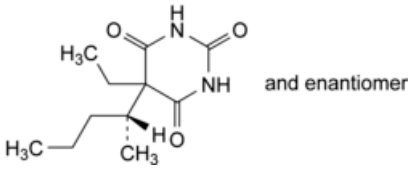
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pentobarbital

General Notices

(Ph. Eur. monograph 0200)



$C_{11}H_{18}N_2O_3$ 226.3 *76-74-4*

Action and use

Barbiturate.

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DEFINITION

5-Ethyl-5-[(2*RS*)-pentan-2-yl]-1,3-diazinane-2,4,6-trione.

Content

98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder or colourless crystals.

Solubility

Very slightly soluble in water, freely soluble in anhydrous ethanol, practically insoluble in heptane. It forms water-soluble compounds with alkali hydroxides and carbonates and with ammonia.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison *pentobarbital CRS*.

If the spectra obtained in the solid state show differences, weigh 10 mg of the substance to be examined and 10 mg of the reference substance separately in glass vials; heat in an oven at 140 °C for 1 h, then allow to stand at room temperature for 3 h. Record new spectra.

TESTS

Appearance of solution

The solution is clear (*2.2.1*) and not more intensely coloured than reference solution B_9 (*2.2.2, Method II*).

Dissolve 1.0 g in a mixture of 4 mL of *dilute sodium hydroxide solution R* and 6 mL of *water R*.

Acidity

Boil 1.0 g with 50 mL of *water R* for 2 min, allow to cool and filter. To 10 mL of the filtrate add 0.15 mL of *methyl red solution R*. The solution is orange-yellow. Not more than 0.1 mL of *0.1 M sodium hydroxide* is required to produce a pure yellow colour.

Related substances

Liquid chromatography (*2.2.29*).

Test solution (a) Dissolve 25.0 mg of the substance to be examined in the mobile phase and dilute to 25.0 mL with the mobile phase.

Test solution (b) Dilute 5.0 mL of test solution (a) to 50.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of test solution (b) to 100.0 mL with the mobile phase.

Reference solution (b) Dissolve 2.5 mg of *pentobarbital impurity E CRS* in the mobile phase and dilute to 25 mL with the mobile phase. Dilute 1 mL of the solution to 100 mL with the mobile phase. Dissolve 5 mg of the substance to be examined in 5 mL of this solution.

Reference solution (c) Dissolve 25.0 mg of *pentobarbital CRS* in the mobile phase and dilute to 25.0 mL with the mobile phase. Dilute 5.0 mL of the solution to 50.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped extra-dense bonded octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase Mix 35 volumes of *acetonitrile R1* and 65 volumes of a 1.36 g/L solution of *potassium dihydrogen phosphate R* previously adjusted to pH 3.5 with *dilute phosphoric acid R*.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 214 nm.

Injection 10 µL of test solution (a) and reference solutions (a) and (b).

Run time 2.5 times the retention time of pentobarbital.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity E.

Relative retention With reference to pentobarbital (retention time = about 10 min): impurity E = about 0.92.

System suitability Reference solution (b):

— *resolution*: minimum 2.0 between the peaks due to impurity E and pentobarbital.

Calculation of percentage contents:

— for each impurity, use the concentration of pentobarbital in reference solution (a).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.1 per cent;

— *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

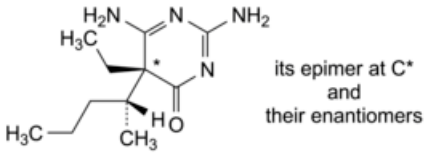
Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

Injection Test solution (b) and reference solution (c).

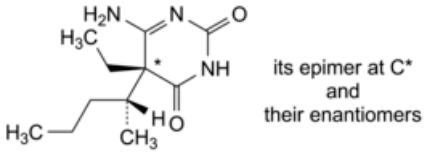
Calculate the percentage content of $C_{11}H_{18}N_2O_3$ taking into account the assigned content of *pentobarbital CRS*.

IMPURITIES

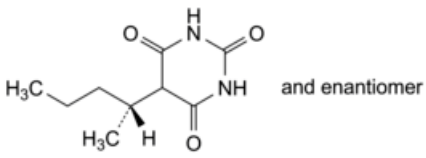
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B, C, D, E, F.



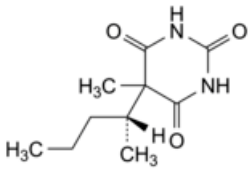
A. mixture of (5*R*)-2,6-diamino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidin-4(5*H*)-one and (5*S*)-2,6-diamino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidin-4(5*H*)-one,



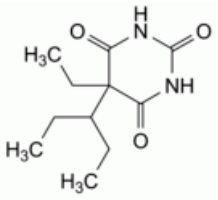
B. mixture of (5*R*)-6-amino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidine-2,4(3*H*,5*H*)-dione and (5*S*)-6-amino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidine-2,4(3*H*,5*H*)-dione,



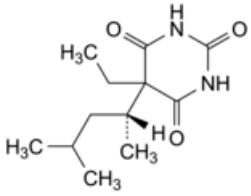
C. 5-[(2*RS*)-pentan-2-yl]-1,3-diazinane-2,4,6-trione,



D. 5-methyl-5-[(2*RS*)-pentan-2-yl]-1,3-diazinane-2,4,6-trione,



E. 5-ethyl-5-(pentan-3-yl)-1,3-diazinane-2,4,6-trione,



F. 5-ethyl-5-[(2*RS*)-4-methylpentan-2-yl]-1,3-diazinane-2,4,6-trione.

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