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Add the following:

▲Cromolyn Sodium Oral Solution

DEFINITION

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

IDENTIFICATION

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

ASSAY

- **Procedure**

Buffer: 10.0 g/L of tetrabutylammonium hydrogen sulfate in water

Mobile phase: Acetonitrile and *Buffer* (25:75)

Standard solution: 0.2 mg/mL of USP Cromolyn Sodium RS in water

Sample solution: Nominally 0.2 mg/mL of cromolyn sodium from Oral Solution prepared as follows. Mix NLT 5 containers of Oral Solution, transfer a suitable volume of the composite Oral Solution to a suitable volumetric flask, and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 330 nm. For *Identification A*, use a diode array detector in the range of 220–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of the cromolyn peak

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

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 Oral Solution taken:

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

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

r_S = peak response of cromolyn sodium 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

• **Deliverable Volume ⟨698⟩:** Meets the requirements

IMPURITIES

• **Organic Impurities**

Solution A: 10.0 g/L of tetrabutylammonium hydrogen sulfate in water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20	60	40
25	60	40
35	50	50
45	90	10
50	90	10

Diluent: Acetonitrile and water (60:40)

System suitability solution: 5 mg/mL of USP Cromolyn Sodium RS and 0.005 mg/mL each of 2-acetylresorcinol, USP Cromolyn Related Compound A RS, and USP Cromolyn Related Compound B RS in *Diluent*

Sensitivity solution: 0.0025 mg/mL of USP Cromolyn Sodium RS in *Diluent*

Standard solution: 0.005 mg/mL of USP Cromolyn Sodium RS in *Diluent*

Sample solution: Nominally 5 mg/mL of cromolyn sodium from Oral Solution prepared as follows. Mix NLT 5 containers of Oral Solution, transfer a suitable volume of the composite Oral Solution to a suitable volumetric flask, and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 330 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between the cromolyn and 2-acetylresorcinol peaks; NLT 3.0 between the cromolyn related compound B and cromolyn related compound A peaks, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Oral Solution taken:

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

r_U = peak response of each impurity 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 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cromolyn	1.0	—
2-Acetylresorcinol[a]	1.15	0.10
Cromolyn related compound B	1.9	0.10
Cromolyn related compound A	2.1	0.10
Any unspecified impurity	—	0.10
Total impurities	—	0.5

[a] 1-(2,6-Dihydroxyphenyl)ethan-1-one; also known as 2,6-Dihydroxyacetophenone.

SPECIFIC TESTS

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **pH ⟨791⟩:** 4.0–7.0

ADDITIONAL REQUIREMENTS

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

• **Labeling:** The label indicates that the Oral Solution is not to be used if it contains a precipitate or is discolored.

• **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▲ (USP 1-Aug-2022)

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

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

Chromatographic Database Information: Chromatographic Database

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