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Indomethacin Suppositories

DEFINITION
Indomethacin Suppositories contain NLT 90.0% and NMT 110.0% of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$).

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*.
- **B.** The UV spectrum of the indomethacin peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **Procedure**

Solution A: Prepare 0.1% of formic acid by diluting 1 mL of formic acid with water to 1 L.

Mobile phase: Acetonitrile and *Solution A* (45:55)

Diluent: *Mobile phase* adjusted with 0.2 M sodium hydroxide (NaOH) to a pH of 8.0

System suitability solution: 0.002 mg/mL of USP Indomethacin RS, 0.002 mg/mL of USP Indomethacin Related Compound A RS, and 0.01 mg/mL of USP Indomethacin Related Compound B RS in *Diluent*

Standard solution: 0.5 mg/mL of USP Indomethacin RS in *Diluent*. Sonicate if necessary.

Sample solution: Prepare a solution nominally equivalent to 0.5 mg/mL of indomethacin in *Diluent* as follows. Mash NLT 10 Suppositories in a beaker, and heat (at about 50°) on a water bath until melted. Mix well and cool. Transfer a portion of the mass equivalent to 10 mg of indomethacin into a 20-mL volumetric flask and add 10 mL of acetonitrile. Heat in a water bath at 50° to dissolve, and dilute with *Diluent* to volume.

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

Mode: LC

Detector: PDA (scan 200–600 nm). Calculations should be based on the chromatograms collected at 240 nm. For *Identification* test *B*, use spectra at the scanned range.

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

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 4 between indomethacin related compound A and indomethacin related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$) in the portion of Suppositories 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 USP Indomethacin RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS
- **Dissolution ⟨711⟩**

Medium: 0.1 M, pH 7.2 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Standard solution: USP Indomethacin RS at a known concentration in *Medium*

Sample solution: Proceed as directed for sample per *Dissolution* ⟨711⟩. Dilute with *Medium* as needed.

Instrumental conditions

Mode: UV

Analytical wavelength: 320 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: NLT 75% (*Q*) of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$) is dissolved.

Change to read:

• **Uniformity of Dosage Units** ⟨905⟩**:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Diluent: Methanol and glacial acetic acid (199:1)

Standard solution: 25 µg/mL of USP Indomethacin RS in *Diluent*

Sample solution: Place 1 Suppository into a 100-mL volumetric flask containing 80 mL of *Diluent*, shake by mechanical means until the Suppository is dissolved, and dilute with *Diluent* to volume. Filter a portion of the solution, discarding the first 15 mL of the filtrate, and dilute a volume of the clear filtrate with the *Diluent* to obtain a solution having a concentration of 25 µg/mL of indomethacin.

Instrumental conditions

Mode: UV

Detector: 320 nm

Blank: *Diluent*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$) in the Suppository taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

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

▲▲ (CN 1-Aug-2023)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Indomethacin RS

USP Indomethacin Related Compound A RS

5-Methoxy-2-methyl-3-indoleacetic acid.

$C_{12}H_{13}NO_3$ 219.24

USP Indomethacin Related Compound B RS

4-Chlorobenzoic acid.

$C_7H_5ClO_2$ 156.57

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

Topic/Question	Contact	Expert Committee
INDOMETHACIN SUPPOSITORIES	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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