Limits:

- *impurity C*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (2 per cent);
- *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (d) (1 per cent);
- *any other impurity*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (e) (0.5 per cent);
- *total*: not more than 6 times the area of the principal peak in the chromatogram obtained with reference solution (e) (3.0 per cent);
- *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (e) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 20 ppm.

1.00 g complies with test D. Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*): maximum 0.25 per cent, determined on 1.00 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 (a).

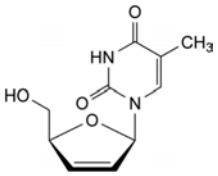
Calculate the content of $C_{10}H_{13}N_5O_4$ from the declared content of *zidovudine CRS*.

STORAGE

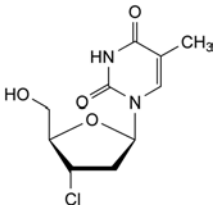
Protected from light.

IMPURITIES

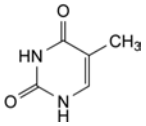
Specified impurities: A, B, C, D.



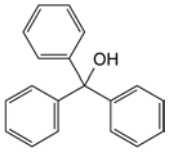
A. 1-[(2*R*,5*S*)-5-(hydroxymethyl)-2,5-dihydrofuran-2-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione,



B. 1-(3-chloro-2,3-dideoxy-β-D-*erythro*-pentofuranosyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione,



C. 5-methylpyrimidine-2,4(1*H*,3*H*)-dione (thymine),



D. triphenylmethanol.

01/2008:1482
corrected 7.0

ZINC ACETATE DIHYDRATE

Zinci acetas dihydricus

$C_4H_6O_4Zn,2H_2O$ M_r 219.5
[5970-45-6]

DEFINITION

Content: 99.0 per cent to 101.0 per cent of $C_4H_6O_4Zn,2H_2O$.

CHARACTERS

Appearance: white or almost white crystalline powder or flakes.

Solubility: freely soluble in water, soluble in ethanol (96 per cent).

IDENTIFICATION

A. It gives reaction (a) of acetates (*2.3.1*).

B. It gives the reaction of zinc (*2.3.1*).

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

pH (*2.2.3*): 5.8 to 7.0.

Dilute 10 mL of solution S to 20 mL with *carbon dioxide-free water R*.

Reducing substances. Boil for 5 min a mixture of 10 mL of solution S, 90 mL of *water R*, 5 mL of *dilute sulfuric acid R* and 1.5 mL of a 0.3 g/L solution of *potassium permanganate R*. The pink colour of the solution remains.

Chlorides (*2.4.4*): maximum 50 ppm.

Dilute 10 mL of solution S with 15 mL of *water R*.

Sulfates (*2.4.13*): maximum 100 ppm, determined on solution S.

Aluminium: maximum 5 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Dissolve 2.50 g in 20 mL of a 200 g/L solution of *cadmium- and lead-free nitric acid R* and dilute to 25.0 mL with the same acid solution.

Reference solutions. Prepare the reference solutions using *aluminium standard solution (200 ppm Al) R*, diluted with a 200 g/L solution of *cadmium- and lead-free nitric acid R*.

Source: aluminium hollow-cathode lamp.

Wavelength: 309.3 nm.

Atomisation device: air-acetylene or acetylene-nitrous oxide flame.

Arsenic (*2.4.2, Method A*): maximum 2 ppm, determined on 0.5 g.

Cadmium: maximum 2 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Use the solution described in the test for aluminium.

Reference solutions. Prepare the reference solutions using *cadmium standard solution (0.1 per cent Cd) R*, diluted with a 200 g/L solution of *cadmium- and lead-free nitric acid R*.

Source: cadmium hollow-cathode lamp.

Wavelength: 228.8 nm.

Atomisation device: air-acetylene flame.

Copper: maximum 50 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Use the solution described in the test for iron.

Reference solutions. Prepare the reference solutions using *copper standard solution (10 ppm Cu) R*, diluted with a 200 g/L solution of *cadmium- and lead-free nitric acid R*.

Source: copper hollow-cathode lamp.

Wavelength: 324.8 nm.

Atomisation device: air-acetylene flame.

Iron: maximum 50 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Dissolve 1.25 g in 20 mL of a 200 g/L solution of *cadmium- and lead-free nitric acid R* and dilute to 25.0 mL with the same acid solution.

Reference solutions. Prepare the reference solutions using *iron standard solution (20 ppm Fe) R*, diluted with a 200 g/L solution of *cadmium- and lead-free nitric acid R*.

Source: iron hollow-cathode lamp.

Wavelength: 248.3 nm.

Atomisation device: air-acetylene flame.

