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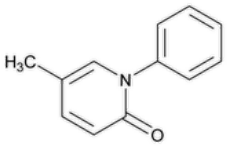
Add the following:

▲Pirfenidone



$C_{12}H_{11}NO$ 185.23

2(1*H*)-Pyridinone, 5-methyl-1-phenyl-;

5-Methyl-1-phenyl-2(1*H*)-pyridone CAS RN®: 53179-13-8; UNII: D7NLD2JX7U.

DEFINITION

Pirfenidone contains NLT 98.0% and NMT 102.0% of pirfenidone ($C_{12}H_{11}NO$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K or 197A

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

ASSAY

• **Procedure**

[Note—Protect solutions containing pirfenidone from light.]

Solution A: 3.0 g/L of sodium phosphate monobasic anhydrous in water. Adjust with 0.1 N sodium hydroxide to a pH of 4.8 ± 0.2.

Solution B: Methanol

Solution C: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	93	5	2
10	72.5	12.5	15
20	40	25	35
35	40	25	35
35.1	93	5	2
50	93	5	2

Standard solution: 1.3 mg/mL of USP Pirfenidone RS prepared as follows. Transfer a suitable amount of USP Pirfenidone RS to a suitable volumetric flask, and add 10% of the final volume of acetonitrile to dissolve. Dilute with *Solution A* to volume.

Sample solution: 1.3 mg/mL of Pirfenidone prepared as follows. Transfer a suitable amount of Pirfenidone to a suitable volumetric flask, and add 10% of the final volume of acetonitrile to dissolve. Dilute with *Solution A* to volume.

[NOTE—It is recommended not to exceed 1.45 mg/mL of USP Pirfenidone RS or Pirfenidone for the preparation of the *Standard solution* or the *Sample solution*, respectively.]

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 4-µm packing L1

Column temperature: 35°

Flow rate: 1.25 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pirfenidone ($C_{12}H_{11}NO$) in the portion of Pirfenidone 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 = concentration of Pirfenidone in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%

• **ORGANIC IMPURITIES**

[NOTE—Protect solutions containing pirfenidone from light.]

Solution A, Solution B, Solution C, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

Diluent: Acetonitrile and *Solution A* (10:90)

System suitability stock solution: 0.15 mg/mL each of USP Pirfenidone Related Compound A RS and USP Pirfenidone Related Compound B RS in *Diluent* prepared as follows. Transfer a suitable amount of USP Pirfenidone Related Compound A RS and USP Pirfenidone Related Compound B RS to a suitable volumetric flask, and add 10% of the final volume of acetonitrile to dissolve. Dilute with *Solution A* to volume.

System suitability solution: 1.5 µg/mL each of USP Pirfenidone Related Compound A RS and USP Pirfenidone Related Compound B RS from the *System suitability stock solution* in *Diluent*

Standard stock solution: 1.3 mg/mL of USP Pirfenidone RS prepared as follows. Transfer a suitable amount of USP Pirfenidone RS to a suitable volumetric flask, and add 10% of the final volume of acetonitrile to dissolve. Dilute with *Solution A* to volume.

Standard solution: 1.6 µg/mL of USP Pirfenidone RS from the *Standard stock solution* in *Diluent*

Sample solution: 3.0 mg/mL of Pirfenidone in *Diluent* prepared as follows. Transfer a suitable amount of Pirfenidone to a suitable volumetric flask, and add 10% of the final volume of acetonitrile to dissolve. Dilute with *Solution A* to volume.

System suitability

Samples: *System suitability solution* and *Standard 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	0.27

Name	Relative Retention Time
Pirfenidone related compound B	0.39
Phenol	0.72
Pirfenidone dimer[a]	0.96
Pirfenidone	1.00
Bromobenzene	1.48

[a] 1,1'-(1,4-Phenylene)bis(5-methylpyridin-2(1*H*)-one).

Suitability requirements

Resolution: NLT 6.5 between pirfenidone related compound A and pirfenidone related compound B, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Signal-to-noise ratio: NLT 20, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Pirfenidone taken:

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

r_U = peak response of each impurity 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 = concentration of pirfenidone in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.03%.

Table 3

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Pirfenidone related compound A	0.65	0.05
Pirfenidone related compound B	0.94	0.05
Phenol	0.75	0.05
Bromobenzene	0.55	0.05
Any unspecified impurity	1.00	0.05
Total impurities	—	0.2

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry under vacuum (740 mbar) at 80° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. 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	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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