Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Nov-2020
Document Type: USP Monographs
DocId: GUID-FDEED382-612A-455B-9925-A9ED734F7329_2_en-US
DOI: https://doi.org/10.31003/USPNF_M20539_02_01
DOI Ref: whv6u

Cromolyn Sodium Inhalation Solution

DEFINITION

Cromolyn Sodium Inhalation Solution is a sterile, aqueous solution of Cromolyn Sodium. It contains NLT 90.0% and NMT 110.0% of the labeled amount of cromolyn sodium ($C_{23}H_{14}Na_2O_{11}$).

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*.

Add the following:

▲• **B.** The UV absorption spectrum of the major peak of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the *Standard solution,* as obtained in the *Assay*.▲ (USP 1-Aug-2020)

ASSAY

Change to read:

• **Procedure**

Buffer: 5.6 g/L of monobasic potassium phosphate and 22.2 g/L of myristyltrimethylammonium bromide in water. Adjust with ▲50% sodium hydroxide TS▲ (USP 1-Aug-2020) to a pH of 6.5.

Mobile phase: Methanol and *Buffer* (55:45)

Diluent: Acetonitrile and water (30:70)

System suitability solution: 0.5 mg/mL of USP Cromolyn Sodium RS and 0.02 mg/mL each of USP Cromolyn Related Compound A RS and USP Cromolyn Related Compound B RS in *Diluent*

Standard solution: 0.5 mg/mL of USP Cromolyn Sodium RS in *Diluent*

Sample solution: Nominally equivalent to 0.5 mg/mL of cromolyn sodium from a volume of Inhalation Solution in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 326 nm. ▲For *Identification B*, use a diode array detector in the range of 220–400 nm.▲ (USP 1-Aug-2020)

Column: 4.6-mm × 10-cm; 3.5-µm packing L7

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2 times the retention time of cromolyn▲ (USP 1-Aug-2020)

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between cromolyn related compound B and cromolyn related compound A; ▲NLT 2.0 between cromolyn related compound A and cromolyn,▲ (USP 1-Aug-2020) *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cromolyn sodium ($C_{23}H_{14}Na_2O_{11}$) in the portion of Inhalation Solution taken:

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

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

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

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

C_U = nominal concentration of cromolyn sodium in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

▲▲ (USP 1-Aug-2020) **Mobile phase, Diluent,** and **System suitability solution:** Prepare as directed in the *Assay*.

Standard solution: 0.002 mg/mL each of USP Cromolyn Related Compound A RS, USP Cromolyn Related Compound B RS, and USP Cromolyn Sodium RS in *Diluent*

Sample solution: Nominally equivalent to 2 mg/mL of cromolyn sodium from a volume of Inhalation Solution in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 326 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L7

Temperatures

Autosampler: 4°

Column: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: ▲NLT▲ (USP 1-Aug-2020) 2 times the retention time of cromolyn

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between cromolyn related compound B and cromolyn related compound A; NLT 2.0 between cromolyn related compound A and cromolyn, *System suitability solution*

Relative standard deviation: NMT 3% for 6 replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cromolyn related compound A or cromolyn related compound B in the portion of Inhalation Solution taken:

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

r_U = peak response of cromolyn related compound A or cromolyn related compound B from the *Sample solution*

r_S = peak response of cromolyn related compound A or cromolyn related compound B from the *Standard solution*

C_S = concentration of ▲USP Cromolyn Related Compound A RS or USP Cromolyn Related Compound B RS▲ (USP 1-Aug-2020) in the *Standard solution* (mg/mL)

C_U = nominal concentration of cromolyn sodium in the *Sample solution* (mg/mL)

Calculate the percentage of any individual unspecified degradation product in the portion of Inhalation Solution taken:

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

r_U = peak response of each ▲individual▲ (USP 1-Aug-2020) unspecified degradation product from the *Sample solution*

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

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

C_U = nominal concentration of cromolyn sodium in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cromolyn related compound B	0.4	1.0
Cromolyn related compound A	0.5	1.0
Cromolyn	1.0	—
Any individual unspecified degradation product	—	1.0
Total impurities	—	2.0

SPECIFIC TESTS

- **pH** ⟨791⟩**:** 4.0–7.0
- **Sterility Tests** ⟨71⟩**:** Meets the requirements

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-unit double-ended glass ampuls or in low-density polyethylene ampuls. Store at controlled room temperature, protected from light.
- **Labeling:** The label indicates that the Inhalation Solution is not to be used if it contains a precipitate.
- **USP Reference Standards** ⟨11⟩

USP Cromolyn Related Compound A RS
1,3-Bis(2-acetyl-3-hydroxyphenoxy) propan-2-ol.
$C_{19}H_{20}O_7$ 360.36

USP Cromolyn Related Compound B RS
Diethyl 5,5'-[(2-hydroxypropane-1,3-diyl)bis(oxy)]bis(4-oxo-4*H*-chromene-2-carboxylate).
$C_{27}H_{24}O_{11}$ 524.48

USP Cromolyn Sodium RS

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

Topic/Question	Contact	Expert Committee
CROMOLYN SODIUM INHALATION SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(3)

Current DocID: GUID-FDEED382-612A-455B-9925-A9ED734F7329_2_en-US
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