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

Tamoxifen Tablets

General Notices

Action and use

Selective estrogen receptor modulator.

DEFINITION

Tamoxifen Tablets contain Tamoxifen Citrate.

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

Content of tamoxifen, $C_{26}H_{29}NO$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

To a quantity of the powdered tablets containing the equivalent of 0.1 g of tamoxifen add 20 mL of *water*, warm, add 2 mL of 5M *sodium hydroxide* and cool. Extract with two 10-mL quantities of *ether*, filtering each extract in turn. Combine the ether extracts and evaporate to dryness in a current of nitrogen at room temperature. Dry the residue at a pressure not exceeding 0.7 kPa for 30 minutes. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of tamoxifen (*RS 328*).

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 150 revolutions per minute.
(b) Use 1000 mL of *0.02M hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, at the maximum at 275 nm, Appendix II B, using 0.02M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of $C_{26}H_{29}NO$ in the medium taking 305 as the value of A(1%, 1 cm) at 275 nm.

Related substances

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

(1) To a quantity of the powdered tablets containing the equivalent of 50 mg of tamoxifen, add 35 mL of the mobile phase, mix with the aid of ultrasound for 5 minutes, dilute to 50 mL with the mobile phase, mix, centrifuge and filter the supernatant liquid through a membrane filter with a nominal pore size of 0.45 µm.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) 0.15% w/v of *tamoxifen citrate for performance test EPCRS* in the mobile phase.
(4) Dilute 1 volume of solution (2) to 20 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Columbus C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 240 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for twice the retention time of the tamoxifen peak.

MOBILE PHASE

40 volumes of *acetonitrile* and 60 volumes of a mixture containing 0.09% w/v of *sodium dihydrogen orthophosphate* and 0.48% w/v of N,N-*dimethyloctylamine*, adjust the final solution to pH 3.0 with *orthophosphoric acid*.

Under the prescribed conditions the retention times relative to tamoxifen (retention time, about 20 minutes) are: *E*-isomer, about 0.8; impurity F, about 0.9).

SYSTEM SUITABILITY

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

the *resolution* between the peaks due to *E*-isomer and to tamoxifen impurity F is at least 3.0;

the resolution between the peaks due to tamoxifen impurity F and tamoxifen is at least 1.5;

the chromatographic profile closely resembles the chromatogram provided with the *tamoxifen citrate for performance test EPCRS.*

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to the *E*-isomer is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the sum of the areas of all the *secondary peaks*, apart from any peak due to the *E*-isomer, is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with a retention time of less than 2.5 minutes and any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.05%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) To a quantity of the powdered tablets containing the equivalent of 5 mg of tamoxifen, add 35 mL of the mobile phase, mix with the aid of ultrasound for 5 minutes, dilute to 50 mL with the mobile phase and filter.
(2) 0.015% w/v of *tamoxifen citrate BPCRS* in the mobile phase.
(3) 0.15% w/v of *tamoxifen citrate for performance test EPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

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

the *resolution* between the peaks due to *E*-isomer and to tamoxifen impurity F is at least 3.0;

the resolution between the peaks due to tamoxifen impurity F and tamoxifen is at least 1.5;

the chromatogram closely resembles the chromatogram provided with the *tamoxifen citrate for performance test EPCRS.*

DETERMINATION OF CONTENT

Calculate the content of tamoxifen, $C_{26}H_{29}NO$, using the declared content of $C_{26}H_{29}NO$, in *tamoxifen citrate BPCRS.*

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of tamoxifen.