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Pioglitazone Tablets

DEFINITION

Pioglitazone Tablets contain an amount of pioglitazone hydrochloride ($C_{19}H_{20}N_2O_3S \cdot HCl$) equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of pioglitazone ($C_{19}H_{20}N_2O_3S$).

IDENTIFICATION

- **A.** The retention time of the pioglitazone peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B. Ultraviolet Absorption**

Sample solution: Dissolve a quantity of finely powdered Tablets in 0.1 N hydrochloric acid to obtain a solution containing 25 µg/mL of pioglitazone. [Note—Vigorous shaking and filtration may be needed.]

Acceptance criteria: The UV absorption spectrum exhibits a maximum between 267 and 271 nm.

ASSAY

- **Procedure**

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

Standard solution: Prepare 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 the *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: Weigh and finely powder NLT 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 23 mg of pioglitazone, to a glass-stoppered flask, and add 50 mL of methanol. Disperse the particles by sonication for about 2 min, then centrifuge. Dilute a portion of the supernatant with *Mobile phase* to obtain a solution having a nominal concentration of 45 µg/mL of pioglitazone.

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: *Standard solution* and *System suitability 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 the labeled amount of $C_{19}H_{20}N_2O_3S$ in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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 = nominal concentration of pioglitazone in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of pioglitazone, 356.44

M_{r2} = molecular weight of pioglitazone hydrochloride, 392.90

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

- **Dissolution ⟨711⟩**

Medium: Hydrochloric acid and potassium chloride buffer, pH 2.0 [mix 50 mL of 0.2 N hydrochloric acid and 150 mL of potassium chloride solution (150 mg/mL), dilute with water to 1 L, and adjust with 5 N hydrochloric acid to a pH of 2.0]; 900 mL

Apparatus 2: 75 rpm

Time: 15 min

Standard solution: Transfer 23 mg of USP Pioglitazone Hydrochloride RS to a 50-mL volumetric flask, dissolve in 10 mL of methanol, and dilute with *Medium* to volume. Dilute this solution with *Medium* to obtain a final concentration of about L/900, where L is the label claim (mg).

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Detector: UV

Analytical wavelength: 269 nm

Cell: 1 cm

Blank: *Medium*

Calculate the percentage of pioglitazone dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = Tablet label claim (mg)

M_{r1} = molecular weight of pioglitazone, 356.44

M_{r2} = molecular weight of pioglitazone hydrochloride, 392.90

V = volume of *Medium* (mL), 900

Tolerances: NLT 80% (Q) of the labeled amount of pioglitazone is dissolved.

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

Procedure for content uniformity

Standard solution: 26 µg/mL of USP Pioglitazone Hydrochloride RS in methanol and 0.1 N hydrochloric acid (9:1)

Sample solution: Transfer 1 Tablet to an appropriate size volumetric flask such that the final concentration does not exceed 0.3 mg of pioglitazone per mL. Add 0.1 N hydrochloric acid at a volume equivalent to 10% of the total volume and shake until the Tablet is completely disintegrated. Add methanol at a volume equivalent to 70% of the total volume and shake vigorously for 10 min. Dilute with methanol to volume, mix well, and centrifuge. Dilute a portion of the supernatant with methanol and 0.1 N hydrochloric acid (9:1) to obtain a solution having a concentration of 24 µg/mL of pioglitazone.

Spectrometric conditions

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

Mode: UV-Vis

Analytical wavelength: 269 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{19}H_{20}N_2O_3S$ in the Tablet taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

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

M_{r1} = molecular weight of pioglitazone, 356.44

M_{r2} = molecular weight of pioglitazone hydrochloride, 392.90

IMPURITIES

Organic Impurities

- **Procedure**

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

Diluent: *Mobile phase* and methanol (4:1)

Standard solution: 1 µg/mL of USP Pioglitazone Hydrochloride RS in *Diluent*. [Note—If necessary, dissolve USP Pioglitazone Hydrochloride RS in a minimal amount of methanol and then dilute with *Diluent* to final concentration.]

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: Weigh and finely powder 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 18 mg of pioglitazone, to a 100-mL volumetric flask and add 20 mL of methanol. Disperse the particles by sonication for about 1 min, then dilute with *Mobile phase* to volume, mix well, centrifuge, and use the supernatant.

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.]

Run time: At least 30 min

Injection size: 40 µL

System suitability

Samples: *Standard solution* and *System suitability 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*

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

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of pioglitazone, 356.44

M_{r2} = molecular weight of pioglitazone hydrochloride, 392.90

Acceptance criteria

Individual impurities: NMT 0.2%

Total impurities: NMT 0.6%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers and store at controlled 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 TABLETS	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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