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Pioglitazone and Glimepiride Tablets

DEFINITION

Pioglitazone and Glimepiride Tablets contain an amount of pioglitazone hydrochloride ($C_{19}H_{20}N_2O_3S \cdot HCl$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of pioglitazone ($C_{19}H_{20}N_2O_3S$), and NLT 90.0% and NMT 110.0% of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$).

IDENTIFICATION

• A. ULTRAVIOLET ABSORPTION

Sample: Transfer 1 Tablet to a suitable container, and add 0.1 N hydrochloric acid to obtain a final concentration of about 0.1 mg/mL of glimepiride. Shake until the Tablet disintegrates. Pass a 2-mL portion of the resulting suspension through a suitable filter of 0.45- μ m pore size. Use the filtrate for the identification of pioglitazone, and use the filter for the identification of glimepiride.

Pioglitazone

Sample solution: Dilute a portion of the filtrate obtained in the *Sample* with 0.1 N hydrochloric acid to obtain a solution containing about 0.03 mg/mL of pioglitazone.

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

Glimepiride

Sample solution: Wash the filter, as obtained in the *Sample*, with 100 mL of 0.1 N hydrochloric acid, and discard the filtrate. Wash the filter with 20 mL of methanol, and use the filtrate.

Acceptance criteria: The UV absorption spectrum exhibits a maximum between 227 and 231 nm.

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

ASSAY

• PROCEDURE

Buffer: 6.9 g/L of monobasic sodium phosphate in water, adjusted with diluted phosphoric acid to a pH of 4.0

Mobile phase: Acetonitrile and *Buffer* (1:1)

Diluent: Acetonitrile and 0.1 N hydrochloric acid (9:1)

Standard stock solution: 0.66 mg/mL of [USP Pioglitazone Hydrochloride RS](#) and 0.08 mg/mL of [USP Glimepiride RS](#) in *Diluent*

Standard solution: 66 μ g/mL of pioglitazone hydrochloride and 8 μ g/mL of glimepiride in *Mobile phase* from the *Standard stock solution*

Resolution stock solution: Dilute 1.0 mL of ethyl benzoate with *Mobile phase* to 100 mL. Further dilute 1.0 mL of the resulting solution with *Mobile phase* to 100 mL.

System suitability solution: Transfer 5.0 mL of the *Standard stock solution* and 5.0 mL of the *Resolution stock solution* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.

Sample stock solution: Transfer 20 Tablets to a suitable container. Add 200.0 mL of *Diluent*, and shake vigorously for at least 20 min. If disintegration is not complete, sonicate until the Tablets are completely disintegrated, and then shake for an additional 10 min. Pass through a suitable filter of 0.2- μ m pore size, discarding the first few mL of filtrate. Further dilute 5.0 mL of the filtrate with *Diluent* to 50.0 mL.

Sample solution: Transfer 10.0 mL of the *Sample stock solution* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume to obtain a solution with the nominal concentrations listed in [Table 1](#).

Table 1

Labeled Amounts of Pioglitazone and Glimepiride (mg/Tablet)	Nominal Concentrations in the Sample solution	
	Pioglitazone (µg/mL)	Glimepiride (µg/mL)
30 and 2	60	4
30 and 4	60	8

Chromatographic system(See [Chromatography \(621\), System Suitability.](#))**Mode:** LC**Detector:** UV 228 nm**Column:** 4.6-mm × 5-cm; 3-µm packing L1**Column temperature:** 25 ± 5°**Flow rate:** 0.8 mL/min. [NOTE—The flow rate may be adjusted to achieve the retention time of the pioglitazone peak of about 2.3 min.]**Injection volume:** 20 µL**System suitability****Samples:** *Standard solution* and *System suitability solution*[NOTE—See [Table 2](#) for the approximate relative retention times.]**Table 2**

Name	Relative Retention Time
Pioglitazone	1.0
Ethyl benzoate	1.7
Glimepiride	2.3

Suitability requirements**Resolution:** NLT 4 between pioglitazone and ethyl benzoate; NLT 3 between ethyl benzoate and glimepiride, *System suitability solution***Relative standard deviation:** NMT 1.0% for the pioglitazone peak; NMT 1.0% for the glimepiride 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, 392.90Calculate the percentage of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) in the portion of Tablets taken:

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

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

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

C_S = concentration of [USP Glimepiride RS](#) in the *Standard solution* (µg/mL)

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

Acceptance criteria: 90.0%–110.0% for each of the labeled amounts of pioglitazone and glimepiride

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Pioglitazone

Medium: Hydrochloric acid buffer pH 2.0 (see [Reagents, Indicators, and Solutions—Buffer Solutions](#)); 900 mL

Apparatus 2: 75 rpm

Time: 15 min

Mobile phase and Chromatographic system: Proceed as directed in the Assay.

Standard stock solution: 0.37 mg/mL of [USP Pioglitazone Hydrochloride RS](#) dissolved first in methanol using 20% of the final volume, and then diluted with *Medium* to volume

Standard solution: Transfer 10.0 mL of the *Standard stock solution* to a 100-mL volumetric flask, and dilute with *Medium* to volume.

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

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

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 = labeled amount 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

Tolerances: NLT 80% (Q) of the labeled amount of pioglitazone ($C_{19}H_{20}N_2O_3S$) is dissolved.

Glimepiride

Medium: pH 6.8 sodium phosphate buffer containing 0.2% of sodium dodecyl sulfate (6.9 g/L of monobasic sodium phosphate, 0.896 g/L of sodium hydroxide, and 2 g/L of sodium dodecyl sulfate in water, adjusted with 1 N sodium hydroxide to a pH of 6.8); 900 mL

Apparatus 2: 75 rpm

Time: 15 min

Mobile phase and Chromatographic system: Proceed as directed in the Assay. The flow rate may be adjusted to achieve the retention time of the glimepiride peak of about 5.4 min.

Standard stock solution: 0.22 mg/mL of [USP Glimepiride RS](#) in acetonitrile

Standard solution: $L/900$ mg/mL of [USP Glimepiride RS](#) in *Medium*, where L is the labeled amount of glimepiride, in mg/Tablet, from the *Standard stock solution*

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

System suitability