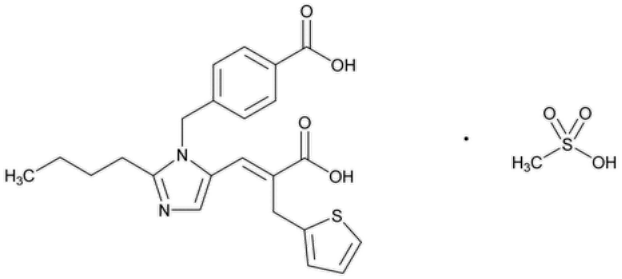
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-4B89A31F-5DA2-4451-8832-C166B28C0CA5_2_en-US
DOI: https://doi.org/10.31003/USPNF_M29712_02_01
DOI Ref: 9kcu6

Eprosartan Mesylate



$C_{23}H_{24}N_2O_4S \cdot CH_4O_3S$ 520.62

2-Thiophenepropropanoic acid, α-[[2-butyl-1-[(4-carboxyphenyl)methyl]-1*H*-imidazol-5-yl]methylene]-, (*E*)-monomethanesulfonate;

(*E*)-2-Butyl-1-(*p*-carboxybenzyl)-α-2-thenylimidazole-5-acrylic acid, monomethanesulfonate CAS RN®: 144143-96-4.

Free base CAS RN®: 133040-01-4.

DEFINITION

Eprosartan Mesylate contains NLT 98.0% and NMT 101.5% of eprosartan mesylate ($C_{23}H_{24}N_2O_4S \cdot CH_4O_3S$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197A or 197K▲ (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**

Mobile phase: Acetonitrile and water (22:78) containing 0.1% trifluoroacetic acid

Standard solution: 0.2 mg/mL of USP Eprosartan Mesylate RS in *Mobile phase*. Sonication may be necessary to dissolve.

Sample solution: 0.2 mg/mL of Eprosartan Mesylate in *Mobile phase*. Sonication may be necessary to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm × 15-cm; 5-µm packing L60

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of eprosartan mesylate ($C_{23}H_{24}N_2O_4S \cdot CH_4O_3S$) in the portion of Eprosartan Mesylate taken:

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

r_U = peak area of eprosartan from the *Sample solution*

r_S = peak area of eprosartan from the *Standard solution*

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

C_U = concentration of Eprosartan Mesylate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–101.5% on the anhydrous and solvent-free basis

IMPURITIES

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

Solution A: Use *Mobile phase* described in the *Assay*.

Solution B: Acetonitrile and water (40:60) containing 0.1% trifluoroacetic acid

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
35	0	100
40	0	100
40.1	100	0
55	100	0

Standard solution and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.2 µg/mL of USP Eprosartan Mesylate RS in *Solution A* from the *Standard solution*

Sample solution: 0.5 mg/mL of Eprosartan Mesylate in *Solution A*. Sonication may be necessary to dissolve.

System suitability: Proceed as directed in the *Assay* except for the *Signal-to-noise ratio*.

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Eprosartan Mesylate taken:

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

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

r_T = sum of all the peak areas from the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard peaks below 0.03%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Dealkyl eprosartan[a]	0.36	0.5
Hydroxy eprosartan[b]	0.79	0.3
Eprosartan	1.0	—
Any unspecified impurity	—	0.10
Total impurities	—	1.0

[a] (*E*)-4-{[2-Butyl-5-(2-carboxyvinyl)-1*H*-imidazol-1-yl]methyl}benzoic acid.

[b] 4-({2-Butyl-5-[2-carboxy-1-hydroxy-3-(thiophen-2-yl)propyl]-1*H*-imidazol-1-yl}methyl)benzoic acid.

• **Limit of Ethyl Methanesulfonate**

Standard stock solution: 0.01 mg/mL of ethyl methanesulfonate in *N,N*-dimethylformamide

Standard solution: 0.004 µg/mL of ethyl methanesulfonate prepared as follows. Weigh 20 µL of *Standard stock solution* into a 50-mL volumetric flask and add 2 mL of *N,N*-dimethylformamide. Dilute with acetonitrile to volume, mix, and add 5 boiling stones.

Sensitivity solution: 0.00054 µg/mL of ethyl methanesulfonate in *N,N*-dimethylformamide from *Standard solution*

Sample solution: 20 mg/mL of Eprosartan Mesylate prepared as follows. Weigh about 1 g of Eprosartan Mesylate into a 50-mL volumetric flask, and pipette 2.0 mL of *N,N*-dimethylformamide into the flask. Dissolve and dilute with acetonitrile to volume, and mix. Add 5 boiling stones, allow the solution to precipitate for at least 2 h, and use the supernatant.

Chromatographic system

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

Mode: GC-MS

Detector: Mass spectrometer, (+) ionization, a selected single-ion monitoring mode with m/z = 79 (CH_2SOOH^+ ion)

Column: 0.25-mm × 30-m; coated with a 0.25-µm layer of phase G27

Temperatures

Injection port: 160°

Column: See *Table 3*.

Table 3

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	20	170	0
170	10	280	2

Carrier gas: Helium

Flow rate: Constant pressure 46 kPa (0.9 mL/min at 50°)

Injection volume: 2 µL

Injection type: Split ratio, 1:4

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 10%, *Standard solution*

Signal-to-noise ratio: NLT 2.5, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the amount of ethyl methanesulfonate in the portion of Eprosartan Mesylate taken:

$$\text{Result} = (r_U/r_S) \times (C_S \times C_U) \times 10^6$$

r_U = peak response of ethyl methanesulfonate from the *Sample solution*

r_S = peak response of ethyl methanesulfonate from the *Standard solution*

C_S = concentration of ethyl methanesulfonate in the *Standard solution* (µg/mL)

C_U = concentration of Eprosartan Mesylate in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 0.2 ppm

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 1.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers and store at NMT 25°.

• **USP Reference Standards ⟨11⟩**

USP Eprosartan Mesylate RS

Topic/Question	Contact	Expert Committee
EPROSARTAN MESYLATE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(3)

Current DocID: GUID-4B89A31F-5DA2-4451-8832-C166B28C0CA5_2_en-US

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