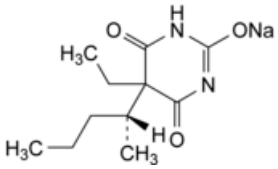
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pentobarbital Sodium

General Notices

(Ph. Eur. monograph 0419)



and enantiomer

$C_{11}H_{17}N_2NaO_3$ 248.3 *57-33-0*

Action and use

Barbiturate.

Preparation

Pentobarbital Tablets

Ph Eur

DEFINITION

Sodium 5-ethyl-4,6-dioxo-5-[(2*RS*)-pentan-2-yl]-1,4,5,6-tetrahydropyrimidin-2-olate.

Content

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

CHARACTERS

Appearance

White or almost white, hygroscopic, crystalline powder.

Solubility

Very soluble in water, freely soluble in ethanol (96 per cent), practically insoluble in heptane.

It shows polymorphism (*5.9*).

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *pentobarbital sodium CRS*.

If the spectra obtained in the solid state show differences, dissolve 10 mg of the substance to be examined and 10 mg of the reference substance separately in 0.2 mL of *methanol R*. Evaporate the solvent by heating in an oven at 80 °C for 2 h. Record new spectra using the residues.

B. Ignite 1 g. The residue gives reaction (a) of sodium (2.3.1).

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 10 mL of *ethanol (50 per cent V/V) R*. Examine immediately after preparation.

pH (2.2.3)

9.6 to 11.0, measured immediately after preparation.

Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 10 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29).

Test solution (a) Dissolve 27.0 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 sodium 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.

Free pentobarbital

Maximum 3.5 per cent.

Dissolve 2.00 g in 75 mL of *dimethylformamide R*, heating gently if necessary. Titrate with *0.1 M sodium methoxide* until the colour changes from olive-green to blue, using 0.25 mL of a 10 g/L solution of *thymol blue R* in *dimethylformamide R* as indicator. Carry out a blank titration.

1 mL of *0.1 M sodium methoxide* is equivalent to 22.63 mg of pentobarbital.

Loss on drying (*2.2.32*)

Maximum 3.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

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).

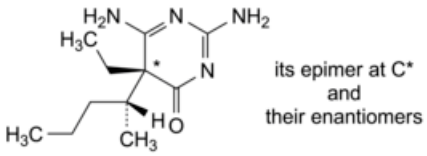
Calculate the percentage content of $C_{11}H_{17}N_2NaO_3$ taking into account the assigned content of *pentobarbital CRS* and a conversion factor of 1.097.

STORAGE

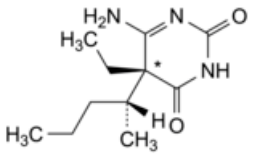
In an airtight container.

IMPURITIES

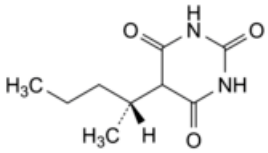
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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.



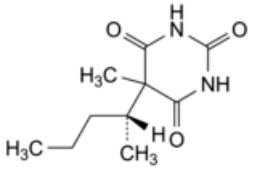
A. mixture of (5*R*)-2,6-diamino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidin-4(5*H*)-one and (5*S*)-2,6-diamino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidin-4(5*H*)-one,



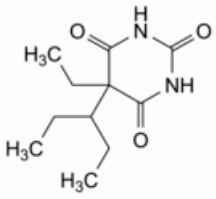
B. mixture of (5*R*)-6-amino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidine-2,4(3*H*,5*H*)-dione and (5*S*)-6-amino-5-ethyl-5-[(2*RS*)-pentan-2-yl]pyrimidine-2,4(3*H*,5*H*)-dione,



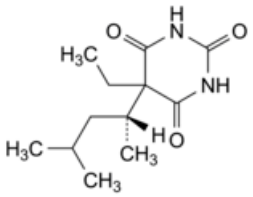
C. 5-[(2*RS*)-pentan-2-yl]-1,3-diazinane-2,4,6-trione,



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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