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

Tamoxifen Oral Solution

General Notices

Action and use

Selective estrogen receptor modulator.

DEFINITION

Tamoxifen Oral Solution contains Tamoxifen Citrate in a suitable vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

To a quantity of the oral solution containing the equivalent of 0.1 g of tamoxifen add 20 mL of *water*, warm, add 2 mL of 5 M *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* obtained with *tamoxifen citrate BPCRS* treated in the same manner.

TESTS

Related substances

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

(1) Dilute a quantity of the oral solution containing the equivalent of 50 mg of tamoxifen to 50 mL with the mobile phase.
(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 10 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 area of any other *secondary peak* is not greater than 0.2 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than 1.2 times the area of the principal peak in the chromatogram obtained with solution (2) (1.2%).

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) (0.1%).

ASSAY

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

(1) Dilute a weighed quantity of the oral solution containing the equivalent of 5 mg of tamoxifen to 50 mL with the mobile phase.
(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 chromatographic profile closely resembles the chromatogram provided with the *tamoxifen citrate for performance test EPCRS.*

DETERMINATION OF CONTENT

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

STORAGE

Tamoxifen Oral Solution should be stored at room temperature and in accordance with the manufacturer's instruction.

LABELLING

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