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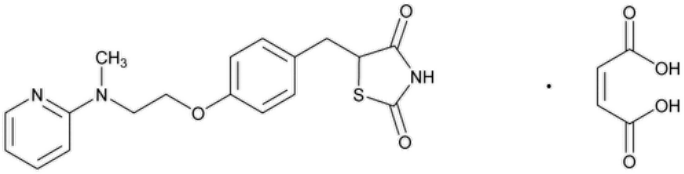
Rosiglitazone Maleate



$C_{18}H_{19}N_3O_3S \cdot C_4H_4O_4$ 473.50

(±)-5-[*p*-[2-(Methyl-2-pyridylamino)ethoxy]benzyl]-2,4-thiazolidinedione maleate (1:1);

(*RS*)-5-{[4-({2-[Methyl(2-pyridinyl)amino]ethyl}oxy) phenyl]methyl}-1,3-thiazolidine-2,4-dione (*Z*)-2-butenedioate CAS RN®: 155141-29-0; UNII: KX2339DP44.

DEFINITION

Rosiglitazone Maleate contains NLT 98.0% and NMT 102.0% of $C_{18}H_{19}N_3O_3S \cdot C_4H_4O_4$, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

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

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

ASSAY

• **Procedure**

Buffer: Dissolve 5.75 g of phosphoric acid in 800 mL water, adjust with 4 N sodium hydroxide to a pH of 3.0, and dilute with water to 1 L.

Mobile phase: Acetonitrile and *Buffer* (25:75)

System suitability solution: Transfer 2.5 mg of USP Rosiglitazone Maleate RS and 1 mg of USP Rosiglitazone Related Compound A RS to a 50-mL volumetric flask, dissolve in 1 mL of stabilizer-free tetrahydofuran, and dilute with *Mobile phase* to volume.

Standard solution: 0.05 mg/mL of USP Rosiglitazone Maleate RS in *Mobile phase*

Sample solution: 0.05 mg/mL of Rosiglitazone Maleate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

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

Suitability requirements

Resolution: Greater than 2.0 between rosiglitazone and rosiglitazone related compound A, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of rosiglitazone maleate ($C_{18}H_{19}N_3O_3S \cdot C_4H_4O_4$) in the portion of Rosiglitazone Maleate 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 Rosiglitazone Maleate RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the anhydrous and solvent-free basis

OTHER COMPONENTS

• **Content of Maleic Acid**

Buffer: Prepare 0.1 M sodium phosphate buffer as follows. Add 11.5 g of phosphoric acid to 800 mL of water, adjust with 2 N sodium hydroxide to a pH of 3.0, and dilute with water to 1 L.

Mobile phase: Methanol and *Buffer* (50:50)

Diluent: Methanol and water (50:50)

System suitability solution: 0.1 µg/mL of USP Fumaric Acid RS and 0.04 mg/mL of USP Rosiglitazone Maleate RS in *Diluent*

Standard solution: 0.01 mg/mL of USP Maleic Acid RS in *Diluent*

Sample solution: 0.04 mg/mL of Rosiglitazone Maleate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 212 nm

Column: 4.6-mm × 15-cm; 5-µm packing L14

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection size: 20 µL

System suitability

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

[Note—The relative retention times for rosiglitazone, maleic acid, and fumaric acid are 0.5, 1.0, and 1.8, respectively.]

Suitability requirements

Resolution: NLT 2.0 between maleic acid and fumaric acid, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of maleic acid in the portion of Rosiglitazone Maleate taken:

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

r_U = peak response of maleic acid from the *Sample solution*

r_S = peak response of maleic acid from the *Standard solution*

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

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

Acceptance criteria: 23.5%–26.0%

IMPURITIES

• **Residue on Ignition, ⟨281⟩:** NMT 0.2%, using an ignition temperature of 800 ± 25°

• **Organic Impurities**

[Note—Protect the *System suitability solution* and *Sample solution* from light.]

Buffer 1: Prepare 0.05 M dibasic potassium phosphate buffer as follows. Dissolve 11.4 g of dibasic potassium phosphate trihydrate in 800 mL of water, adjust with a mixture of phosphoric acid and water (1:1) to a pH of 7.0, and dilute with water to 1 L.

Solution A: Acetonitrile and *Buffer 1* (30:70)

Solution B: Acetonitrile and *Buffer 1* (70:30)

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
25.0	100	0
50.0	0	100

Buffer 2: Prepare 0.05 M monobasic potassium phosphate buffer by dissolving 6.8 g of monobasic potassium phosphate in 1 L of water.

Diluent: Acetonitrile and *Buffer 2* (30:70)

System suitability solution: 0.5 mg/mL of USP Rosiglitazone Maleate RS in *Diluent*, using sonication, if necessary, to dissolve. [NOTE—USP Rosiglitazone Maleate RS contains rosiglitazone related compound A as a minor component.]

Sample solution: 0.5 mg/mL of Rosiglitazone Maleate in *Diluent*, using sonication, if necessary, to dissolve

Chromatographic system

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

Mode: LC

Detector: UV 246 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *System suitability solution*

[NOTE—Identify the peak due to rosiglitazone related compound A based on its relative retention time shown in *Table 2*.]

Suitability requirements

Resolution: NLT 2.0 between rosiglitazone and rosiglitazone related compound A

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual impurity in the portion of Rosiglitazone Maleate taken:

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

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

r_T = sum of the peak responses from the *Sample solution*, except for the peak response of maleic acid

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Maleic acid	0.09	Disregard
Impurity 1[a]	0.15	0.1
Impurity 2[b]	0.81	0.5
Rosiglitazone	1.0	—
Rosiglitazone related compound A[c]	1.15	0.5

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any other individual impurity	—	0.1
Total impurities	—	1.0

[a] 2-(5-{[4-({2-[Methyl(2-pyridinyl)amino]ethyl}oxy)phenyl]methyl}-2,4-dioxo-1,3-thiazolidin-3-yl)butanedioic acid.

[b] 3-[4-({2-[Methyl(2-pyridinyl)amino]ethyl}oxy)phenyl]propanamide.

[c] (5*Z*)-5-{[4-({2-[Methyl(2-pyridinyl)amino]ethyl}oxy)phenyl]methylidene}-1,3-thiazolidine-2,4-dione.

SPECIFIC TESTS

• **Water Determination,** *Method 1a*⟨921⟩**:** NMT 0.5%

[Note—Because maleic acid will react with methanol thereby producing water, both titrant and solvent must be methanol free.]

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Fumaric Acid RS
USP Maleic Acid RS
USP Rosiglitazone Maleate RS
USP Rosiglitazone Related Compound A RS

(5*Z*)-5-{[4-({2-[Methyl(2-pyridinyl)amino]ethyl}oxy) phenyl]methylidene}-1,3-thiazolidine-2,4-dione.
$C_{18}H_{17}N_3O_3S$ 355.41

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

Topic/Question	Contact	Expert Committee
ROSIGLITAZONE MALEATE	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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