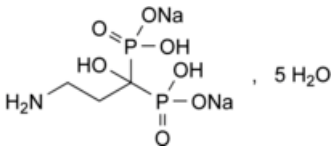
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pamidronate Disodium Pentahydrate

General Notices

Disodium Pamidronate

(Ph. Eur. monograph 1779)



$C_3H_9NNa_2O_7P_2,5H_2O$ 369.1 *109552-15-0*

Action and use

Bisphosphonate; treatment of osteolytic lesions; Paget's disease; hypercalcaemia of malignancy.

Preparation

Pamidronate Disodium Infusion

Ph Eur

DEFINITION

Disodium dihydrogen (3-amino-1-hydroxypropylidene)bisphosphonate pentahydrate.

Content

98.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Soluble in water, practically insoluble in methylene chloride. It is sparingly soluble in dilute mineral acids and dissolves in dilute alkaline solutions.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *pamidronate disodium pentahydrate CRS*.

B. Dissolve 0.5 g in 10 mL of *water R*. The solution 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 Y_6 (2.2.2, *Method II*).

Dissolve 0.20 g in *carbon dioxide-free water R* and dilute to 10 mL with the same solvent.

pH (2.2.3)

7.8 to 8.8.

Dissolve 0.100 g in *carbon dioxide-free water R* and dilute to 10 mL with the same solvent.

Impurity A

Thin-layer chromatography (2.2.27).

Test solution Dissolve 30 mg of the substance to be examined in *water R* and dilute to 10.0 mL with the same solvent.

Reference solution Dissolve 15 mg of *3-aminopropionic acid R* in *water R* and dilute to 100.0 mL with the same solvent. Dilute 1.0 mL of this solution to 10.0 mL with *water R*.

Plate *TLC silica gel plate R*.

Mobile phase *concentrated ammonia R*, *di-isopropyl ether R*, *methanol R* (4:8:9 *V/V/V*).

Application 10 µL.

Development Over 2/3 of the plate.

Drying In a current of warm air.

Detection Spray with a *ninhydrin solution R*. Heat at 100-105 °C for 15 min.

Limit:

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

Impurities B and C

Liquid chromatography (2.2.29).

Test solution Dissolve 20.0 mg of the substance to be examined in *water R* and dilute to 10.0 mL with the same solvent.

Reference solution To 2.0 mL of a 0.3 g/L solution of *phosphoric acid R* add 2.0 mL of a 0.25 g/L solution of *phosphorous acid R* and dilute to 50.0 mL with *water R*.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm,

— *stationary phase*: *anion-exchange resin R* (5 µm),

— *temperature*: 35 °C.

Mobile phase To 0.5 mL of *anhydrous formic acid R* add 2500 mL of *water R*; adjust to pH 3.5 with an 80 g/L solution of *sodium hydroxide R*.

Flow rate 1.0 mL/min.

Detection Refractometer.

Injection 100 µL.

Relative retention With reference to pamidronate (retention time = about 13 min): impurity B = about 1.3; impurity C = about 1.6.

System suitability Reference solution:

— *resolution*: minimum 2.5 between the peaks due to impurities B and C.

Limits:

— *impurities B, C*: for each impurity, not more than the area of the corresponding peaks in the chromatogram obtained with the reference solution (0.5 per cent).

Water (*2.5.12*)

23.0 per cent to 27.0 per cent, determined on 0.100 g.

ASSAY

Dissolve 0.250 g in 70 mL of *water R*. Titrate with *0.1 M hydrochloric acid* determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M hydrochloric acid* is equivalent to 27.91 mg of $C_3H_9NNa_2O_7P_2$.

IMPURITIES

Specified impurities *A, B, C.*

A. 3-aminopropanoic acid (β-alanine),

B. H_3PO_4: phosphoric acid,

C. H_3PO_3: phosphorous acid.