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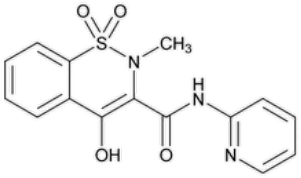
Piroxicam



$C_{15}H_{13}N_3O_4S$ 331.35

2*H*-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-*N*-2-pyridinyl-, 1,1-dioxide;

4-Hydroxy-2-methyl-*N*-2-pyridyl-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide CAS RN®: 36322-90-4; UNII: 13T4O6VMAM.

DEFINITION

Piroxicam contains NLT 97.0% and NMT 103.0% of piroxicam ($C_{15}H_{13}N_3O_4S$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M.** Do not dry specimens.

Delete the following:

▲• **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

Solution: 10 µg/mL

Medium: Hydrochloric acid in methanol (1 in 1200)

Acceptance criteria: Meets the requirements ▲ (USP 1-Dec-2020)

Delete the following:

▲• **C. Thin-Layer Chromatography ⟨201⟩**

Diluent: Chloroform and methanol (1:1)

Standard solution: 1 mg/mL of USP Piroxicam RS in *Diluent*

Sample solution: 1 mg/mL in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Absorbent: 0.25-mm layer of chromatographic silica gel

Application volume: 20 µL

Developing solvent system: Toluene and glacial acetic acid (95:5)

Analysis

Samples: *Standard solution* and *Sample solution*

Allow the spots to dry, and develop the chromatogram in the *Developing solvent system* until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, and air-dry. Place the plate in the developing chamber, and develop as before. Remove the plate from the chamber, mark the solvent front, and air-dry. Locate the spots on the plate by viewing under short-wavelength UV light.

Acceptance criteria: The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*. ▲ (USP 1-Dec-2020)

Add the following:

▲• **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-Dec-2020)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** Mix 1 mL of phosphoric acid with 1000 mL of water.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
2.0	65	35
6.0	5	95
6.1	65	35
11.0	65	35

Diluent: Methanol

Standard solution: 0.05 mg/mL of USP Piroxicam RS in *Diluent*. Sonicate to dissolve, if needed.

Sample solution: 0.05 mg/mL of Piroxicam in *Diluent*. Sonicate to dissolve, if needed.

Chromatographic system

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

Mode: LC

Detector: UV 340 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Temperatures

Autosampler: 4°

Column: 35°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%▲ (USP 1-Dec-2020)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of piroxicam ($C_{15}H_{13}N_3O_4S$) in the portion of Piroxicam taken:

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

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

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

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

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

Acceptance criteria: 97.0%–103.0%

IMPURITIES

Add the following:

▲• **Limit of Piroxicam Related Compound B**

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

System suitability solution: 1000 µg/mL of USP Piroxicam RS and 10 µg/mL each of USP Piroxicam Related Compound B RS and USP Piroxicam Related Compound G RS in *Diluent*. Sonicate to dissolve, if needed. Use freshly prepared solution.

Standard solution: 2 µg/mL of USP Piroxicam Related Compound B RS in *Diluent*. Sonicate to dissolve, if needed. Use freshly prepared solution.

Sample solution: 1.0 mg/mL of Piroxicam in *Diluent*. Sonicate to dissolve, if needed. Use freshly prepared solution.

System suitability

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

[NOTE—The relative retention times for piroxicam related compound B, piroxicam related compound G, and piroxicam are 0.89, 0.95, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between piroxicam related compound B and piroxicam related compound G, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of piroxicam related compound B in the portion of Piroxicam taken:

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

r_U = peak response of piroxicam related compound B from the *Sample solution*

r_s = peak response of piroxicam related compound B from the *Standard solution*

C_S = concentration of USP Piroxicam Related Compound B RS in the *Standard solution* (µg/mL)

C_U = concentration of Piroxicam in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 0.2%▲ (USP 1-Dec-2020)

Add the following:

▲• **ORGANIC IMPURITIES**

Solution A: 0.5% of glacial acetic acid in water. Adjust with ammonium hydroxide to a pH of 6.2.

