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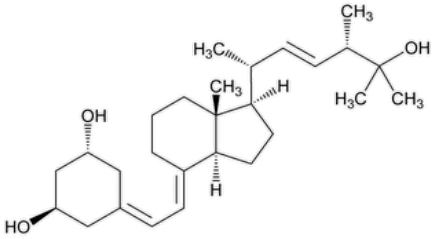
Paricalcitol



$C_{27}H_{44}O_3$ 416.64

19-Nor-1-α,25-dihydroxyvitamin D_2;

(1α,3β,7*E*,22*E*)-19-Nor-9,10-secoergosta-5,7,22-triene-1,3,25-triol;

(7*E*,22*E*)-19-Nor-9,10-secoergosta-5,7,22-triene-1α,3β,25-triol CAS RN®: 131918-61-1; UNII: 6702D36OG5.

DEFINITION

Paricalcitol contains NLT 97.0% and NMT 103.0% of paricalcitol ($C_{27}H_{44}O_3$), calculated on the dried basis.

[**Caution—**Handle Paricalcitol with exceptional care because it is very potent. Care should be taken to prevent inhaling particles of Paricalcitol and exposing the skin to it.]

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩**,** *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** 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 containing 5.0 µg/mL of paricalcitol.

Sample solution: Transfer an accurately weighed amount of Paricalcitol to a suitable volumetric flask, add dehydrated alcohol (approximately 1 mL of dehydrated alcohol per each 0.5 mg of paricalcitol), sonicate to dissolve, and dilute with *Diluent* to volume. Further dilute this solution with *Diluent* to obtain a solution containing 5.0 µg/mL of paricalcitol.

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 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of paricalcitol ($C_{27}H_{44}O_3$) in the portion of Paricalcitol 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* (µg/mL)

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

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

• **Organic Impurities**

[Note—Unless otherwise specified, protect paricalcitol solutions from light.]

Diluent: Dehydrated alcohol and water (50:50)

Solution A: Acetonitrile and water (5:95)

Solution B: Acetonitrile and methanol (75:25)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	42	58
11[a]	42	58
20	0	100
27	0	100
27.1	42	58
30	42	58

[a] Determine the retention time of the paricalcitol peak using the *Standard solution*. Adjust the start of the gradient to be 1.0 ± 0.1 min prior to the retention time of paricalcitol and accordingly adjust the remaining gradient times.

System suitability stock solution: Prepare a 50-µg/mL solution of paricalcitol from USP Paricalcitol Solution RS in dehydrated alcohol. Using a colorless glass container, expose the solution to ultraviolet light at 254 nm. Paricalcitol undergoes partial degradation to 7*Z*-paricalcitol. A degradation of at least 0.2% of paricalcitol to 7*Z*-paricalcitol [(7*Z*,22*E*)-19-nor-9,10-secoergosta-5,7,22-triene-1α,3β,25-triol] must be obtained, based on the corresponding peaks. If it is not obtained, expose the solution to ultraviolet light again.

System suitability solution: *System suitability stock solution* and water (1:1)

Standard stock solution: 5 µg/mL of paricalcitol from USP Paricalcitol Solution RS in *Diluent*

Standard solution: 0.15 µg/mL of paricalcitol from *Standard stock solution* in *Diluent*

Sensitivity solution: 0.05 µg/mL of paricalcitol from *Standard solution* in *Diluent*

Sample stock solution: 200 µg/mL of Paricalcitol in dehydrated alcohol

Sample solution: 100 µg/mL of Paricalcitol from *Sample stock solution* in water

Chromatographic system

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

Mode: LC

Detector: UV 252 nm

Column: 4.6-mm × 10-cm; 2.7-µm packing L1

Column temperature: 30°

Flow rate: 0.9 mL/min

Injection volume: 25 µL

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

[NOTE—The relative retention times for paricalcitol and 7*Z*-paricalcitol are 1.0 and 1.06, respectively.]

Suitability requirements

Resolution: NLT 1.5 between paricalcitol and 7*Z*-paricalcitol, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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* (µg/mL)

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Paricalcitol	1.0	—	—
22*Z*-Paricalcitol[a]	1.23	0.64	0.15
Any other individual impurity	—	1.0	0.1
Total impurities	—	—	0.5

[a] (7*E*,22*Z*)-19-Nor-9,10-secoergosta-5,7,22-triene-1α,3β,25-triol.

SPECIFIC TESTS

• **LOSS ON DRYING**

(See *Thermal Analysis* ⟨891⟩.)

Sample: 8 mg of Paricalcitol

Analysis: Determine the percentage of volatile substances by thermogravimetric analysis on an appropriately calibrated instrument. Heat at a rate of 5°/min between ambient temperature and 150° in an atmosphere of nitrogen at a flow rate of 40 mL/min. Determine the accumulated loss in weight from the thermogram.

Acceptance criteria: NMT 2.0%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store under argon in a freezer.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Paricalcitol RS

USP Paricalcitol Solution RS

Topic/Question	Contact	Expert Committee
PARICALCITOL	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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