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Paricalcitol Injection

DEFINITION

Paricalcitol Injection is a sterile solution of Paricalcitol in a mixture of Water for Injection, Propylene Glycol, and Alcohol, or other suitable solvents. It contains NLT 90.0% and NMT 110.0% of the labeled amount of paricalcitol ($C_{27}H_{44}O_3$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

[Note—Protect paricalcitol solutions from light.]

Mobile phase: Methanol and water (4:1)

Diluent: Methanol and water (1:1)

Standard solution: Dilute USP Paricalcitol Solution RS with *Diluent* to obtain a solution having a concentration of paricalcitol similar to that of the Injection.

Sample solution: Use the Injection.

Chromatographic system

(See *Chromatography (621), System Suitability*.)

Mode: LC

Detector: UV 252 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 100–200 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of paricalcitol ($C_{27}H_{44}O_3$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of paricalcitol in the *Standard solution*, calculated on the basis of the content of paricalcitol in the USP Paricalcitol Solution RS (µg/mL)

C_U = nominal concentration of paricalcitol in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• **Content of Propylene Glycol and Alcohol** (if present)

Mobile phase: 0.01 N sulfuric acid solution, filtered and degassed

Alcohol stock solution: Transfer 2.0 mL of dehydrated alcohol to a 10-mL volumetric flask, and dilute with water to volume.

Propylene glycol stock solution: Transfer 3.0 mL of propylene glycol to a 10-mL volumetric flask, and dilute with water to volume.

Standard solution: Transfer 5.0 mL each of *Alcohol stock solution* and *Propylene glycol stock solution* to a 50-mL volumetric flask, and dilute with water to volume.

Sample solution: Transfer 5.0 mL of Injection to a 50-mL volumetric flask, and dilute with water to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Refractive index

Column: 7.8-mm × 30-cm; packing L17

Column temperature: 60°

Flow rate: 0.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[NOTE—Elution order is propylene glycol followed by alcohol.]

Suitability requirements

Resolution: NLT 4.0 between propylene glycol and alcohol

Relative standard deviation: NMT 2.0% for each peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of propylene glycol and alcohol in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of alcohol or propylene glycol from the *Sample solution*

r_S = peak response of alcohol or propylene glycol from the *Standard solution*

C_S = concentration of alcohol or propylene glycol in the *Alcohol stock solution* or *Propylene glycol stock solution* (% v/v)

C_U = nominal concentration of alcohol or propylene glycol (if present) in the Injection (% v/v)

Acceptance criteria

Alcohol: 80.0%–120.0%

Propylene glycol: 80.0%–120.0%

IMPURITIES

• **ALUMINUM ⟨206⟩**

Diluent: Dilute 4 mL of nitric acid with water to 2000 mL.

Matrix modifier: 1.5 mg/mL of magnesium nitrate

Standard stock solution: Proceed as directed for *Standard preparations* in the chapter, beginning with “Treat some aluminum wire” and ending with “Cool, and transfer the solution, with the aid of water, to a 100-mL volumetric flask, and dilute with water to volume”. Transfer 2 mL of this solution to a second 100-mL volumetric flask, and dilute with water to volume. Transfer 2 mL of this solution to a third 100-mL volumetric flask, and dilute with water to volume. This solution contains 0.4 µg/mL of aluminum.

Standard solution A: 2.5 ng/mL of aluminum in *Diluent*, from the *Standard stock solution*

Standard solution B: 5.0 ng/mL of aluminum in *Diluent*, from the *Standard stock solution*

Standard solution C: 10 ng/mL of aluminum in *Diluent*, from the *Standard stock solution*

Standard solution D: 20 ng/mL of aluminum in *Diluent*, from the *Standard stock solution*

Standard solution E: 50 ng/mL of aluminum in *Diluent*, from the *Standard stock solution*

Sample solution: Dilute 4.0 mL of Injection with 6.0 mL of *Diluent*, or use an appropriate dilution to obtain a solution having a concentration of NMT 0.02 µg/mL of aluminum.

System suitability solution: Dilute 9.5 mL of the *Sample solution* with 0.5 mL of the *Standard stock solution*. If the resulting solution contains more than 0.04 µg/mL of aluminum, prepare an alternate dilution having a concentration of about 0.02–0.04 µg/mL of aluminum.

Instrumental conditions

(See *Atomic Absorption Spectroscopy ⟨852⟩*.)

