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Cilostazol Tablets

DEFINITION
Cilostazol Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of cilostazol ($C_{20}H_{27}N_5O_2$).

IDENTIFICATION

Delete the following:

▲• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197S

Standard solution: 100 mg/mL of USP Cilostazol RS in chloroform

Sample solution: Transfer the equivalent of 100 mg of cilostazol from finely powdered Tablets into a glass container. Add 1 mL of chloroform, shake for 1 min, and pass through a suitable filter of 0.5-µm or finer pore size.▲ (USP 1-May-2021)

Add the following:

▲• **A.** The UV spectrum of the major peak for cilostazol of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

• **B.** The retention time of the major peak for cilostazol of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

▲**Mobile phase:** Acetonitrile, methanol, and water (35:15:50)

Standard solution: 0.1 mg/mL of USP Cilostazol RS in *Mobile phase* prepared as follows. Transfer a quantity of USP Cilostazol RS to a suitable volumetric flask. Add *Mobile phase* to 80% of the total volume and sonicate for at least 15 min. Dilute with *Mobile phase* to volume, and mix well.

Sample stock solution: Transfer 10 Tablets to a 500-mL volumetric flask. Add *Mobile phase* to 80% of the total volume and shake mechanically for 30 min. Sonicate for at least 5 min. Dilute with *Mobile phase* to volume, and mix well.

Sample solution: Nominally 0.1 mg/mL of cilostazol in *Mobile phase* from the *Sample stock solution*. Pass through a suitable nylon filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. *For Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 2 times the retention time of the cilostazol peak

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cilostazol ($C_{20}H_{27}N_5O_2$) in the portion of Tablets taken:

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

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

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

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

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

▲ (USP 1-May-2021)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.30% sodium lauryl sulfate in water; 900 mL

Apparatus 2: 75 rpm

Time: 60 min

▲**Standard stock solution:** 0.28 mg/mL of USP Cilostazol RS in methanol▲ (USP 1-May-2021)

Standard solution: ▲5.6 µg/mL of USP Cilostazol RS in *Medium* from the *Standard stock solution*▲ (USP 1-May-2021)

Sample solution: ▲Nominally 5.6 µg/mL of cilostazol in *Medium* prepared as follows. Pass NLT 20 mL of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 10 mL. Dilute with *Medium*.▲ (USP 1-May-2021)

Instrumental conditions

Mode: UV

Analytical wavelength: 257 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲the labeled amount of▲ (USP 1-May-2021) cilostazol ▲($C_{20}H_{27}N_5O_2$)▲ (USP 1-May-2021) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V^{\blacktriangle} \times D_{\blacktriangle\ (\text{USP 1-May-2021})} \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

▲D = dilution factor for the *Sample solution*▲ (USP 1-May-2021)

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of cilostazol ▲($C_{20}H_{27}N_5O_2$)▲ (USP 1-May-2021) is dissolved.

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

Medium: 0.3% sodium lauryl sulfate in water; 900 mL, deaerated

Apparatus 2: 75 rpm

Time: 30 min

▲**Standard stock solution:** 1.1 mg/mL of USP Cilostazol RS in methanol▲ (USP 1-May-2021)

Standard solution: ▲(L/900) mg/mL of USP Cilostazol RS in 0.5% sodium lauryl sulfate in water from the *Standard stock solution*, where L is the label claim in mg/Tablet▲ (USP 1-May-2021)

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

Mode: UV

Analytical wavelength: 258 nm

Cell: 0.2 cm

Blank: *Medium*

▲**Analysis**

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cilostazol ($C_{20}H_{27}N_5O_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

▲ (USP 1-May-2021)

Tolerances: NLT 75% (*Q*) of the labeled amount of cilostazol ▲($C_{20}H_{27}N_5O_2$)▲ (USP 1-May-2021) is dissolved.

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

Medium: 0.3% sodium lauryl sulfate in water; 900 mL

Apparatus 2: 75 rpm

Time: 60 min

▲**Standard stock solution,**▲ (USP 1-May-2021) **Standard solution, Sample solution,** and **Instrumental conditions:** Proceed as directed for *Test 1*.

▲**Analysis**

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cilostazol ($C_{20}H_{27}N_5O_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution*

L = label claim (mg/Tablet)

▲ (USP 1-May-2021)

Tolerances: NLT 70% (*Q*) of the labeled amount of cilostazol ▲($C_{20}H_{27}N_5O_2$)▲ (USP 1-May-2021) is dissolved.

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

IMPURITIES

Add the following:

▲• **Organic Impurities**

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

System suitability solution: 0.1 mg/mL of USP Cilostazol RS and 1 µg/mL of USP Cilostazol Related Compound B RS in *Mobile phase*

Sensitivity solution: 0.05 µg/mL of USP Cilostazol RS in *Mobile phase* from the *Standard solution*

System suitability

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

[Note—The relative retention times for cilostazol related compound A, cilostazol related compound B, and cilostazol are 0.25, 0.81, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between cilostazol related compound B and cilostazol, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

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

r_U = peak response of each degradation product from the *Sample solution*

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

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

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

Acceptance criteria

Any individual degradation product: NMT 0.2%

Total degradation products: NMT 0.3%▲ (USP 1-May-2021)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight and light-resistant containers. Store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Cilostazol RS

▲ USP Cilostazol Related Compound B RS

6-[4-(1-Cyclohexyl-1*H*-tetrazol-5-yl)butoxy]-1*H*-quinolin-2-one.

$C_{20}H_{25}N_5O_2$ 367.45▲ (USP 1-May-2021)

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

Topic/Question	Contact	Expert Committee
CILOSTAZOL TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

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