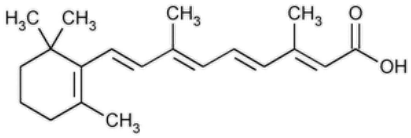
Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-23BED26C-1C53-40B7-AB97-12B20ECCF72A_4_en-US
DOI: https://doi.org/10.31003/USPNF_M84520_04_01
DOI Ref: z7wjh

Tretinoin



$C_{20}H_{28}O_2$ 300.44
Retinoic acid;
all-*trans*-Retinoic acid CAS RN®: 302-79-4; UNII: 5688UTC01R.

DEFINITION

Tretinoin contains NLT 97.0% and NMT 103.0% of tretinoin ($C_{20}H_{28}O_2$), calculated on the dried basis.

Avoid exposure to strong light, and use low-actinic glassware in the performance of the following procedures.

IDENTIFICATION

Change to read:

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

Change to read:

• **B.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

Analytical wavelength: 352 nm

Medium: Dilute 1 mL of 0.01 N hydrochloric acid with isopropyl alcohol to 1000 mL.

Sample solution: 4 µg/mL in *Medium*

Acceptance criteria: Absorptivities do not differ by more than 3.0%, calculated on the dried basis.

ASSAY

• **Procedure**

Sample: 240 mg of Tretinoin

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N sodium methoxide VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 50 mL of dimethylformamide, and add 3 drops of a 1-in-100 solution of thymol blue in dimethylformamide. Titrate with *Titrant* to a greenish endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N sodium methoxide is equivalent to 30.04 mg of tretinoin ($C_{20}H_{28}O_2$).

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Limit of Isotretinoin**

Mobile phase: Isooctane, isopropyl alcohol, and glacial acetic acid (99.65:0.25:0.1)

System suitability stock solution: 250 µg/mL of USP Tretinoin RS in isooctane prepared as follows. Dissolve a quantity of USP Tretinoin RS in a minimum amount of methylene chloride, and add a suitable amount of isooctane to the known concentration.

Standard stock solution: 250 µg/mL of USP Isotretinoin RS in isooctane prepared as follows. Dissolve a quantity of USP Isotretinoin RS in a minimum amount of methylene chloride, and add a suitable amount of isooctane to the known concentration.

System suitability solution: Transfer 5 mL of *Standard stock solution* into a 100-mL volumetric flask, and add *System suitability stock solution* to volume.

Standard solution: 12.5 µg/mL of USP Isotretinoin RS in isooctane from *Standard stock solution*

Sample solution: Transfer 25 mg of Tretinoin into a 100-mL volumetric flask. Dissolve in a minimum amount of methylene chloride, and add isooctane to volume.

Chromatographic system

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

Mode: LC

Detector: UV 352 nm

Column: 4.0-mm × 25-cm; packing L3

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for isotretinoin and tretinoin are about 0.84 and 1.00, respectively.]

Suitability requirements

Resolution: NLT 2.0 between isotretinoin and tretinoin

Relative standard deviation: NMT 2.0% for the isotretinoin peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of isotretinoin in the portion of Tretinoin taken:

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

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

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

C_S = concentration of USP Isotretinoin RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: NMT 5.0%

SPECIFIC TESTS

- **LOSS ON DRYING ⟨731⟩**

Analysis: Dry a sample under vacuum at room temperature for 16 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, preferably under an atmosphere of an inert gas, protected from light.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Isotretinoin RS

USP Tretinoin RS

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

Topic/Question	Contact	Expert Committee
TRETINOIN	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 41(4)

Current DocID: GUID-23BED26C-1C53-40B7-AB97-12B20ECCF72A_4_en-US

DOI: https://doi.org/10.31003/USPNF_M84520_04_01
DOI ref: z7wjh