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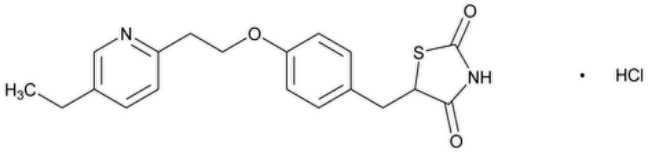
Pioglitazone Hydrochloride



$C_{19}H_{20}N_2O_3S \cdot HCl$ 392.90

2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-, monohydrochloride, (±)-;

(±)-5-[*p*-[2-(5-Ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedione monohydrochloride CAS RN®: 112529-15-4; UNII: JQT35NPK6C.

DEFINITION

Pioglitazone Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{19}H_{20}N_2O_3S \cdot HCl$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B. Identification Tests—General, *Chloride*⟨191⟩:** Dissolve 25 mg of Pioglitazone Hydrochloride in 0.5 mL of nitric acid, and add 2 mL of dilute nitric acid. It meets the requirements of the test for *Chloride*.

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

ASSAY

• **Procedure**

Mobile phase: Acetonitrile, 0.1 M ammonium acetate, and glacial acetic acid (25:25:1)

Standard solution: Prepare a 0.5 mg/mL solution of USP Pioglitazone Hydrochloride RS in methanol, and dilute with *Mobile phase* to obtain a solution containing 50 µg/mL of pioglitazone hydrochloride.

System suitability stock solution: 0.5 mg/mL of USP Pioglitazone Hydrochloride RS and 0.13 mg/mL of benzophenone in methanol

System suitability solution: Dilute *System suitability stock solution* with *Mobile phase* to obtain a solution containing 50 µg/mL of pioglitazone hydrochloride and 13 µg/mL of benzophenone.

Sample solution: Prepare a 0.5 mg/mL solution of pioglitazone hydrochloride in methanol, and dilute with *Mobile phase* to obtain a solution containing 50 µg/mL of pioglitazone hydrochloride.

Chromatographic system

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

Mode: LC

Detector: UV 269 nm

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

Column temperature: 25 ± 2.5°

Flow rate: 0.7 mL/min

[Note—Adjust the flow rate so that the retention time of the pioglitazone peak is about 7 min.]

Injection size: 20 µL

System suitability

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

[Note—The approximate relative retention times for pioglitazone and benzophenone are 1.0 and 2.6, respectively.]

Suitability requirements

Tailing factor: NMT 1.5 for pioglitazone and benzophenone, *System suitability solution*

Resolution: NLT 15 between pioglitazone and benzophenone, *System suitability solution*

Relative standard deviation: NMT 2.0% for six replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{19}H_{20}N_2O_3S \cdot HCl$ in the portion of Pioglitazone Hydrochloride 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 Pioglitazone Hydrochloride RS in the *Standard solution* (µg/mL)

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

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

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.1%

Organic Impurities

- **Procedure**

Mobile phase and **System suitability stock solution:** Proceed as directed in the *Assay*.

System suitability solution: Dilute the *System suitability stock solution* with *Mobile phase* to obtain a solution containing 25 µg/mL of pioglitazone hydrochloride and 6.5 µg/mL of benzophenone.

Sample solution: 0.2 mg/mL of pioglitazone hydrochloride dissolved in 20% of the final volume with methanol, then diluted with *Mobile phase* to final volume

Standard solution: 1 µg/mL of pioglitazone hydrochloride prepared by diluting the *Sample solution* with *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 269 nm

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

Column temperature: 25 ± 2.5°

Flow rate: 0.7 mL/min

[Note—Adjust the flow rate so that the retention time of the pioglitazone peak is about 7 min.]

Injection size: 40 µL

Run time: At least four times the retention time of pioglitazone

System suitability

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

Suitability requirements

Tailing factor: NMT 1.5 for pioglitazone and benzophenone, *System suitability solution*

Resolution: NLT 15 between pioglitazone and benzophenone, *System suitability solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Pioglitazone Hydrochloride taken:

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

r_U = peak response of each individual impurity from the *Sample solution*

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

D = dilution factor used to prepare the *Standard solution*, 0.005

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.5%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Hydroxypioglitazone[a]	0.7	0.15
Pioglitazone	1.0	—
Didehydropioglitazone[b]	1.4	0.15
N-Alkylpioglitazone[c]	3.0	0.15
Any other individual impurity	—	0.10

[a] (±)-5-{4-[2-(5-Ethylpyridin-2-yl)ethoxy]benzyl}-5-hydroxythiazolidine-2,4-dione.

[b] (*Z*)-5-{4-[2-(5-Ethylpyridin-2-yl)ethoxy]benzylidene}thiazolidine-2,4-dione.

[c] (±)-5-{4-[2-(5-Ethylpyridin-2-yl)ethoxy]benzyl}-3-[2-(5-ethylpyridin-2-yl)ethyl]thiazolidine-2,4-dione.

SPECIFIC TESTS

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at room temperature.

• **USP Reference Standards** ⟨11⟩
USP Pioglitazone Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
PIOGLITAZONE HYDROCHLORIDE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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