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Phenobarbital Elixir

General Notices

Phenobarbital Oral Solution

Phenobarbital Elixir from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable.

Action and use

Barbiturate.

DEFINITION

Phenobarbital Elixir is an *oral solution* containing 0.3% w/v of Phenobarbital in a suitable flavoured vehicle containing a sufficient volume of *ethanol (96 %)* or of an appropriate Dilute Ethanol to give a final concentration of 38% v/v of ethanol.

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

Content of phenobarbital, $C_{12}H_{12}N_2O_3$

0.285 to 0.315% w/v.

IDENTIFICATION

Extract 50 mL with three 50-mL quantities of ether, wash the combined ether extracts with 20 mL of water, discard the washings, extract the ether solution with a mixture of 5 mL of 2M *sodium hydroxide* and 25 mL of *water* and then with two 5-mL quantities of *water*. Acidify the combined aqueous extracts to *litmus paper* with *2M hydrochloric acid*, extract with four 25-mL quantities of *ether*, wash the combined ether extracts with two 2-mL quantities of *water*, wash the combined aqueous washings with 10 mL of *ether*, add the ether washings to the combined ether extracts, evaporate the ether and dry the residue of phenobarbital to constant weight at 105°. The *infrared absorption spectrum* of the residue Appendix II A, is concordant with the reference spectrum of phenobarbital *(RS 270)*.

TESTS

Ethanol content

36 to 40% v/v, Appendix VIII F.

Related substances

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

(1) Dilute a quantity of the elixir containing 100 mg of Phenobarbital in 100 mL of the mobile phase.
(2) Dilute 1 volume of solution (1) to 10 volumes with the mobile phase. Dilute 1 volume of the resulting solution to 50 volumes with the mobile phase.
(3) 0.0005% w/v of *phenobarbital impurity A EPCRS* and 0.0005% w/v of *phenobarbital impurity B EPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb S5 ODS 2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for twice the run time of phenobarbital.

MOBILE PHASE

25 volumes of *acetonitrile* and 75 volumes of a solution containing 0.66% w/v of *sodium acetate* in *water*, adjusted to pH 4.5 using *glacial acetic acid*.

When the chromatograms are recorded under the prescribed conditions the retention times relative to phenobarbital (retention time, about 9 minutes) are: impurity A, about 0.4; impurity B, about 0.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and impurity B is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

(1) Dissolve a weighed quantity of the elixir containing 100 mg of Phenobarbital in 100 mL of the mobile phase. Dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.
(2) 0.01% of *phenobarbital BPCRS* in the mobile phase.
(3) A solution of 0.0005% w/v of *phenobarbital impurity A EPCRS* and 0.0005% w/v of *phenobarbital impurity B EPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

Use the chromatographic conditions described under the test for Related substances.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and impurity B is at least 1.5.

DETERMINATION OF CONTENT

Determine the weight per mL of the elixir, Appendix V G, and calculate the content of $C_{12}H_{12}N_2O_3$, weight in volume, using the declared content of $C_{12}H_{12}N_2O_3$ in *phenobarbital BPCRS*.

STORAGE

Phenobarbital Elixir should be protected from light.