCRS* in *acetonitrile* to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used but inject 20 µL of each solution.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{24}O_2$ in the transdermal patch using the declared content of $C_{18}H_{24}O_2$ in *estradiol hemihydrate BPCRS*.

ASSAY

Use the average of the 10 results obtained in the test for Uniformity of content.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of estradiol per patch.