Solution B: Acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0.0	95	5
3.0	95	5
5.0	77	23
10.0	77	23
15.0	40	60
15.1	95	5
20.0	95	5

Sensitivity solution: 0.5 µg/mL of USP Piroxicam RS in methanol. Sonicate to dissolve, if needed. Use freshly prepared solution.

Standard solution: 2 µg/mL each of USP Piroxicam RS, USP Piroxicam Related Compound A RS, USP Piroxicam Related Compound D RS, USP Piroxicam Related Compound G RS, and USP Piroxicam Related Compound J RS in methanol. Sonicate to dissolve, if needed. Use freshly prepared solution.

Sample solution: 1.0 mg/mL of Piroxicam in methanol. Sonicate to dissolve, if needed. Use freshly prepared solution.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm for quantitation of piroxicam, piroxicam related compound A, piroxicam related compound D, and any unspecified impurity; UV 355 nm for quantitation of piroxicam related compound G, and piroxicam related compound J

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Temperatures

Autosampler: 4°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Resolution: NLT 5.0 between piroxicam and piroxicam related compound G, *Standard solution*

Relative standard deviation: NMT 5.0% for piroxicam and piroxicam related compounds A, D, G, and J; *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of piroxicam related compounds A, D, G, and J in the portion of the Piroxicam taken:

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

r_U = peak response of piroxicam related compound A, D, G, or J from the *Sample solution*

r_s = peak response of piroxicam related compound A, D, G, or J from the *Standard solution*

C_S = concentration of the corresponding Reference Standard in the *Standard solution* (µg/mL)

C_U = concentration of Piroxicam in the *Sample solution* (µg/mL)

Calculate the percentage of any unspecified impurity in the portion of the Piroxicam taken:

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

r_U = peak response of any unspecified impurity from the *Sample solution*

r_s = peak response of piroxicam from the *Standard solution*

C_S = concentration of USP Piroxicam RS in the *Standard solution* (µg/mL)

C_U = concentration of Piroxicam in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Piroxicam related compound A	0.35	0.2
Piroxicam related compound G (as the anhydrous form)[a]	0.86	0.2
Piroxicam	1.0	—
Piroxicam related compound B[b]	1.2	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Piroxicam related compound D	1.36	0.2
Piroxicam related compound J	1.42	0.2
Any unspecified impurity	—	0.10
Total impurities[c]	—	0.4▲ (USP 1-Dec-2020)

[a] Methyl 4-hydroxy-2*H*-benzothiazine-3-carboxylate 1,1-dioxide

[b] For peak identification only; quantitated by the test for *Limit of Piroxicam Related Compound B*.

[c] Total impurities is the sum of piroxicam related compound B from the test for *Limit of Piroxicam Related Compound B* and each specified and any unspecified impurities from the *Organic Impurities* test.

• **Residue on Ignition ⟨281⟩:** NMT 0.3%

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Piroxicam RS

▲

USP Piroxicam Related Compound A RS

Pyridin-2-amine.

$C_5H_6N_2$ 94.11

USP Piroxicam Related Compound B RS

4-Hydroxy-*N*-(pyridin-2-yl)-2*H*-benzothiazine-3-carboxamide 1,1-dioxide.

$C_{14}H_{11}N_3O_4S$ 317.32

USP Piroxicam Related Compound D RS

Methyl 2-[1,1-dioxido-3-oxobenzoisothiazol-2(3*H*)-yl]acetate.

$C_{10}H_9NO_5S$ 255.25

USP Piroxicam Related Compound G RS

Methyl 4-hydroxy-2*H*-benzothiazine-3-carboxylate 1,1-dioxide monohydrate.

$C_{10}H_9NO_5S \cdot H_2O$ 273.26

USP Piroxicam Related Compound J RS

Methyl 4-hydroxy-2-methyl-2*H*-benzothiazine-3-carboxylate 1,1-dioxide.

$C_{11}H_{11}NO_5S$ 269.27

▲ (USP 1-Dec-2020)

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

Topic/Question	Contact	Expert Committee
PIROXICAM	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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