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Risedronate Sodium Tablets

General Notices

Action and use

Bisphosphonate; treatment of osteoporosis, Paget's disease.

DEFINITION

Risedronate Sodium Tablets contain Risedronate Sodium 2.5-Hydrate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of anhydrous risedronate sodium, $C_7H_{10}NNaO_7P_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 25 mg of anhydrous risedronate sodium with 10 mL of *water* and filter (a 0.45-µm nylon filter is suitable). Mix the filtrate with 10 mL of 0.2M *copper(II) chloride* and allow to stand for 10 minutes. Add 2 mL of *ethanol* to this solution, mix and allow to stand for 1 hour (a precipitate is produced). Filter the suspension through a Whatman No. 1 filter and wash the precipitate with 10 mL of *ethanol*, discarding the washings and allow the residue to dry in air. The infrared absorption spectrum of the dried residue, Appendix II A, is concordant with the reference spectrum of anhydrous risedronate sodium *(RS 498)*.

TESTS

Dissolution

Comply with the requirements in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 500 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and filter. Use the filtered medium, diluted with *water* if necessary, to produce a solution containing 0.001% w/v of anhydrous risedronate sodium.
(2) 0.0012% w/v of *risedronate sodium 2.5-hydrate BPCRS* in *water.*
(3) 0.00075% w/v of *risedronate impurity E EPCRS* and 0.005% w/v of *risedronate sodium 2.5-hydrate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.0 mm) packed with *anion exchange resin* (10 µm) (Dionex Ionpac AS7 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.8 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 263 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

0.18% w/v solution of *disodium edetate* adjusted to pH 9.5 with 1M *sodium hydroxide*.

SYSTEM SUITABILITY

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

DETERMINATION OF CONTENT

Calculate the total content of anhydrous risedronate sodium, $C_7H_{10}NNaO_7P_2$, in the medium from the chromatograms obtained and using the declared content of $C_7H_{10}NNaO_7P_2$, in *risedronate sodium 2.5-hydrate BPCRS*.

LIMITS

The amount of anhydrous risedronate sodium released is not less than 75% (Q) of the stated amount.

Related substances

A. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. *Prepare and store all solutions in plastic containers.*

Solution A Dissolve 0.410 g of *sodium edetate*, 1.7 g of *dipotassium hydrogen phosphate* and 1.7 g of *tetrabutylammonium dihydrogen phosphate* in 900 mL of *water*. Adjust to pH 7.5 with 1M *sodium hydroxide*, and dilute to 1000 mL with *water*.
(1) To a quantity of the powdered tablets containing 25 mg of anhydrous risedronate sodium, add 10 mL of the mobile phase and swirl for 10 minutes in a water-bath at 30° and filter (a nylon 0.45-µm filter is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase. Dilute 1 volume of this solution to 10 volumes with the mobile phase.
(3) 0.001% w/v solution of *risedronate impurity E EPCRS* and 0.00115% w/v of *risedronate sodium 2.5-hydrate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Luna C18 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 a column temperature of 40°.
(e) Use a detection wavelength of 263 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for twice the run time of risedronate.

MOBILE PHASE

10 volumes of *acetonitrile* and 90 volumes of solution A.

When the chromatograms are recorded under the prescribed conditions, the relative retention with reference to risedronate (retention time of about 16 minutes) of impurity E is about 0.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between the peaks due to impurity E and risedronate is at least 3.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than twice 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 4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%).

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

B. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. *Prepare and store all solutions in plastic containers.*

Solution A Dissolve 0.41 g of *sodium edetate*, 1.7 g of *dipotassium hydrogen phosphate* and 1.7 g of *tetrabutylammonium dihydrogen phosphate* in 900 mL of *water*. Adjust to pH 7.5 with 1M *sodium hydroxide*, and dilute to 1000 mL with *water*.
(1) To a quantity of the powdered tablets containing 25 mg of anhydrous risedronate sodium, add 10 mL of the mobile phase and swirl for 5 to 10 minutes in a water-bath at 30° and filter (a nylon 0.45-µm filter is suitable).
(2) Dilute 1 volume of solution (1) to 50 volumes with the mobile phase. Dilute 1 volume of this solution to 10 volumes with the mobile phase.
(3) 0.000115% w/v of *risedronate sodium 2.5-hydrate BPCRS* and 0.00075% w/v of *risedronate impurity A EPCRS* in the mobile phase.
(4) Dissolve 0.1 g of *sodium chloride* in the mobile phase and dilute to 10 mL with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Luna C18 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 a column temperature of 40°.
(e) Use a detection wavelength of 263 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 8 times the retention time of risedronate.

MOBILE PHASE

25 volumes of *acetonitrile* and 75 volumes of solution A.

When the chromatograms are recorded under the prescribed conditions, the relative retention with reference to risedronate (retention time of about 4 minutes) of impurity A is about 2.2.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than 0.5 times the area of the peak due to risedronate in the chromatogram obtained with solution (3) (0.15%);

the area of any other *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 twice the area of the principal peak in the chromatogram obtained with solution (2) (0.4%).

Disregard any peak eluting before the peak due to risedronate, any peak corresponding to the peak obtained with solution (4) and any peak with an area less than half 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.

(1) Mix with the aid of ultrasound 10 whole tablets with 150 mL of the mobile phase and dilute to 250 mL with the mobile phase. Filter (a nylon 0.45-µm filter is suitable) and dilute a volume of the filtrate, if necessary, with sufficient mobile phase to produce a solution containing 0.016% w/v solution of anhydrous risedronate sodium.
(2) 0.018% w/v of *risedronate sodium 2.5-hydrate BPCRS* in the mobile phase.
(3) 0.00075% w/v of *risedronate impurity E EPCRS* and 0.005% w/v of *risedronate sodium 2.5-hydrate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

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

DETERMINATION OF CONTENT

Calculate the content of $C_7H_{10}NNaO_7P_2$, in the tablets using the declared content of $C_7H_{10}NNaO_7P_2$, in *risedronate sodium 2.5-hydrate BPCRS*.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of *risedronic acid*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Risedronate Sodium 2.5-Hydrate.