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Add the following:

▲Pirfenidone Capsules

DEFINITION
Pirfenidone Capsules contain NLT 95.0% and NMT 105.0% of the labeled amount of pirfenidone ($C_{12}H_{11}NO$).

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 pirfenidone peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **Procedure**

Buffer: Dissolve 1.4 mL of triethylamine in each liter of water.Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile, methanol, and *Buffer* (22:13:65)

Standard solution: 0.1 mg/mL of USP Pirfenidone RS in *Mobile phase*

Sample stock solution: Nominally 1.1 mg/mL of pirfenidone in *Mobile phase* prepared as follows. Transfer a portion of contents from Capsules (NLT 10), equivalent to 267 mg of pirfenidone, to a 250-mL volumetric flask. Add 150 mL of *Mobile phase*, and shake on a mechanical shaker for 10 min. Sonicate for 10 min and cool to ambient temperature. Dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.11 mg/mL of pirfenidone from the *Sample stock solution* in *Mobile phase*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, and discard the initial 2–3 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 15 µL

Run time: NLT 1.5 times the retention time of pirfenidone

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pirfenidone ($C_{12}H_{11}NO$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Tier 1

Medium: Water; 1000 mL

Apparatus 2: 50 rpm, with a suitable sinker

Time: 30 min

Standard solution: 0.134 mg/mL of USP Pirfenidone RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first 3 mL of filtrate. Transfer 5.0 mL of the filtrate to a 10-mL volumetric flask and dilute with *Medium* to volume.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 318 nm

Path length: 2.0 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pirfenidone ($C_{12}H_{11}NO$) 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 Pirfenidone RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 1000 mL

D = dilution factor, 2

L = label claim (mg/Capsule)

Tolerances: NLT 85% (Q) of the labeled amount of pirfenidone ($C_{12}H_{11}NO$) is dissolved

Tier 2

Medium: pH 7.0 phosphate buffer containing 1750 units of pancreatin/L, 1000 mL, deaerated

Apparatus 2: 50 rpm, with a suitable sinker

Time: 30 min

Standard solution: 0.134 mg/mL of USP Pirfenidone RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first 3 mL of filtrate.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 318 nm

Path length: 1.0 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pirfenidone ($C_{12}H_{11}NO$) 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 Pirfenidone RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Capsule)

Tolerances: NLT 85% (Q) of the labeled amount of pirfenidone ($C_{11}H_{12}NO$) is dissolved

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

IMPURITIES

- **Organic Impurities**

Buffer, Sample stock solution, and **Sample solution:** Prepare as directed in the *Assay*.

Solution A: Acetonitrile, methanol, and *Buffer* (22:13:65)

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
26	100	0
26.01	85	15
40	85	15
42	100	0
52	100	0

System suitability solution: 0.10 µg/mL each of USP Pirfenidone Related Compound A RS and USP Pirfenidone Related Compound B RS in *Solution A*

Standard solution: 0.15 µg/mL of USP Pirfenidone RS in *Solution A*

Sensitivity solution: 0.05 µg/mL of USP Pirfenidone RS from the *Standard solution* in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

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

[Note—The relative retention times in *Table 2* are provided as information that could aid in peak assignment.]

Table 2

Name	Relative Retention Time
Pirfenidone related compound A	0.25
Pirfenidone related compound B	0.34
Phenol	0.82

Name	Relative Retention Time
Pirfenidone	1.00
Bromobenzene	3.89

Suitability requirements

Resolution: NLT 6.0 between pirfenidone related compound A and pirfenidone 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 any specified or unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of any specified or unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: The reporting threshold is 0.05%.

Any unspecified degradation product: NMT 0.10%

Total degradation products: NMT 0.3%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards** ⟨11⟩

USP Pirfenidone RS

USP Pirfenidone Related Compound A RS

5-Methylpyridin-2-amine.

$C_6H_8N_2$ 108.14

USP Pirfenidone Related Compound B RS

5-Methylpyridin-2(1*H*)-one.

C_6H_7NO 109.13▲ (USP 1-May-2024)

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

Topic/Question	Contact	Expert Committee
PIRFENIDONE CAPSULES	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

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