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Ketoprofen Extended-Release Capsules

DEFINITION
Ketoprofen Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of ketoprofen ($C_{16}H_{14}O_3$).

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.*

Change to read:

• **B.** ▲**Spectroscopic Identification Tests ⟨197⟩*Ultraviolet-Visible Spectroscopy*: 197U.**▲ (CN 1-May-2020) The UV spectrum from the *Sample solution* in the *Analysis* for the *Dissolution* section corresponds to the spectrum from the *Standard solution.*

ASSAY

• **Procedure**

[Note—Protect the *Standard solution* and *Sample solution* from light.]

Mobile phase: Acetonitrile, water, and glacial acetic acid (90:110:1)

Standard stock solution: 0.24 mg/mL of USP Ketoprofen RS in *Mobile phase*

Standard solution: 0.024 mg/mL of USP Ketoprofen RS in *Mobile phase,* from the *Standard stock solution*

System suitability solution: 0.25 mg/mL of USP Ketoprofen RS and 0.5 mg/mL of USP Ketoprofen Related Compound A RS in *Mobile phase.* Pipet 4.0 mL of this solution into a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: Remove completely the contents of NLT 20 Capsules, and transfer a quantity of the beads, equal to 200 mg of ketoprofen, to a 250-mL volumetric flask. Add 150 mL of *Mobile phase* and mix; bring to volume. Centrifuge, and pipet 3.0 mL of clear supernatant that contains about 2.4 mg of ketoprofen into a 100-mL volumetric flask. Dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 1.2 mL/min

Injection size: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between ketoprofen and ketoprofen related compound A, *System suitability solution*

Tailing factor: NMT 1.5 for the ketoprofen peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{16}H_{14}O_3$ in the portion of Capsules 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 Ketoprofen RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 2: 50 rpm

Time: 1, 4, and 8 h

Detector: UV 258 nm

Standard solution: About 0.1 mg/mL of USP Ketoprofen RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 10-µm pore size, then pass the filtrate through a suitable filter of 0.45-µm pore size.

Capsules labeled to contain 200 mg: In a test tube, dilute 5.0 mL of filtrate with 5.0 mL of *Medium.*

Capsules labeled to contain 150 mg: In a test tube, dilute 6.0 mL of filtrate with 3.0 mL of *Medium.*

Capsules labeled to contain 100 mg: No dilution is necessary.

Capsule blank: Place 10 empty, clean Capsules of the appropriate dosage into a 1000-mL volumetric flask. Add about 800 mL of *Medium* at 37°. Stir until Capsule shells are disintegrated. After equilibration to room temperature, dilute with *Medium* to volume. Transfer 100.0 mL to a 1000-mL volumetric flask, and dilute with *Medium* to volume. Pass through a suitable filter of 10-µm pore size, then pass the filtrate through a suitable filter of 0.45-µm pore size.

Capsules labeled to contain 200 mg: In a flask, dilute 25.0 mL with 25.0 mL of *Medium*.

Capsules labeled to contain 150 mg: In a flask, dilute 30.0 mL with 15.0 mL of *Medium*.

Capsules labeled to contain 100 mg: No dilution is necessary.

Analysis

Samples: *Standard solution*, *Sample solution*, and *Capsule blank*, using *Medium* as the blank

Calculate the concentration, in mg/mL, of ketoprofen in the sample withdrawn at each time point:

$$\text{Result} = (A_U - A_{CB}) \times (C_S/A_S)$$

A_U = absorbance of the *Sample solution*

A_{CB} = absorbance of the *Capsule blank*

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

A_S = absorbance of the *Standard solution*

Calculate the percentage of ketoprofen dissolved at each time point:

$$\text{Result} = (D + \Sigma R) \times 100/L$$

D = [amount dissolved (mg)] = volume (mL) remaining before draw × concentration (mg/mL) of sample withdrawn at the sampling time point

R = [amount removed (mg)] = volume (mL) of sample withdrawn × concentration (mg/mL) of sample withdrawn at each time point

100 = conversion factor for percentage

L = Capsule label claim (mg)

Tolerances: The percentage of the labeled amount of ketoprofen released at the times specified conforms to *Acceptance Table 2.*

Time (h)	Amount Dissolved
1	10%–25%
4	55%–80%
8	NLT 80%

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

Procedure for content uniformity:

[Note—Protect the *Standard solution* and *Sample solution* from light.]

Mobile phase, Standard solution, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sample solution: Transfer the contents of 10 Capsules, 1 Capsule each, to each of 10 250-mL volumetric flasks, add about 150 mL of *Mobile phase* to each flask, and stir for 2 h. Dilute with *Mobile phase* to volume, and mix. Centrifuge, and pipet a volume of clear supernatant that contains about 2.4 mg of ketoprofen into a 100-mL volumetric flask. Dilute with *Mobile phase* to volume.

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between ketoprofen and ketoprofen related compound A, *System suitability solution*

Tailing factor: NMT 1.5 for the ketoprofen peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{16}H_{14}O_3$ in each Capsule:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

SPECIFIC TESTS

• **Water Determination, *Method I*⟨921⟩:** NMT 3.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Ketoprofen RS

USP Ketoprofen Related Compound A RS

α-Methyl-3-(4-methylbenzoyl) benzeneacetic acid.

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

Topic/Question	Contact	Expert Committee
KETOPROFEN EXTENDED-RELEASE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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