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Metoclopramide Injection

DEFINITION

Metoclopramide Injection is a sterile solution of Metoclopramide Hydrochloride in Water for Injection. It contains the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of metoclopramide ($C_{14}H_{22}ClN_3O_2$).

IDENTIFICATION

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

ASSAY

- **Procedure**

Mobile phase: Dissolve 2.7 g of sodium acetate in 500 mL of water. Add 500 mL of acetonitrile and 2 mL of tetramethylammonium hydroxide solution in methanol (1 in 5), and mix. Adjust with glacial acetic acid to a pH of 6.5, filter, and degas.

System suitability stock solution: Transfer 12.5 mg of benzenesulfonamide to a 25-mL volumetric flask. Add 15 mL of methanol, and shake to dissolve. Dilute with 0.01 M phosphoric acid to volume.

Standard stock solution: 0.9 mg/mL of USP Metoclopramide Hydrochloride RS in 0.01 M phosphoric acid

System suitability solution: Transfer 5 mL of *System suitability stock solution* and 5 mL of *Standard stock solution* into a 100-mL volumetric flask, and dilute with 0.01 M phosphoric acid to volume.

Standard solution: 45 µg/mL of USP Metoclopramide Hydrochloride RS (equivalent to 40 µg/mL of metoclopramide) from *Standard stock solution*. Dilute with 0.01 M phosphoric acid.

Sample solution: Nominally 40 µg/mL of metoclopramide, prepared as follows. Transfer a volume of Injection, equivalent to about 40 mg of metoclopramide, to a 100-mL volumetric flask, and dilute with 0.01 M phosphoric acid to volume. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, and dilute with 0.01 M phosphoric acid to volume.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm or diode array. [Note—Use the diode array detector to perform *Identification* test *B*.]

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

[Note—The relative retention times for benzenesulfonamide and metoclopramide are 0.7 and 1.0, respectively.]

Resolution: NLT 1.5 between the benzenesulfonamide and metoclopramide peaks, *System suitability solution*

Tailing factor: NMT 2.0 for the metoclopramide peak, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metoclopramide ($C_{14}H_{22}ClN_3O_2$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of metoclopramide, 299.80

M_{r2} = molecular weight of anhydrous metoclopramide hydrochloride, 336.26

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

Mobile phase: Prepare a 1.88 g/L solution of sodium 1-hexanesulfonate solution (0.01 M solution) in a mixture of acetonitrile and water (60:40), and adjust with glacial acetic acid to a pH of 4.0.

Standard solution: 5.5 µg/mL of USP Metoclopramide Hydrochloride RS in *Mobile phase*

Sample solution: Dilute a volume of Injection with *Mobile phase* to obtain a solution containing about 1.0 mg/mL of metoclopramide.

Chromatographic system

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

Mode: LC

Detector: UV 265 nm

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

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.8

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of metoclopramide, 299.80

M_{r2} = molecular weight of anhydrous metoclopramide hydrochloride, 336.26

Acceptance criteria: NMT 0.5% of any individual impurity is found.

SPECIFIC TESTS

• **pH ⟨791⟩:** 2.5–6.5

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 2.5 USP Endotoxin Units/mg of metoclopramide

• **Particulate Matter in Injections ⟨788⟩:** It meets the requirements for small-volume injections.

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass, protected from light. [Note—Injection containing an antioxidant agent does not require protection from light.] Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Metoclopramide Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
METOCLOPRAMIDE INJECTION	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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