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

Ursodeoxycholic Acid Tablets

General Notices

Action and use

Bile acid; treatment of gallstones.

DEFINITION

Ursodeoxycholic Acid Tablets contain Ursodeoxycholic Acid. They may be coated.

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

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

92.5 to 107.5% of the stated amount.

IDENTIFICATION

A. Extract a quantity of the powdered tablets 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 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of phosphate buffer as the dissolution medium, prepared using 0.68% w/v *potassium dihydrogen orthophosphate* adjusted to pH 8.0 using 2M *sodium hydroxide* at a temperature of 37°.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the dissolution medium and filter. Dilute with dissolution medium, if necessary, to produce a solution containing 0.017% w/v of Ursodeoxycholic Acid.

(2) Dissolve 17 mg of *ursodeoxycholic acid BPCRS* in 1 mL of *ethanol* (*96%*) and dilute to 100 mL with the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS is suitable), fitted with a stainless steel guard column packed with the same material (Lichrospher 100-RP 18E is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 40°C for both columns.
(e) Use a detection wavelength of 210 nm.
(f) Inject 200 µL of each solution.

MOBILE PHASE

280 volumes of *acetonitrile R1* and 720 volumes of a 0.05M phosphate buffer prepared by dissolving 6.81 g of *potassium dihydrogen orthophosphate* in 1000 mL of *water* and adjusting the pH to 6.5 with 2M *sodium hydroxide*.

DETERMINATION OF CONTENT

Calculate the total content of ursodeoxycholic acid, $C_{24}H_{40}O_4$, in the medium 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 tablets 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) 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 times 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 the peak due 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 and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D using the following solutions in Solvent B.

Solvent B Prepare a solution containing 535 mL of *water*, 6.0 g of *sodium dihydrogen orthophosphate dihydrate*, 2.0 g of *disodium hydrogen orthophosphate dihydrate*, 65 mL of *tetrabutylammonium hydroxide solution* and 400 mL of *acetonitrile R1*.

(1) Mix a quantity of the powdered tablets containing 0.3 g of Ursodeoxycholic Acid with 20 mL of solvent B with the aid of ultrasound for 15 minutes, shake intermittently and filter, if necessary.
(2) 1.5% w/v of *ursodeoxycholic acid BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS 1 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 a detection wavelength of 210 nm.
(f) Inject 10 µL of each solution.
(g) Allow the chromatography to proceed for twice the retention time of ursodeoxycholic acid.

MOBILE PHASE

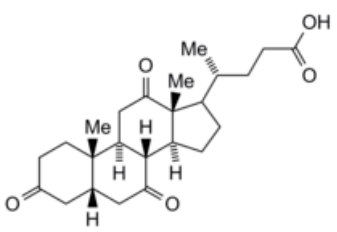
500 volumes of *acetonitrile R1* and 500 volumes of a solution containing 1.2% w/v of *sodium dihydrogen orthophosphate dihydrate*, 0.4% w/v of *disodium hydrogen orthophosphate dihydrate* and 1.08% w/v of *tetrabutylammonium hydrogen sulfate* in *water*.

DETERMINATION OF CONTENT

Calculate the content of $C_{24}H_{40}O_4$ in the tablets 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).