Saccharin Sodium

**Add the following:**

Additions to the monograph that are national USP text, are not part of the harmonized text, are marked with symbols (△) to specify this fact.

\[ C_7H_4NNaO_3S \cdot 2H_2O \]

C₇H₄NNaO₃S · 2H₂O 241.20

C₇H₄NNaO₃S 205.17

1,2-Benzisothiazol-3(2H)-one, 1,1-dioxide, sodium salt, dihydrate; 1,2-Benzisothiazolin-3-one 1,1-dioxide sodium salt dihydrate [6155-57-3].

**IMPURITIES**

**Change to read:**

**Organic Impurities**

- **PROCEDURE 1: LIMIT OF TOLUENESULFONAMIDES**

  **Internal standard solution:** 0.25 mg/mL of caffeine in methylene chloride

  **Standard stock solution:** 20.0 µg/mL of USP o-Toluenesulfonamide RS and 20.0 µg/mL of USP p-Toluenesulfonamide RS in methylene chloride

  **Sample stock solution:** 50 mL of the Sample stock solution with four quantities each of 50 mL of methylene chloride. Combine the lower layers, dry over anhydrous sodium sulfate, and filter. Wash the filter and the sodium sulfate with 10 mL of methylene chloride. Combine the solution and the washings, and evaporate almost to dryness in a water bath at a temperature not exceeding 40°C. Use a small quantity of methylene chloride, quantitatively transfer the residue into a suitable 10-mL tube, evaporate to dryness in a stream of nitrogen, and dissolve the residue in 1.0 mL of the Internal standard solution.

  **Blank solution:** Evaporate 200 mL of methylene chloride to dryness in a water bath at a temperature not exceeding 40°C. Dissolve the residue in 1 mL of methylene chloride.

  **Chromatographic system**

  (See Chromatography (621), System Suitability.)

  **Mode:** GC

  **Detector:** Flame ionization

  **Column:** 0.53-mm × 10-m fused silica, coated with G3 phase (film thickness, 2 µm)

  **Temperatures**

  **Injection port:** 250°C

  **Detector:** 250°C

  **Column:** 180°C

  **Carrier gas:** Nitrogen

  **Flow rate:** 10 mL/min

  **Injection volume:** 1 µL

  **Split ratio:** 2:1

**System suitability samples:**

- **Standard solution and Blank solution**

  [NOTE—The substances are eluted in the following order: o-toluenesulfonamide, p-toluenesulfonamide, and caffeine.]
Saccharin

Suitability requirements: No peaks at the retention times for the internal standard, o-toluenesulfonamide, or p-toluenesulfonamide, Blank solution
Resolution: NLT 1.5 between o-toluenesulfonamide and p-toluenesulfonamide, Standard solution
Analysis
Samples: Standard solution and Sample solution
Acceptance criteria: If any peaks due to o-toluenesulfonamide and p-toluenesulfonamide appear in the chromatogram of the Sample solution, the ratio of their areas to that of caffeine (internal standard) in USP 39 (2014) is NMT the corresponding ratio in the chromatogram of the Standard solution.
Individual impurities: See Table 1.

<table>
<thead>
<tr>
<th>Name</th>
<th>Acceptance Criteria, NMT (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>o-Toluenesulfonamide</td>
<td>10</td>
</tr>
<tr>
<td>p-Toluenesulfonamide</td>
<td>10</td>
</tr>
</tbody>
</table>

**Procedure 2: Limit of Benzoate and Salicylate**

Sample solution: 50 mg/mL
Analysis: To 10 mL of the Sample solution add 5 drops of 6 N acetic acid, and then add 3 drops of ferric chloride TS.
Acceptance criteria: No precipitate or violet color appears.

**SPECIFIC TESTS**

**Water Determination (921), Method 1** NMT 15.0%

**Change to read:**

- **Readily Carbonizable Substances (271)**
  - Matching fluid A: Cobaltous chloride CS, ferric chloride CS, cupric sulfate CS, and water (0.1: 0.4: 0.1: 4.4)
  - Sample solution: 40 mg/mL in sulfuric acid [94.5%–95.5% (w/w) of H₂SO₄], maintained at 48°–50° for 10 min
  - Acceptance criteria: The Sample solution has no more color than Matching fluid A, when viewed against a white background.

**Change to read:**

- **Acidity or Alkalinity**
  - Sample solution: 100 mg/mL in carbon dioxide-free water
  - Analysis: To 10 mL of the Sample solution add 1 drop of phenolphthalein TS.
  - Acceptance criteria: No red or pink color is produced. Then add 1 drop of 0.1 N sodium hydroxide: a red or pink color is produced.

**Change to read:**

- **Clarity of Solution**
  - Hydrazine solution: 10.0 mg/mL of hydrazine sulfate in water (Note—Allow to stand for 4–6 h.)
  - Methenamine solution: Transfer 2.5 g of methenamine to a 100-mL glass-stoppered flask, add 25.0 mL of water, insert the glass stopper, and mix to dissolve.
  - Primary opalescent suspension: Transfer 25.0 mL of Hydrazine solution to the Methenamine solution in the 100-mL glass-stoppered flask. Mix, and allow to stand for 24 h. [Note—This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. The suspension must not adhere to the glass and must be well mixed before use.]
  - Opalescence standard: Transfer 15.0 mL of the Primary opalescent suspension, dilute with water to 1000 mL, and mix. [Note—This suspension should not be used beyond 24 h after preparation.]

**Reference Suspension A**: Opalescence standard and water (1 in 20)

**Reference Suspension B**: Opalescence standard and water (1 in 10)

Sample solution: 200 mg/mL in water
Analysis
Samples: Reference suspension A, Reference suspension B, Sample solution, and water
Transfer a sufficient portion of the Sample solution to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of Reference suspension A, Reference suspension B, and water to separate matching test tubes. Compare solutions in diffused daylight, viewing vertically against a black background (see Spectrophotometry and Light-Scattering (851), Visual Comparison).

Acceptance criteria: The Sample solution shows the same clarity as that of water, or its opalescence is NMT that of Reference suspension A.

**Change to read:**

- **Color of Solution**
  - Diluent: 10-g/L solution of hydrochloric acid
  - Standard stock solution: Ferric chloride CS, cobaltous chloride CS, cupric sulfate CS, and Diluent (3.0: 3.0: 2.4: 1.6)
  - Standard solution: Standard stock solution and Diluent (1 in 100). [Note—Prepare the Standard solution immediately before use.]

Sample solution: Use the Sample solution from the test for Clarity of Solution.
Analysis
Samples: Standard solution, Sample solution, and water
Transfer a sufficient portion of the Sample solution to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of the Standard solution and water to separate, matching test tubes. Compare the solutions in diffused daylight, viewing vertically against a white background (see Spectrophotometry and Light-Scattering (851), Visual Comparison).

Acceptance criteria: The Sample solution has the appearance of water or is not more intensely colored than the Standard solution.
ADDITIONAL REQUIREMENTS

Change to read:

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at room temperature.

Change to read:

- **LABELING:** Where the quantity of saccharin sodium is indicated in the labeling of any preparation containing Saccharin Sodium, this shall be expressed in terms of saccharin (C₇H₅NO₃S).

**USP REFERENCE STANDARDS**

- USP Saccharin Sodium RS
- USP o-Toluenesulfonamide RS
  - C₇H₆NO₂S 171.22
- USP p-Toluenesulfonamide RS
  - C₇H₅NO₂S 171.22