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Indomethacin Extended-Release Capsules

DEFINITION

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

IDENTIFICATION

Change to read:

- **A.** **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: (197K)** (USP 1-May-2020)

Standard: (USP 1-May-2020) Prepare a solution of 5 mg/mL of [USP Indomethacin RS](#) in [acetone](#). Transfer 5 mL of this solution to a stoppered flask, add 20 mL of [water](#), and shake for 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. (USP 1-May-2020)

Sample: (USP 1-May-2020) Shake a portion of Capsule contents, nominally equivalent to 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 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. (USP 1-May-2020)

Acceptance criteria: The IR absorption spectrum of the *Sample* exhibits maxima only at the same wavelengths as that of the *Standard*. (USP 1-May-2020)

Change to read:

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay. (USP 1-May-2020)

Delete the following:

• C.

Sample solution: Equivalent to 1 mg/mL of indomethacin in [sodium hydroxide](#) solution (0.4 mg/mL) from powdered Capsule contents

Analysis: Shake the *Sample solution* for 5 min, and filter. To 1 mL of the clear filtrate add 1 mL of 1 mg/mL [sodium nitrite](#) solution, mix, and allow to stand for 5 min. Add 0.5 mL of [sulfuric acid](#).

Acceptance criteria: A golden yellow color develops. (USP 1-May-2020)

ASSAY

Change to read:

• PROCEDURE

Mobile phase: [Methanol](#), [water](#), and [phosphoric acid](#) (600:400:0.8)

Diluent: [Phosphoric acid](#) and [water](#) (1:99)

Standard solution: (USP 1-May-2020) 0.8 mg/mL of [USP Indomethacin RS](#), prepared as follows. Transfer a suitable quantity of [USP Indomethacin RS](#) to a suitable volumetric flask, dissolve with 60% of the flask volume of [acetonitrile](#), and dilute with *Diluent* to volume. (USP 1-May-2020)

Sample solution: Nominally 0.75 mg/mL of indomethacin prepared as follows. (USP 1-May-2020) Weigh and finely powder the contents of NLT 20 Capsules. Transfer a portion of the powder, nominally equivalent to 75 mg of indomethacin, to a 100-mL volumetric flask, add 40 mL of *Diluent*, and shake for 1 h. Sonicate for 15 min, add 40 mL of [acetonitrile](#), sonicate for 15 min, and dilute with [acetonitrile](#) to volume. Centrifuge a portion of this solution, and use the supernatant. (USP 1-May-2020)

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 240 nm**Column:** 3.9-mm × 30-cm; ▲10-μm▲ (USP 1-May-2020) packing [L1](#)**Flow rate:** 2 mL/min**Injection volume:** 20 μL**System suitability****Sample:** *Standard solution* ▲▲ (USP 1-May-2020)**Suitability requirements**

▲▲ (USP 1-May-2020)

Tailing factor: NMT 2.0 ▲▲ (USP 1-May-2020)**Relative standard deviation:** NMT 2.0% ▲▲ (USP 1-May-2020)**Analysis****Samples:** ▲*Standard solution*▲ (USP 1-May-2020) and *Sample solution*Calculate the percentage of ▲the labeled amount of▲ (USP 1-May-2020) 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▲ (USP 1-May-2020) from the *Sample solution* r_S = peak response ▲of indomethacin from the *Standard solution*▲ (USP 1-May-2020) C_S = concentration of [USP Indomethacin RS](#) in ▲the *Standard solution*▲ (USP 1-May-2020) (mg/mL) C_U = nominal concentration of indomethacin in the *Sample solution* (mg/mL)**Acceptance criteria:** 90.0%–110.0%**PERFORMANCE TESTS****Change to read:**

- [DISSOLUTION \(711\)](#).

Test 1

▲▲ (USP 1-May-2020)

Medium: pH 6.2 phosphate buffer (see [Reagents and Reference Tables, Solutions, Buffer Solutions](#)); 750 mL**Apparatus 1:** 75 rpm**Times:** 1, 2, 4, 6, 12, and 24 h**Standard solution:** [USP Indomethacin RS](#) at a known concentration in *Medium***Sample solution:** ▲Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary.▲ (USP 1-May-2020)**Instrumental conditions**(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)**Mode:** UV**Analytical wavelength:** 318 nm**Analysis****Samples:** *Standard solution* and *Sample solution***Tolerances:** See [Table 1](#).**Table 1**

Time (h)	Amount Dissolved
1	10%–25%
2	20%–40%
4	30%–55%

Time (h)	Amount Dissolved
6	45%–65%
12	60%–80%
24	NLT 80%

The percentages of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$) dissolved at the times specified conform to [Dissolution <711>](#).

[Acceptance Table 2.](#)

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: pH 6.2 phosphate buffer (see [Reagents and Reference Tables, Solutions, Buffer Solutions](#)); 900 mL

▲Apparatus 1: 75 rpm▲ (USP 1-May-2020)

Standard solution, Sample solution, and Analysis: Proceed as directed in *Test 1*.

Tolerances: See [Table 2](#).

Table 2

Time (h)	Amount Dissolved
1	12%–32%
2	27%–52%
4	50%–80%
12	NLT 80%

The percentages of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$) dissolved at the times specified conform to [Dissolution <711>](#).

[Acceptance Table 2.](#)

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: pH 6.8 phosphate buffer (see [Reagents and Reference Tables, Solutions, Buffer Solutions](#)); 750 mL

▲Apparatus 1: 75 rpm▲ (USP 1-May-2020)

Standard solution, Sample solution, and Analysis: Proceed as directed in *Test 1*.

Tolerances: See [Table 3](#).

Table 3

Time (h)	Amount Dissolved
1	15%–40%
2	35%–55%
4	55%–75%
6	65%–85%
12	NLT 75%
24	NLT 85%

The percentages of the labeled amount of indomethacin ($C_{19}H_{16}ClNO_4$) dissolved at the times specified conform to [Dissolution <711>](#).

[Acceptance Table 2.](#)