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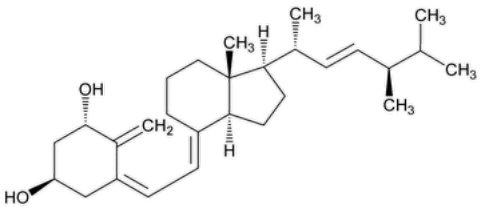
Doxercalciferol



$C_{28}H_{44}O_2$ 412.65

1α-Hydroxyvitamin D_2;

1α-Hydroxyergocalciferol;

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, (1α,3β,5*Z*,7*E*,22*E*)-;

(5*Z*,7*E*,22*E*)-9,10-Secoergosta-5,7,10(19),22-tetraene-1α,3β-diol CAS RN®: 54573-75-0.

DEFINITION

Doxercalciferol contains NLT 98.0% and NMT 102.0% of doxercalciferol ($C_{28}H_{44}O_2$), calculated on the dried basis.

[Caution—Great care should be taken in handling Doxercalciferol, because it is a potentially cytotoxic agent.]

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 doxercalciferol solutions from light.]

Solution A: Water

Solution B: Acetonitrile

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system for 5 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	25	75
15	23	77
20	10	90
25	10	90

Standard solution: 1.0 mg/mL of USP Doxercalciferol RS in acetonitrile. Use sonication to dissolve if necessary.

System suitability solution: Heat a portion of the *Standard solution* at 40° for 1 h to obtain at least 0.1%–0.2% of pre-doxercalciferol.

Sample solution: 1.0 mg/mL of Doxercalciferol in acetonitrile. Use sonication to dissolve if necessary.

[Note—Doxercalciferol solutions are stable for at least 9 h when stored at room temperature, and up to 7 days when stored at 5°.]

Chromatographic system

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

Mode: LC

Detector: UV 265 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 35°

Flow rate: 1.7 mL/min

Injection volume: 5 µL

System suitability

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

[NOTE—The relative retention times for pre-doxercalciferol and doxercalciferol are 0.94 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between pre-doxercalciferol and doxercalciferol, *System suitability solution*

Tailing factor: 0.7–1.3, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of doxercalciferol ($C_{28}H_{44}O_2$) in the portion of Doxercalciferol taken:

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

r_U = peak response of doxercalciferol from the *Sample solution*

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

C_S = concentration of USP Doxercalciferol RS in the *Standard solution* (mg/mL)

C_U = concentration of Doxercalciferol in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **ORGANIC IMPURITIES**

[NOTE—Protect doxercalciferol solutions from light.]

Solution A, Solution B, and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: See *Table 2*. Return to original conditions and re-equilibrate the system for 5 min.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	25	75
15	23	77
20	10	90
30	10	90
36	0	100
50	0	100

Standard stock solution: 4.0 mg/mL of USP Doxercalciferol RS. Dissolve first in ethyl acetate using about 20% of the final volume with sonication in an ice-water bath, if necessary, and dilute with acetonitrile to volume.

Standard solution: 0.004 mg/mL of USP Doxercalciferol RS in acetonitrile from the *Standard stock solution*

System suitability solution: Heat a portion of the *Standard stock solution* at 40° for 1 h or let it stand at room temperature for about 4–6 h, to obtain at least 0.1%–0.2% of pre-doxercalciferol

Sample solution: 4.0 mg/mL of Doxercalciferol. Dissolve first in ethyl acetate using about 20% of the final volume with sonication in an ice-water bath, if necessary, and dilute with acetonitrile to volume. [NOTE—The *Sample solution* should be prepared fresh before injection and injected within 5 min of completing its preparation.]

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.0 between pre-doxercalciferol and doxercalciferol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Doxercalciferol taken:

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

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

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

C_S = concentration of USP Doxercalciferol RS in the *Standard solution* (mg/mL)

C_U = concentration of Doxercalciferol in the *Sample solution* (mg/mL)

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

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pre-doxercalciferol	0.94	0.15
trans-Doxercalciferol (if present)[a,b]	0.96	0.30
Doxercalciferol	1.0	—
β-Doxercalciferol (if present)[b,c]	1.07	0.50
Dihydrodoxercalciferol (if present)[b,d]	1.10	0.50
Any other individual impurity	—	0.50
Total impurities	—	1.0

[a] (5*E*,7*E*,22*E*)-9,10-Secoergosta-5,7,10(19),22-tetraene-1α,3β-diol.

[b] If possible from manufacturing process.

[c] (5*Z*,7*E*,22*E*)-9,10-Secoergosta-5,7,10(19),22-tetraene-1β,3β-diol.

[d] (5*Z*,7*E*)-9,10-Secoergosta-5,7,10(19)-triene-1α,3β-diol.

SPECIFIC TESTS

• **Loss on Drying**

(See *Thermal Analysis* ⟨891⟩.)

Analysis: Determine the percentage of volatile substances by thermogravimetric analysis on an appropriately calibrated instrument, using 5–10 mg of Doxercalciferol. Heat the specimen under test at a rate of 5°/min in a stream of nitrogen at a flow rate of about 40 mL/min. Record the thermogram from ambient temperature to 150°.

Acceptance criteria: NMT 0.50%

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 10 mg/mL in alcohol

Acceptance criteria: +45° to +52°

• **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** [Note—This requirement applies only if the drug substance is intended for use in the manufacture of parenteral dosage forms.] The total aerobic microbial count is NMT 10^3 cfu/g, and the total combined yeasts and molds count is NMT 10^2 cfu/g.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at a lowered temperature not exceeding 8°.

• **USP Reference Standards** ⟨11⟩

USP Doxercalciferol RS

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

Topic/Question	Contact	Expert Committee
DOXERCALCIFEROL	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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