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

Ursodeoxycholic Acid Capsules

General Notices

Action and use

Bile acid; treatment of gallstones.

DEFINITION

Ursodeoxycholic Acid Capsules contain Ursodeoxycholic Acid.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of ursodeoxycholic acid, $C_{24}H_{40}O_4$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Extract a quantity of the contents of the capsules containing 0.1 g of Ursodeoxycholic Acid with 10 mL of *ethanol (96%)*, centrifuge and evaporate the supernatant liquid to dryness in a stream of nitrogen in a water bath at room temperature. Dry the residue at room temperature at a pressure of 0.7 kPa for 2 hours. The *infrared absorption spectrum*, Appendix II A, of the dried residue is concordant with the *reference spectrum* of ursodeoxycholic acid (*RS 402*).
B. In the Assay, 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

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 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of phosphate buffer of pH 7.5, prepared using equal volumes of 0.05M *potassium dihydrogen orthophosphate* and 0.05M *disodium hydrogen orthophosphate*, and adjusting the pH to 7.5 using 1M *sodium hydroxide*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the medium and filter. Dilute, if necessary, with sufficient dissolution medium to produce a solution expected to contain 0.028% w/v of Ursodeoxycholic Acid.

(2) Add 0.7 mL of 0.1M *sodium hydroxide* to 28 mg of *ursodeoxycholic acid BPCRS* and add sufficient dissolution medium to produce 100 mL, mix with the aid of ultrasound for 20 minutes and leave to cool at room temperature.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Assay may be used with an injection volume of 250 µL.

DETERMINATION OF CONTENT

Calculate the total content of ursodeoxycholic acid, $C_{24}H_{40}O_4$, in the medium from the chromatograms obtained and using the declared content of $C_{24}H_{40}O_4$ in *ursodeoxycholic acid BPCRS*.

Related substances

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

Solvent A 20 volumes of *methanol* and 80 volumes of the mobile phase.

(1) Add a quantity of the contents of the capsules containing 250 mg of Ursodeoxycholic Acid to 15 mL of Solvent A and mix with the aid of ultrasound for 15 minutes. Dilute to 50 mL and filter (0.45-µm PVDF filter is suitable).
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.5% w/v of *ursodeoxycholic acid impurity standard BPCRS* and 0.0055% w/v of *chenodeoxycholic acid BPCRS* (impurity A).
(4) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 2.1 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Uptisphere HDO C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.6 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a refractive index detector.
(f) Inject 8 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 5 times the retention time of ursodeoxycholic acid.

MOBILE PHASE

25 volumes of *acetonitrile*, 34 volumes of *methanol* and 47 volumes of a solution prepared by dissolving 0.8 g of *sodium dihydrogen orthophosphate dihydrate* in 1000 mL of *water* and adjusting the pH to 3.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions the retention time relative to ursodeoxycholic acid (retention time, about 5 minutes) are: 7-ketolithocholic acid (impurity F), about 1.3 and chenodeoxycholic acid, about 2.8.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to ursodeoxycholic acid and 7-ketolithocholic acid is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peaks corresponding to chenodeoxycholic acid is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of any *secondary peak* is not greater than 4.2 times the area of the principal peak in the chromatogram obtained with solution (2) (2.1%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.05%).

ASSAY

Weigh a quantity of the mixed contents of 20 capsules. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) To a quantity of the mixed contents of the capsules containing 0.125 g of Ursodeoxycholic Acid add 15 mL of *methanol*, mix with the aid of ultrasound for 10 minutes and dilute to 50 mL with the mobile phase.
(2) Dissolve 50 mg of *ursodeoxycholic acid BPCRS* in 2 mL of *methanol* with the aid of ultrasound for 10 minutes and dilute to 20 mL with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (4 µm) (Superspher 100 RP 18E 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 40°.
(e) Use a detection wavelength of 210 nm.
(f) Inject 30 µL of each solution.

MOBILE PHASE

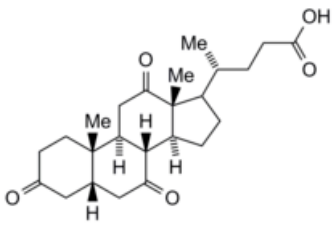
To 40 volumes of *acetonitrile R1* add 60 volumes of 0.001M *potassium dihydrogen orthophosphate*, allow to equilibrate to room temperature, adjust to pH 2.0 with *orthophosphoric acid* (*85%*) and filter.

DETERMINATION OF CONTENT

Calculate the content of $C_{24}H_{40}O_4$ using the declared content of $C_{24}H_{40}O_4$ in *ursodeoxycholic acid BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include A, D, E and F listed under Ursodeoxycholic Acid and the following:



1. 3,7,12-trioxo-(5β)-cholan-24-oic acid (dehydrocholic acid).