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Add the following:

▲Phentolamine Mesylate Injection

DEFINITION

Phentolamine Mesylate Injection is a clear, colorless, sterile solution. It contains NLT 90.0% and NMT 105.0% of the labeled amount of phentolamine mesylate ($C_{17}H_{19}N_3O \cdot CH_4O_3S$). It contains no preservatives.

IDENTIFICATION

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

ASSAY

- **Procedure**

Buffer: Transfer 10.2 g of monobasic potassium phosphate to a suitable container. Add 3000 mL of water to dissolve. Adjust with phosphoric acid to a pH of 2.5.

Solution A: Methanol and *Buffer* (20:80)

Solution B: Methanol and *Buffer* (70:30)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5.0	100	0
28.0	0	100
44.0	0	100
45.0	100	0
55.0	100	0

Diluent: Transfer 1.36 g of sodium acetate and 0.5 g of ethylenediamine tetraacetate disodium dihydrate to a 1000-mL volumetric flask. Add 1000 mL of water to dissolve. Adjust with glacial acetic acid to a pH of 3.8.

Standard solution A: 0.22 mg/mL of USP Phentolamine Mesylate RS in *Diluent*.
[Note—Sonication may be needed to aid the dissolution.]

Standard solution B: 0.22 mg/mL of USP Phentolamine Related Compound A RS in *Diluent*.
[Note—Sonication may be needed to aid the dissolution.]

Standard solution C: 0.22 mg/mL of USP Phentolamine Keto Analog RS prepared as follows. Transfer a suitable amount of USP Phentolamine Keto Analog RS in a suitable volumetric flask. Add methanol to 15% of the flask volume, and sonicate. Dilute with *Diluent* to volume.

System suitability solution: 0.22 mg/mL of USP Phentolamine Mesylate RS and 1.1 µg/mL each of USP Phentolamine Related Compound A RS from *Standard solution B* and USP Phentolamine Keto Analog RS from *Standard solution C* in *Diluent*

Sample solution: Nominally 0.24 mg/mL of phentolamine mesylate prepared from a suitable volume of the pooled Injection (NLT 4 cartridges)

Chromatographic system

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

Mode: LC

Detector: UV 232 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 4-µm packing L87

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for phentolamine keto analog, phentolamine, and phentolamine related compound A are about 0.84, 1.00, and 1.09, respectively.]

Suitability requirements

Resolution: NLT 2.0 between phentolamine and phentolamine related compound A, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution A*

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

Analysis

Samples: *Standard solution A* and *Sample solution*

Calculate the percentage of the labeled amount of phentolamine mesylate ($C_{17}H_{19}N_3O \cdot CH_4O_3S$) in the portion of Injection taken:

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

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

r_S = peak response of phentolamine from *Standard solution A*

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

C_U = nominal concentration of phentolamine mesylate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–105.0%

IMPURITIES

- **ORGANIC IMPURITIES**

Buffer, Solution A, Solution B, Mobile phase, Diluent, Standard solution B, Standard solution C, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.11 µg/mL of USP Phentolamine Mesylate RS in *Diluent*

Standard solution: 1.2 µg/mL of USP Phentolamine Mesylate RS, 2.8 µg/mL of USP Phentolamine Keto Analog RS from *Standard solution C*, and 5.2 µg/mL of USP Phentolamine Related Compound A RS from *Standard solution B* in *Diluent*

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between phentolamine and phentolamine related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0% for phentolamine keto analog, phentolamine, and phentolamine related compound A, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phentolamine related compound A and phentolamine keto analog in the portion of Injection taken:

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

r_U = peak response of phentolamine related compound A or phentolamine keto analog from the *Sample solution*

r_S = peak response of phentolamine related compound A or phentolamine keto analog from the *Standard solution*

C_S = concentration of USP Phentolamine Related Compound A RS or USP Phentolamine Keto Analog RS in the *Standard solution* (µg/mL)

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

Calculate the percentage of any unspecified degradation product in the portion of Injection taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phentolamine keto analog	0.84	1.2
Phentolamine	1.00	—
Phentolamine related compound A	1.09	2.2
Any unspecified degradation product	—	0.5
Total degradation products	—	4.2

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** Meets the requirements
- **pH ⟨791⟩:** 3.5–4.5
- **Particulate Matter in Injections ⟨788⟩, *Method 1*:** Meets the requirements
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Protect from direct heat and light. Protect from freezing. Store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**

USP Phentolamine Keto Analog RS

N-(3-Hydroxyphenyl)-*N*-(4-tolyl)-4,5-dihydro-1*H*-imidazole-2-carboxamide.

$C_{17}H_{17}N_3O_2$ 295.34

USP Phentolamine Mesylate RS

USP Phentolamine Related Compound A RS

N-(2-Aminoethyl)-2-[(3-hydroxyphenyl)(4-tolyl)amino]acetamide.

$C_{17}H_{21}N_3O_2$ 299.37▲ (USP 1-May-2022)

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

Topic/Question	Contact	Expert Committee
PHENTOLAMINE MESYLATE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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