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Metoprolol Tartrate Injection

DEFINITION

Metoprolol Tartrate Injection is a sterile solution of Metoprolol Tartrate in Water for Injection. It contains Sodium Chloride as a tonicity-adjusting agent. It contains NLT 90.0% and NMT 110.0% of the labeled amount of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$.

IDENTIFICATION

Change to read:

• **A.** ▲The retention time of metoprolol of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

Add the following:

▲• **B.** The UV-Vis spectrum of the major peak of the *Diluted sample stock solution* corresponds to that of the *Diluted standard stock solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

ASSAY

Change to read:

• **Procedure**

Solution A: 9.0 mg/mL of sodium chloride in water

Mobile phase: 961 mg of 1-pentanesulfonic acid sodium salt (monohydrate) and 82 mg of anhydrous sodium acetate in a mixture of 550 mL of methanol and 470 mL of water. Add 0.57 mL of glacial acetic acid.

Internal standard solution: 0.72 mg/mL of USP Oxprenolol Hydrochloride RS in freshly prepared *Mobile phase*

Standard stock solution: 1 mg/mL of USP Metoprolol Tartrate RS in *Solution A*

Standard solution: *Standard stock solution* and *Internal standard solution* (1:1)

▲**Diluted standard stock solution:** 0.1 mg/mL of USP Metoprolol Tartrate RS from *Standard stock solution* in *Solution A*▲ (USP 1-May-2019)

Sample stock solution: Nominally 1 mg/mL of metoprolol tartrate from Injection prepared as follows. Transfer an accurately measured volume of Injection, if necessary, into *Solution A*.

Sample solution: *Sample stock solution* and *Internal standard solution* (1:1)

▲**Diluted sample stock solution:** Nominally 0.1 mg/mL of metoprolol tartrate from *Sample stock solution* in *Solution A*▲ (USP 1-May-2019)

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2019)

Column: 3.9-mm × 30-cm; ▲10-µm▲ (USP 1-May-2019) packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for metoprolol and oxprenolol are 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between metoprolol and oxprenolol

Relative standard deviation: NMT 2.0% from three replicate injections

Analysis

Samples: *Standard solution*, ▲*Diluted standard stock solution*,▲ (USP 1-May-2019) *Sample solution*, and ▲*Diluted sample stock solution*. [Note—The *Diluted standard stock solution* and *Diluted sample stock solution* are used for *Identification B*.]▲ (USP 1-May-2019)

Calculate the percentage of the labeled amount of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$ in the portion of Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of metoprolol to oxprenolol from the *Sample solution*

R_S = peak response ratio of metoprolol to oxprenolol from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Add the following:

▲• **Organic Impurities**

Solution A: 1.3 g/L of sodium dodecyl sulfate in 0.1% (w/v) phosphoric acid

Solution B: 9.0 mg/mL of sodium chloride in water. [Note—This solution is only needed when sample dilution is required.]

Mobile phase: Acetonitrile and *Solution A* (40:60)

System suitability solution: 5 µg/mL each of USP Metoprolol Tartrate RS, USP Metoprolol Related Compound A RS, USP Metoprolol Related Compound B RS, and USP Metoprolol Related Compound C RS in *Mobile phase*

Standard solution: 2.5 µg/mL each of USP Metoprolol Tartrate RS and USP Metoprolol Related Compound C RS in *Mobile phase*

Sample solution: Nominally 1 mg/mL of metoprolol tartrate from a volume of Injection. Transfer an accurately measured volume of Injection, if necessary, into *Solution B*.

Chromatographic system

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

Mode: LC

Detector: UV 223 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for metoprolol and metoprolol related compounds are listed in *Table 1*.]

Suitability requirements

Resolution: NLT 1.5 between metoprolol related compound A and metoprolol related compound B; NLT 2.5 between metoprolol related compound B and metoprolol related compound C, *System suitability solution*

Relative standard deviation: NMT 3% for metoprolol and metoprolol related compound C, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of metoprolol related compound C in the portion of Injection taken:

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

r_U = peak response of metoprolol related compound C from the *Sample solution*

r_S = peak response of metoprolol related compound C from the *Standard solution*

C_S = concentration of USP Metoprolol Related Compound C RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of metoprolol tartrate 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 each unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tartaric acid	0.13	—
Metoprolol related compound C	0.64	0.4
Metoprolol related compound B[a]	0.73	—
Metoprolol related compound A[a]	0.83	—
Metoprolol	1.0	—
Any unspecified degradation product	—	0.2
Total degradation products	—	1.0▲ (USP 1-May-2019)

[a] Specified impurities controlled in the drug substance. They are not to be included in the calculation of the total degradation products.

SPECIFIC TESTS

- **pH ⟨791⟩:** 5.0–8.0
- **Bacterial Endotoxins Test ⟨85⟩:** NMT 25.0 USP Endotoxin Units/mg of metoprolol tartrate
- **Sterility Tests ⟨71⟩**, *Test for Sterility of the Product to be Examined, Membrane Filtration*: Meets the requirements
- **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

Change to read:

- **Packaging and Storage:** Preserve in single-dose, light-resistant containers, preferably of Type I or Type II glass. ▲Store at controlled room temperature.▲ (USP 1-May-2019)

Change to read:

- **USP Reference Standards ⟨11⟩**

USP Metoprolol Tartrate RS

▲USP Metoprolol Related Compound A RS

1-(Ethylamino)-3-[4-(2-methoxyethyl)phenoxy]propan-2-ol.

$C_{14}H_{23}NO_3$ 253.34

USP Metoprolol Related Compound B RS

1-Chloro-3-[4-(2-methoxyethyl)phenoxy]propan-2-ol.

$C_{12}H_{17}ClO_3$ 244.71

USP Metoprolol Related Compound C RS

4-[2-Hydroxy-3-(isopropylamino)propoxy]benzaldehyde hydrochloride.

$C_{13}H_{19}NO_3 \cdot HCl$ 273.76▲ (USP 1-May-2019)

USP Oxprenolol Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
METOPROLOL TARTRATE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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