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

Naproxen Gastro-resistant Tablets

General Notices

Gastro-resistant Naproxen Tablets

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Naproxen Gastro-resistant Tablets contain Naproxen. They are made gastro-resistant by enteric-coating or by other means.

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

Content of naproxen, $C_{14}H_{14}O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Remove the coating from a number of tablets and powder the uncoated cores. Extract a quantity of the powdered tablets containing 0.2 g of Naproxen with 20 mL of *methanol*, shake for 15 minutes, filter, evaporate the filtrate and dry the residue at 105°. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of naproxen *(RS 244)*.

TESTS

Dissolution

Carry out the *dissolution test for tablets and capsules*, Appendix XII B1. The solutions should be protected from light.

Prepare a phosphate buffer pH 7.4 by dissolving 2.62 g of *sodium dihydrogen orthophosphate monohydrate* and 11.5 g of *anhydrous disodium hydrogen orthophosphate* in sufficient *water* to produce 1000 mL and adjusting the pH to 7.4, with either 0.1M *sodium hydroxide* or 0.1M *hydrochloric acid*, if necessary.

First stage

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 2 hours, withdraw a 10-mL sample of the medium, filter through a 5-µm filter and measure the *absorbance* of the filtrate, Appendix II B, diluted with the dissolution medium, if necessary, at 332 nm using 0.1M *hydrochloric acid* in the reference cell.
(2) Measure the *absorbance* of a suitable solution of *naproxen BPCRS* in the phosphate buffer pH 7.4.

DETERMINATION OF CONTENT

Calculate the total content of naproxen, $C_{14}H_{14}O_3$, in the medium using the declared content of $C_{14}H_{14}O_3$ in *naproxen BPCRS*.

LIMITS

The amount of naproxen released is not more than 5% of the stated amount.

Final stage

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Replace the 0.1M *hydrochloric acid* in the vessel with 900 mL of the phosphate buffer pH 7.4, previously held at 36.5° to 37.5°.

PROCEDURE

(1) After 45 minutes, withdraw a 10-mL sample of the medium and filter. Immediately measure the *absorbance* of the filtrate, Appendix II B, diluted with the phosphate buffer pH 7.4, if necessary, at 332 nm using the phosphate buffer pH 7.4 in the reference cell.
(2) Measure the *absorbance* of a suitable solution of *naproxen BPCRS* in the phosphate buffer pH 7.4.

DETERMINATION OF CONTENT

Calculate the total content of naproxen, $C_{14}H_{14}O_3$, in the medium using the declared content of $C_{14}H_{14}O_3$ in *naproxen BPCRS*.

LIMITS

The amount of naproxen released is not less than 75% (Q) of the stated amount.

Related substances

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

(1) Mix with the aid of ultrasound a quantity of powdered tablets containing 30 mg of Naproxen with 40 mL of the mobile phase, dilute with sufficient mobile phase to produce 50 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase. Further dilute 1 volume of this solution to 10 volumes with the mobile phase.
(3) 0.03% w/v of *naproxen impurity standard BPCRS* in *acetonitrile*. Dilute 1 volume of this solution to 100 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Nucleosil 120-3 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 50°.
(e) Use an autosampler temperature of 8°.
(f) Use a detection wavelength of 230 nm.
(g) Inject 20 µL of each solution.
(h) Allow the chromatography to proceed for 10 times the retention time of naproxen.

MOBILE PHASE

42 volumes of *acetonitrile* and 58 volumes of 0.01M *potassium dihydrogen orthophosphate* previously adjusted to pH 2.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to naproxen (retention time about 2 minutes) are: impurity O, about 0.8; impurity K, about 0.9; impurity L, about 1.5 and impurity N, about 5.6.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity K and naproxen is at least 2.2;

in the chromatogram obtained with solution (2), the *signal-to-noise* ratio of the peak due to naproxen is at least 50.

LIMITS

In the chromatogram obtained with solution (1), identify any peaks corresponding to impurities L, N and O using the chromatogram obtained with solution (3), and multiply the areas of these peaks by the following correction factors: L, 3.5 and O, 1.8.

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than 1.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.16%);

the sum of the areas of any *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. The solutions should be protected from light.

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 0.1 g of Naproxen with 10 mL of *water*. Add 80 mL of *acetonitrile* and further mix. Dilute to produce 100 mL with *acetonitrile*. Dilute 1 volume of the filtrate to 100 volumes with the mobile phase and filter.
(2) 0.001% w/v of *naproxen BPCRS* in the mobile phase.
(3) 0.03% w/v of *naproxen impurity standard BPCRS* in *acetonitrile*. Dilute 1 volume of this solution to 100 volumes with 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 impurity K and naproxen is at least 2.2.

DETERMINATION OF CONTENT

Calculate the content of naproxen, $C_{14}H_{14}O_3$, in the tablets from the chromatograms obtained and using the declared content of $C_{14}H_{14}O_3$ in *naproxen BPCRS*.

STORAGE

Naproxen Gastro-resistant Tablets should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Naproxen.