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Pioglitazone and Metformin Hydrochloride Tablets

DEFINITION

Pioglitazone and Metformin Hydrochloride 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 ($C_{19}H_{20}N_2O_3S$), and NLT 95.0% and NMT 105.0% of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$).

IDENTIFICATION

Change to read:

- A. [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy: 197U](#) ▲ (CN 1-MAY-2020)

[NOTE—The UV spectra of the major peaks of the *Sample solution* and the *Standard solution* as obtained in the Assay may also be used to meet the *Acceptance criteria*.]

Pioglitazone

Sample solution: Transfer a quantity of finely powdered Tablets to a suitable container, and add [water](#) to obtain a final concentration of about 0.03 mg/mL of pioglitazone. Sonicate for about 30 s. Pass through a 5-mL portion of the resulting suspension using a suitable filter of 0.45-μm pore size, then wash the filter with 10 mL of [water](#), and discard the filtrate. Wash the filter with 5 mL of [0.1 N hydrochloric acid](#), and use the filtrate.

Acceptance criteria: The UV absorption spectrum exhibits a maximum between 265 and 271 nm.

Metformin hydrochloride

Sample solution: Transfer a quantity of finely powdered Tablets to a suitable container, and add a suitable quantity of [water](#), based on the labeled amount of metformin hydrochloride in the sample, to obtain a final concentration of about 0.4 mg/mL of metformin hydrochloride. Sonicate for about 30 s, and pass through a suitable filter of 0.45-μm pore size, discarding the first few mL of filtrate. Dilute a portion of the filtrate with [water](#) to obtain a solution containing about 8 μg/mL of metformin hydrochloride.

Acceptance criteria: The UV absorption spectrum exhibits a maximum between 230 and 235 nm.

- B. The retention times of the pioglitazone and metformin peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

• PROCEDURE

Mobile phase: 7.2 g/L of [sodium dodecyl sulfate](#) in a mixture of 0.05 M [monobasic ammonium phosphate](#) and acetonitrile (1:1)

Diluent: Methanol and [0.1 N hydrochloric acid](#) (1:1)

System suitability stock solution: 0.5 mg/mL of [p-methoxyacetophenone](#) and 0.4 mg/mL of [butylparaben](#) in *Diluent*

Pioglitazone standard stock solution: 0.84 mg/mL of [USP Pioglitazone Hydrochloride RS](#) in *Diluent*

Mixed standard stock solution: 2.5 mg/mL of [USP Metformin Hydrochloride RS](#) and 0.084 mg/mL of [USP Pioglitazone Hydrochloride RS](#) in [0.1 N hydrochloric acid](#) from the *Pioglitazone standard stock solution*

System suitability solution: Transfer 10.0 mL of the *Mixed standard stock solution* and 5.0 mL of the *System suitability stock solution* to a 50-mL volumetric flask, and dilute with [0.1 N hydrochloric acid](#) to volume.

Standard solution: 16.8 μg/mL of [USP Pioglitazone Hydrochloride RS](#) and 0.5 mg/mL of [USP Metformin Hydrochloride RS](#) in [0.1 N hydrochloric acid](#) from the *Mixed standard stock solution*

Sample stock solution: Weigh and finely powder NLT 10 Tablets. Transfer an amount of powdered Tablets, equivalent to about 15 mg of pioglitazone, to a 200-mL volumetric flask. Add 120 mL of [0.1 N hydrochloric acid](#), shake for about 30 min, and then sonicate for about 5 min. Dilute with [0.1 N hydrochloric acid](#) to volume, and mix well. Pass through a suitable filter of 0.45-μm pore size, discarding the first few mL of filtrate.

Sample solution: Transfer a suitable volume of the *Sample stock solution* (see [Table 1](#)) to a 50-mL volumetric flask, and dilute with [0.1 N hydrochloric acid](#) to volume.

Table 1

Labeled Amount of Pioglitazone and Metformin Hydrochloride (mg/Tablet)	Volume of Sample Stock Solution Used to Prepare the Sample Solution (mL)	Nominal Concentrations in the Sample Solution	
		Pioglitazone (µg/mL)	Metformin Hydrochloride (mg/mL)
15 and 500	10	15	0.5
15 and 850	5	7.5	0.425

Chromatographic system(See [Chromatography \(621\)](#), [System Suitability](#).)**Mode:** LC**Detector:** UV 255 nm for metformin and *p*-methoxyacetophenone; UV 225 nm for pioglitazone and butylparaben. If this procedure is used for *Identification A*, use a diode-array detector set at 200–400 nm.**Column:** 6.0-mm × 15-cm; 5-µm packing [L7](#)**Column temperature:** 25 ± 5°**Flow rate:** 1 mL/min. [NOTE—The flow rate may be adjusted to achieve the retention time of the metformin peak of about 5 min.]**Injection volume:** 10 µL**System suitability****Samples:** *System suitability solution* and *Standard solution*[NOTE—See [Table 2](#) for the approximate relative retention times.]**Table 2**

Name	Relative Retention Time
Metformin	1.0
<i>p</i> -Methoxyacetophenone	1.2
Pioglitazone	1.8
Butylparaben	2.1

Suitability requirements**Resolution:** NLT 2.5 between metformin and *p*-methoxyacetophenone; NLT 2.5 between pioglitazone and butylparaben, *System suitability solution***Relative standard deviation:** NMT 1.0% for the metformin peak; NMT 1.0% for pioglitazone peak, *Standard solution***Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the percentage of the labeled amount of pioglitazone ($C_{19}H_{20}N_2O_3S$) 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 of pioglitazone 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

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) in the portion of Tablets taken:

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

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

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

C_S = concentration of [USP Metformin Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 95.0%–105.0% for each of the labeled amounts of pioglitazone and metformin hydrochloride

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Medium: pH 2.5 McIlvaine buffer (could be prepared by adjusting 0.1 M [citric acid](#) with 0.2 M [dibasic sodium phosphate](#) to a pH of 2.5); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Diluent and Mobile phase: Proceed as directed in the Assay.

Pioglitazone standard stock solution: 0.37 mg/mL of [USP Pioglitazone Hydrochloride RS](#) in *Diluent*

Standard solution: 0.0185 mg/mL of [USP Pioglitazone Hydrochloride RS](#) from the *Pioglitazone standard stock solution* and ($L/900$) mg/mL of [USP Metformin Hydrochloride RS](#) in *Medium*, where L is the label claim, in mg/Tablet, of metformin hydrochloride

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

Chromatographic system: Proceed as directed in the Assay, except use an *Injection volume* of 5 μ L.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5 for the metformin peak; NMT 2.0 for the pioglitazone peak

Relative standard deviation: NMT 2.0% for the metformin peak; NMT 2.0% for the pioglitazone peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pioglitazone ($C_{19}H_{20}N_2O_3S$) dissolved:

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

r_U = peak response of pioglitazone 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* (mg/mL)

L = label claim of pioglitazone (mg/Tablet)

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of pioglitazone, 356.44

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

Calculate the percentage of the labeled amount of metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) dissolved:

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

r_U = peak response of metformin hydrochloride from the *Sample solution*