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Indomethacin Capsules

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

IDENTIFICATION

- **A.**

Standard: A solution of 25 mg of USP Indomethacin RS in 5 mL of acetone recrystallized and prepared similarly as for the *Sample*.

Sample: Shake a portion of the contents of Capsules, nominally equivalent to about 50 mg of indomethacin, with 10 mL of acetone for about 2 min, and filter. Transfer 5 mL of the filtrate to a stoppered flask, add 20 mL of water, and shake for about 2 min until a precipitate forms and crystallizes. Filter, and collect the crystals. Dry the crystals in air, then dry at a pressure below 5 mm of mercury at 100° for 2 h.

Acceptance criteria: The IR absorption spectrum of a potassium bromide dispersion of the *Sample* exhibits maxima only at the same wavelengths as those of the *Standard*.

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

ASSAY

- **Procedure**

Solution A: Phosphoric acid and water (2:1000)

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

Diluent: *Mobile phase* adjusted with 0.2 N sodium hydroxide to a pH of 6.0

Standard stock solution: 1 mg/mL of USP Indomethacin RS prepared as follows. Transfer a suitable quantity of USP Indomethacin RS to an adequate volumetric flask, add 50% of the final volume of acetonitrile, and dilute with *Diluent* to final volume.

Standard solution: 0.04 mg/mL of USP Indomethacin RS in *Diluent* from *Standard stock solution*

Sample stock solution: Nominally 1 mg/mL of indomethacin prepared as follows. Transfer a suitable portion of the contents from NLT 20 Capsules to an adequate volumetric flask, add 50% of the final volume of acetonitrile, and sonicate for about 10 min with intermittent shaking. Add about 25% of the final volume of *Diluent* and sonicate for about 10 min with intermittent shaking. Dilute with *Diluent* to final volume and mix. Allow the resulting mixture to stand until a clear supernatant is obtained. Use the clear supernatant.

Sample solution: Nominally 0.04 mg/mL of indomethacin in *Diluent* from *Sample stock solution*. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

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

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 25 µL

Run time: NLT 2 times the retention time of indomethacin

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 indomethacin ($C_{19}H_{16}ClNO_4$) in the portion of Capsules taken:

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

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

r_S = peak response of indomethacin 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: pH 7.2 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*) and water (1:4); 750 mL

Apparatus 1: 100 rpm

Time: 20 min

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

Sample solution: Filter a portion of the solution under test and suitably dilute with *Medium*, if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 318 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: NLT 80% (*Q*) of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Solution A, Mobile phase, Diluent, Standard stock solution, Sample stock solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability stock solution: 0.2 mg/mL each of USP Indomethacin Related Compound A RS and USP Indomethacin Related Compound B RS prepared as follows. Transfer suitable quantities of USP Indomethacin Related Compound A RS and USP Indomethacin Related Compound B RS to an adequate volumetric flask, add 40% of the final volume of acetonitrile, and sonicate to dissolve. Dilute with *Diluent* to final volume.

System suitability solution: 0.002 mg/mL each of USP Indomethacin Related Compound A RS and USP Indomethacin Related Compound B RS, and 0.4 mg/mL of USP Indomethacin RS in *Diluent* from *System suitability stock solution* and *Standard stock solution*

Sensitivity solution: 0.2 µg/mL of USP Indomethacin RS in *Diluent* from *Standard stock solution*

Standard solution: 0.002 mg/mL of USP Indomethacin RS in *Diluent* from *Standard stock solution*

Sample solution: Nominally 0.4 mg/mL of indomethacin in *Diluent* from *Sample stock solution*

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between indomethacin related compound A and indomethacin related compound B, *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 indomethacin related compound A, indomethacin related compound B, and any unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of indomethacin related compound A, or indomethacin related compound B, or any unspecified degradation product from the *Sample solution*

r_S = peak response of indomethacin 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)

F = relative response factor of each individual impurity (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Indomethacin related compound A	0.3	0.8	0.20
Indomethacin related compound B	0.4	2.1	0.20
Indomethacin	1.0	1.0	—
Any unspecified degradation product	—	1.0	0.20
Total degradation products	—	—	1.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩

USP Indomethacin RS

USP Indomethacin Related Compound A RS

2-(5-Methoxy-2-methyl-1*H*-indol-3-yl)acetic 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 CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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