Mode: Atomic absorption spectrophotometry; instrument equipped with a flameless, electrically heated furnace

Lamp: Aluminum hollow-cathode

Analytical wavelength: Aluminum emission line at 309.3 nm

Analysis

Samples: *Standard solution A*, *Standard solution B*, *Standard solution C*, *Standard solution D*, *Standard solution E*, *Sample solution*, and *System suitability solution*

Under typical conditions, the sample volume is 20 µL, the volume of the *Matrix modifier* is 5 µL, the injection temperature is 100°, and the oven conditions are as listed in *Table 1*. [NOTE—These conditions may be optimized for each instrument.]

Table 1

Step	Temperature
Drying 1	110°
Drying 2	130°
Drying 3	200°
Pyrrolysis	1100°
Read	2300°
Clean out	2450°

Determine the absorbances of the samples. Plot the absorbances of the *Standard solutions* versus the content of aluminum, in ng/mL, drawing a straight line best fitting the five points. The correlation coefficient is NLT 0.995, the recovery for the *System suitability solution* is 80%–120%, and the duplicate injections must agree within 0.0024 µg/mL. From the graph so obtained, determine the quantity of aluminum, *C*, in µg, found in each mL of the *Sample solution*.

Calculate the quantity, in µg/mL, of aluminum in the portion of Injection taken:

$$\text{Result} = C \times D$$

C = measured concentration of aluminum in the *Sample solution* (µg/mL)

D = dilution factor used to prepare the *Sample solution*

Acceptance criteria: NMT 0.5 µg/mL

- **ORGANIC IMPURITIES**

Diluent: Acetonitrile and water (1:1)

Solution A: Acetonitrile and water (15:85)

Solution B: Acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	65	35
25	5	95
45	5	95

Return to the original conditions, and re-equilibrate the system.

Standard solution: Dilute USP Paricalcitol Solution RS with *Diluent* to obtain a solution having a concentration of paricalcitol equal to 0.5% of the labeled concentration of the Injection.

Degradation stock solution: Dilute 1 mL of USP Paricalcitol Solution RS with *Diluent* to 5 mL.

Degradation solution A: Transfer 1 mL of the *Degradation stock solution* and 0.1 mL of 30% hydrogen peroxide into a 10-mL container, and allow to stand at room temperature for 1 h. Dilute with *Diluent* to 10 mL, and mix.

Degradation solution B: Mix 1 mL of the *Degradation stock solution* and 1 mL of 0.1 N hydrochloric acid, and heat at 70° for 1 h. Cool to room temperature, dilute with *Diluent* to 10 mL, and mix.

Sample solution: Use the Injection.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 252 nm

Columns

Guard: 4.6-mm × 7.5-mm or 4.6-mm × 10-mm; packing L1

Analytical: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 100–200 µL

System suitability

Samples: *Standard solution* and *Degradation solution B*

Suitability requirements

Resolution: NLT 1.0 between the paricalcitol peak and the related compound D peak, *Degradation solution B*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Diluent*, *Degradation solution A*, *Degradation solution B*, *Standard solution*, and *Sample solution*

Identify the impurities in the *Sample solution* on the basis of the relative retention times of the components of *Degradation solution A* and *Degradation solution B* in *Table 3*.

Table 3

Name[a]	Degradation Solution	Relative Retention Time	Acceptance Criteria, NMT (%)
Related compound A	A	0.63	1.0
Related compound B	A	0.79	1.0
Related compound C	B	0.89	1.0
Related compound D	B	0.95	1.0
Related compound E[b]	B	1.32	1.0
Related compound F	B	1.57	1.0
Related compound G	B	1.66	1.0
Related compound H	B	1.74	1.0
Related compound I	B	1.79	1.0
Total impurities	—	—	2.0

[a] Related compounds A–I are specified unidentified degradation products. No information is available about chemical structures or chemical names for these impurities.

[b] This peak is very small; the signal-to-noise ratio is approximately 3–5.

Calculate the percentage of each impurity in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times C_S \times (100/L)$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of paricalcitol from the *Standard solution*

C_S = concentration of paricalcitol in the *Standard solution*, calculated on the basis of the content of paricalcitol in the USP Paricalcitol Solution RS (µg/mL)

L = labeled amount of paricalcitol in the Injection (µg/mL)

Acceptance criteria: See *Table 3*. Disregard any peak observed in the *Diluent*.

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 10 USP Endotoxin Units/µg of paricalcitol.
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **Other Requirements:** It meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose or multi-dose containers, preferably of Type I glass. Store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**
  USP Paricalcitol Solution RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
PARICALCITOL INJECTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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