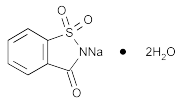
Saccharin Sodium

Add the following:

▲Portions of this monograph that are national *USP* text, and are not part of the harmonized text, are marked with symbols (◆◆) to specify this fact.▲*USP39*



$C_7H_4NNaO_3S \cdot 2H_2O$ 241.20

$C_7H_4NNaO_3S$ 205.17

1,2-Benzisothiazol-3(2*H*)-one, 1,1-dioxide, sodium salt, dihydrate;
1,2-Benzisothiazolin-3-one 1,1-dioxide sodium salt dihydrate [6155-57-3].
Anhydrous [128-44-9].

DEFINITION

Change to read:

Saccharin Sodium contains NLT 99.0% and NMT 101.0% of saccharin sodium ($C_7H_4NNaO_3S$)▲*USP39*, calculated on the anhydrous basis.

IDENTIFICATION

• **A. Infrared Absorption** ⟨197K⟩
Sample: Dry at 105° to constant weight.

Change to read:

• **B. Procedure**
Sample solution: 100 mg/mL
Potassium pyroantimonate solution: Dissolve 2 g of potassium pyroantimonate in 95 mL of hot water. Cool quickly, and add 50 mL of a potassium hydroxide solution (50 mg/mL) and 1 mL of sodium hydroxide solution (8.5 in 100). Allow to stand for 24 h, filter, and dilute with water to 150 mL.
Analysis: ●To 10 mL of the *Sample solution*● (ERR 1-Dec-2014) add 2 mL of 15% potassium carbonate, and heat to boiling. No precipitate is formed. Add 4 mL of *Potassium pyroantimonate solution*, and heat to boiling. Allow to cool in ice water and, if necessary, rub the inside of the test tube with a glass rod.
Acceptance criteria: A dense precipitate is formed.

Change to read:

• ▲◆▲*USP39***C.** Sodium salts impart an intense yellow color to a nonluminous flame.▲◆▲*USP39*

ASSAY

• **Procedure**
Sample solution: Dissolve 150 mg of Saccharin Sodium in 50 mL of glacial acetic acid. [Note—Slight heating may be needed to dissolve the sample.]
Analysis: Titrate the *Sample solution* with 0.1 N perchloric acid, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 20.52 mg of saccharin sodium ($C_7H_4NNaO_3S$).
Acceptance criteria: 99.0%–101.0% on the anhydrous basis

IMPURITIES

Delete the following:

●• **Heavy Metals,** *Method I* ⟨231⟩
Sample: 4 g in 46 mL of water
Analysis: Add 4 mL of dilute hydrochloric acid (1 in 12), mix, and rub the inner wall of the vessel with a glass rod until crystallization begins. Allow the solution to stand for 1 h, then pass through a dry filter, discarding the first 10 mL of the filtrate. Use 25 mL of the subsequent filtrate for the *Test Preparation*.
Acceptance criteria: NMT 10 ppm● (Official 1-Dec-2015)

Change to read:

Organic Impurities

• ▲◆▲*USP39***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
Standard solution: Evaporate 5.0 mL of *Standard stock solution* to dryness in a stream of nitrogen. Dissolve the residue in 1.0 mL of the *Internal standard solution*.
Sample stock solution: 200 mg/mL in water. If necessary, adjust the pH to 7–8 with 1 N sodium hydroxide or 1 N hydrochloric acid before final dilution.
Sample solution: Shake 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°. Using 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°. 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°
Detector: 250°
Column: 180°
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.]

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)• (ERR 1-Dec-2014) is NMT the corresponding ratio in the chromatogram of the *Standard solution*.
Individual impurities: See *Table 1*.

Table 1

Name	Acceptance Criteria, NMT (ppm)
o-Toluenesulfonamide	10
p-Toluenesulfonamide	10

▲◆▲*USP39*

- **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 I***:** 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)▲*USP39*
Sample solution: 40 mg/mL in sulfuric acid [94.5%–95.5% (w/w) of H_2SO_4], 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▲*USP39* color is produced. Then add 1 drop of 0.1 N sodium hydroxide: a ▲red or pink▲*USP39* color is produced.

Change to read:

- **CLARITY OF SOLUTION**

[NOTE—The *Sample solution* is to be compared to *Reference suspension A*▲▲*USP39* in diffused daylight 5 min after preparation of *Reference suspension A*.]▲▲*USP39*
Hydrazine solution: 10.0 mg/mL of hydrazine sulfate ▲in water.▲*USP39* [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. ▲▲*USP39*]
Opalescence standard: Transfer 15.0 mL of the *Primary opalescent suspension*, dilute ▲with water to 1000 mL, and mix.▲*USP39* [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▲*USP39*
Analysis
Samples: ▲▲*USP39**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▲*USP39* to separate matching test tubes. Compare solutions in diffused daylight, viewing vertically against a black background (see *Spectrophotometry and Light-Scattering* ⟨851⟩*, Visual Comparison*).
[NOTE—The diffusion of light must be such that *Reference suspension A* can readily be distinguished from water, and that *Reference suspension B* can readily be distinguished from *Reference suspension A*.]
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**▲▲*USP39*

Diluent▲▲*USP39***:** 10-g/L solution of hydrochloric acid
Standard stock solution: Ferric chloride CS, cobaltous chloride CS, cupric sulfate CS, and *Diluent*▲▲*USP39* (3.0: 3.0: 2.4: 1.6)
Standard solution: *Standard stock solution* and *Diluent* ▲▲*USP39* (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: ▲▲*USP39**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*▲▲*USP39* 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▲▲*USP39* or is not more intensely colored than the *Standard solution*.

ADDITIONAL REQUIREMENTS

Change to read:

- ▲◆▲*USP39* **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at room temperature.▲◆▲*USP39*

Change to read:

- ▲◆▲*USP39* **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 ($C_7H_5NO_3S$).▲◆▲*USP39*
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Saccharin Sodium RS
  USP *o*-Toluenesulfonamide RS
  $C_7H_9NO_2S$ 171.22
  USP *p*-Toluenesulfonamide RS
  $C_7H_9NO_2S$ 171.22