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

Levothyroxine Oral Solution

General Notices

Action and use

Thyroid hormone replacement.

DEFINITION

Levothyroxine Oral Solution is a solution of Levothyroxine Sodium in a suitable aqueous vehicle.

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

Content of anhydrous levothyroxine sodium, $C_{15}H_{10}I_4NNaO_4$

90.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Dilute, if necessary, a weighed quantity of the oral solution with sufficient mobile phase to produce a solution containing the equivalent of 0.0005% w/v of anhydrous levothyroxine sodium.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.000015% w/v of *liothyronine sodium EPCRS*.
(4) 0.0005% w/v of *levothyroxine sodium EPCRS* and 0.0005% w/v of *liothyronine sodium EPCRS*.
(5) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5 µm) (Microsorb CN is suitable).
(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 225 nm.
(f) Inject 100 µL of each solution.
(g) Allow the chromatography to proceed for 5 times the retention time of levothyroxine.

MOBILE PHASE

5 volumes of *orthophosphoric acid*, 300 volumes of *acetonitrile* and 700 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions, the relative retention with reference to levothyroxine (retention time about 6 minutes) for liothyronine is about 2.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to levothyroxine and liothyronine is at least 4.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to liothyronine (impurity A) is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (3.0%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the sum of the areas of all *secondary peaks*, other than the peak due to liothyronine, is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

ASSAY

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

Solution A Equal volumes of *methanol* and 0.1M *sodium hydroxide*.

(1) Dilute, if necessary, a weighed quantity of the oral solution with sufficient solution A to produce a solution containing the equivalent of 0.0005% w/v of anhydrous levothyroxine sodium.
(2) 0.00056% w/v of *levothyroxine sodium EPCRS*.
(3) 0.0005% w/v of *liothyronine sodium EPCRS* and 0.0005% w/v of *levothyroxine sodium EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5 µm) (Spherisorb S5 CN is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 225 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

5 volumes of *orthophosphoric acid*, 300 volumes of *acetonitrile* and 700 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions, the retention time of levothyroxine is about 4 minutes.

SYSTEM SUITABILITY

The Assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to liothyronine and levothyroxine is at least 4.0.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_{15}H_{10}I_4NNaO_4$, weight in volume, using the declared content of $C_{15}H_{10}I_4NNaO_4$ in *levothyroxine sodium EPCRS*.

STORAGE

Levothyroxine Oral Solution should be protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of anhydrous levothyroxine sodium.

IMPURITIES

The impurities limited by the requirements of this monograph include impurity A listed under Levothyroxine Sodium.