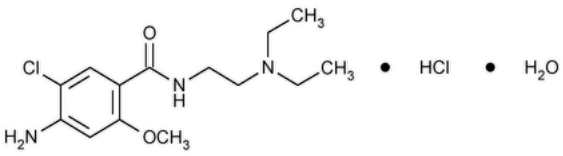
Status: Currently Official on 18-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-EE46DBF9-B185-48F7-8826-31682903A169_2_en-US
DOI: https://doi.org/10.31003/USPNF_M53320_02_01
DOI Ref: aa7rk

Metoclopramide Hydrochloride



$C_{14}H_{22}ClN_3O_2 \cdot HCl \cdot H_2O$ 354.27

Benzamide, 4-amino-5-chloro-*N*-[2-(diethylamino)ethyl]-2-methoxy-, monohydrochloride, monohydrate;

4-Amino-5-chloro-*N*-[2-(diethylamino)ethyl]-*o*-anisamide monohydrochloride monohydrate CAS RN®: 54143-57-6; UNII: W1792A2RVD.

DEFINITION

Metoclopramide Hydrochloride contains NLT 98.0% and NMT 101.0% of metoclopramide hydrochloride ($C_{14}H_{22}ClN_3O_2 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **B.** **Identification Tests—General, *Chloride*⟨191⟩**

Sample solution: Dissolve 100 mg in 2 mL of water, and acidify the solution with dilute nitric acid.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Sample: 250 mg

Analysis: Dissolve the *Sample* in a mixture of 5.0 mL of 0.01 N hydrochloric acid and 50 mL of alcohol. Titrate with 0.1 N sodium hydroxide VS (see *Titrimetry ⟨541⟩*), determining the endpoint potentiometrically. Read the volume of 0.1 N sodium hydroxide added between the two points of inflection. Each mL of 0.1 N sodium hydroxide is equivalent to 33.63 mg of the anhydrous metoclopramide hydrochloride ($C_{14}H_{22}ClN_3O_2 \cdot HCl$).

Acceptance criteria: 98.0%–101.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Buffer: Dissolve 6.8 g of monobasic potassium phosphate in 700 mL of water. Add 0.2 mL of *N*,*N*-dimethyloctylamine, and adjust with dilute phosphoric acid to a pH of 4.0. Dilute with water to 1000 mL.

Mobile phase: Acetonitrile and *Buffer* (250:1000)

Standard stock solution: 0.1 mg/mL each of USP Metoclopramide Hydrochloride RS, USP Metoclopramide Related Compound A RS, USP Metoclopramide Related Compound B RS, and USP Metoclopramide Related Compound D RS in *Mobile phase*

Standard solution: 2.0 µg/mL each of USP Metoclopramide Hydrochloride RS, USP Metoclopramide Related Compound A RS, USP Metoclopramide Related Compound B RS, and USP Metoclopramide Related Compound D RS in *Mobile phase* from the *Standard stock solution*

Sample solution: 1.0 mg/mL of Metoclopramide Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: At least 8 times the retention time of the metoclopramide peak

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 for metoclopramide related compound A and metoclopramide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each of metoclopramide related compounds A, B, and D in the portion of Metoclopramide Hydrochloride taken:

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

r_U = peak response of the relevant metoclopramide related compound from the *Sample solution*

r_S = peak response of the relevant metoclopramide related compound from the *Standard solution*

C_S = concentration of the relevant USP Metoclopramide Related Compound RS in the *Standard solution* (mg/mL)

C_U = concentration of Metoclopramide Hydrochloride in the *Sample solution* (mg/mL)

Calculate the percentage of any other individual impurity in the portion of Metoclopramide Hydrochloride taken:

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

r_U = peak response of any other individual 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* (mg/mL)

C_U = concentration of Metoclopramide Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
N-Acetylmetoclopramide (metoclopramide related compound A)[a]	0.8	0.15
Metoclopramide	1.0	—
Methyl 4-acetamido-2-methoxybenzoate (metoclopramide related compound D)	2.4–2.7	0.15
N-Acetyl methyl ester analog (metoclopramide related compound B)[b]	5.2–6.7	0.15
Any other individual impurity	—	0.10
Total impurities	—	0.50

[a] 4-Acetamido-5-chloro-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide.

[b] Methyl 4-acetamido-5-chloro-2-methoxybenzoate.

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩**:** 4.5%–6.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Metoclopramide Hydrochloride RS

USP Metoclopramide Related Compound A RS

N-Acetylmetoclopramide.

4-Acetamido-5-chloro-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide.

$C_{16}H_{24}ClN_3O_3$ 341.83

USP Metoclopramide Related Compound B RS

N-Acetyl methyl ester analog.

Methyl 4-acetamido-5-chloro-2-methoxybenzoate.

$C_{11}H_{12}ClNO_4$ 257.67

USP Metoclopramide Related Compound D RS

Methyl 4-acetamido-2-methoxybenzoate.

$C_{11}H_{13}NO_4$ 223.23

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

Topic/Question	Contact	Expert Committee
METOCLOPRAMIDE HYDROCHLORIDE	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 39(1)

Current DocID: GUID-EE46DBF9-B185-48F7-8826-31682903A169_2_en-US

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