Lead: maximum 10 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Dissolve 5.00 g in 20 mL of a 200 g/L solution of *cadmium- and lead-free nitric acid R* and dilute to 25.0 mL with the same acid solution.

Reference solutions. Prepare the reference solutions using *lead standard solution (0.1 per cent of Pb) R*, diluting with a 200 g/L solution of *cadmium- and lead-free nitric acid R*.

Source: lead hollow-cathode lamp.

Wavelength: 283.3 nm.

Atomisation device: air-acetylene flame.

ASSAY

Dissolve 0.200 g in 5 mL of *dilute acetic acid R*. Carry out the complexometric titration of zinc (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 21.95 mg of $C_4H_6O_4Zn,2H_2O$.

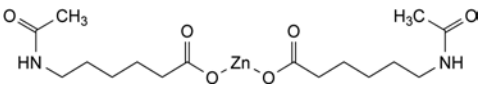
STORAGE

In a non-metallic container.

07/2010:1279
corrected 7.0

ZINC ACEXAMATE

Zinci acexamas



$C_{16}H_{28}N_2O_6Zn$ M_r 409.8

[70020-71-2]

DEFINITION

Zinc 6-(acetylamino)hexanoate.

Content: 97.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: soluble in water, practically insoluble in acetone and in ethanol (96 per cent). It dissolves in dilute nitric acid.

mp: about 198 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *zinc acexamate CRS*.

B. 5 mL of solution S (see Tests) gives the reaction of zinc (*2.3.1*).

TESTS

Solution S. Dissolve 0.5 g in *carbon dioxide-free water R* and dilute to 20 mL with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension IV (*2.2.1*) and is colourless (*2.2.2, Method II*).

pH (*2.2.3*): 5.0 to 7.0 for solution S.

Impurity B. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 0.30 g of the substance to be examined in *water R* and dilute to 10 mL with the same solvent.

Reference solution. Dissolve 15 mg of *6-aminohexanoic acid R* (impurity B) in *water R* and dilute to 10 mL with the same solvent. Dilute 1 mL of this solution to 10 mL with *water R*.

Plate: *TLC silica gel plate R*.

Mobile phase: *ammonia R, water R, ethanol (96 per cent) R* (2:30:68 *V/V/V*).

Application: 5 µL; allow to dry in air.

Development: over a path of 15 cm.

Drying: in a current of warm air.

Detection: spray with *ninhydrin solution R* and heat at 100-105 °C for 15 min.

Limit:

– *impurity B*: any spot due to impurity B is not more intense than the corresponding spot in the chromatogram obtained with the reference solution (0.5 per cent).

Related substances. Liquid chromatography (*2.2.29*).

Test solution (a). Dissolve 0.50 g of the substance to be examined in *water R* and dilute to 100.0 mL with the same solvent.

Test solution (b). To 20.0 mL of test solution (a), add 20 mL of the mobile phase and 0.4 mL of a 100 g/L solution of *phosphoric acid R*, then dilute to 50.0 mL with the mobile phase.

Reference solution (a). Dissolve 40 mg of *N-acetyl-ε-caprolactam R* (impurity C) in *water R* and dilute to 100.0 mL with the same solvent.

Reference solution (b). Dilute 5.0 mL of reference solution (a) to 100.0 mL with *water R*.

Reference solution (c). Dissolve 20 mg of *zinc acexamate impurity A CRS* in *water R* and dilute to 50.0 mL with the same solvent.

Reference solution (d). Dissolve 40 mg of *ε-caprolactam R* (impurity D) in *water R* and dilute to 100.0 mL with the same solvent. Dilute 5.0 mL of this solution to 100.0 mL with *water R*.

Reference solution (e). To 20.0 mL of test solution (a), add 5.0 mL of reference solution (b), 5.0 mL of reference solution (c), 5.0 mL of reference solution (d) and 0.4 mL of a 100 g/L solution of *phosphoric acid R*, then dilute to 50.0 mL with the mobile phase.

Reference solution (f). To 5.0 mL of reference solution (c), add 5.0 mL of reference solution (b), 5.0 mL of reference solution (d) and 0.4 mL of a 100 g/L solution of *phosphoric acid R*, then dilute to 50.0 mL with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.0 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mix 0.2 volumes of *phosphoric acid R*, 8 volumes of *acetonitrile R* and 92 volumes of *water R*, then adjust to pH 4.5 with *dilute ammonia R1*.

Flow rate: 1.2 mL/min.

Detection: spectrophotometer at 210 nm.

Injection: 20 µL of test solution (b) and reference solutions (b), (e) and (f).

Run time: 8 times the retention time of zinc acexamate.