- **FORMIC ACID**

Mobile phase: Diluted perchloric acid (5 in 1000)
Standard solution: 10 µg/mL of formic acid in water
Sample stock solution: 20 mg/mL of Povidone in water
Sample solution: Transfer a suspension of strongly acidic ion exchange resin (use the hydrogen form of ion-exchange resin) in water to a column of about 0.8 cm in inside diameter to give a packing depth of about 20 mm in length, and keep the strongly acidic ion-exchange resin layer constantly immersed in water. Pour 5 mL of water, and adjust the flow rate so that water drops at a rate of about 20 drops/min. When the level of the water is near the top of the strongly acidic ion-exchange resin layer, add 100 mL of the *Sample stock solution* into the column. After dropping 2 mL of the solution, collect 1.5 mL of the solution, and use this as the *Sample solution*.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4- to 8-mm × 25- to 30-cm; 5- to 10-µm packing L17
Column temperature: 30°
[NOTE—Adjust the flow rate so that the retention time of formic acid is about 11 min.]
Injection size: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 2.0% of formic acid for 6 injections, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Record the chromatograms, and measure the responses for the formic acid peak.
Calculate the percentage of formic acid in the sample taken:

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

r_U = peak response of formic acid from the *Sample solution*
r_S = peak response of formic acid from the *Standard solution*
C_S = concentration of formic acid in the *Standard solution* (mg/mL)
C_U = concentration of Povidone in the *Sample solution* (mg/mL), calculated on the anhydrous basis
Acceptance criteria: NMT 0.5%

SPECIFIC TESTS

- **pH** ⟨**791**⟩

Sample solution: 50 mg/mL in water
Acceptance criteria: 3.0–5.0 for Povidone having a nominal K-value of 30 or less; 4.0–7.0 for Povidone having a nominal K-value greater than 30

- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 5.0%
- **K-VALUE**

Sample solution: Weigh a quantity of undried Povidone equivalent on the anhydrous basis to the amount specified in *Table 1*.

Table 1

Nominal K-value	Quantity (g)
≤18	5.00
>18 to ≤95	1.00
>95	0.10

Dissolve it in 50 mL of water in a 100-mL volumetric flask, and dilute to volume. Allow to stand for 1 h.

Analysis
Sample: *Sample solution*
Determine the viscosity of the *Sample solution*, using a capillary-tube viscosimeter (see *Viscosity* ⟨911⟩), at 25 ± 0.2°. Calculate the K-value of Povidone:

$$\text{Result} = \left[\sqrt{300c\log z + (c + 1.5c\log z)^2} + 1.5c\log z - c\right] \Big/ \left(0.15c + 0.003c^2\right)$$

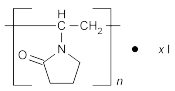
c = weight, on the anhydrous basis, of the specimen tested in each 100.0 mL of solution (g)
z = viscosity of the *Sample solution* relative to that of water

Acceptance criteria
K-value of Povidone having a stated (nominal) K-value of NMT 15: 85.0%–115.0% of the stated values
K-value of Povidone having a stated K-value or a stated K-value range with an average of more than 15: 90.0%–108.0% of the stated value or of the average of the stated range

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **LABELING:** Label it to state, as part of the official title, the K-value or K-value range of Povidone.

Povidone–Iodine



$(C_6H_9NO)_n \cdot xI$
2-Pyrrolidinone, 1-ethenyl-, homopolymer, compd. with iodine.
1-Vinyl-2-pyrrolidinone polymer, compound with iodine [25655-41-8].

» Povidone–Iodine is a complex of Iodine with Povidone. It contains not less than 9.0 percent and not more than 12.0 percent of available iodine (I), calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

Identification—

A: Add 1 drop of a solution (1 in 10) to a mixture of 1 mL of starch TS and 9 mL of water: a deep blue color is produced.

B: Spread 1 mL of a solution (1 in 10) over an area of about 20 cm × 20 cm on a glass plate, and allow to air-dry at room temperature in an atmosphere of low humidity overnight: a brown, dry, non-smearing film is formed, and it dissolves readily in water.

Loss on drying ⟨731⟩**—**Dry 5.0 g of it at 105° until the difference between two successive weighings at 1-hour intervals is not greater than 5.0 mg: it loses not more than 8.0% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.025%, from 2 g.

Iodide ion—

Determination of total iodine—Dissolve about 500 mg of Povidone–Iodine, accurately weighed, in 100 mL of water in a 250-mL conical flask. Add sodium bisulfite TS until the color of iodine has disappeared. Add 25.0 mL of 0.1 N silver nitrate VS and 10 mL of nitric acid, and mix. Titrate the excess silver nitrate with 0.1 N ammonium thiocyanate VS, using ferric ammonium sulfate TS as the indicator. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.1 N silver nitrate is equivalent to 12.69 mg of I. From the percentage of total iodine, calculated on the dried basis, subtract the

percentage of available iodine (see *Assay for available iodine*), to obtain the percentage of iodide ion. Not more than 6.6%, calculated on the dried basis, is found.

Heavy metals, *Method II* ⟨231⟩**:** 0.002%.

Nitrogen content, *Method II* ⟨461⟩**—**Not less than 9.5% and not more than 11.5% of N is found, calculated on the dried basis.

Assay for available iodine—Place about 5 g of Povidone–Iodine, accurately weighed, in a 400-mL beaker, and add 200 mL of water. Cover the beaker, and stir by mechanical means at room temperature for not more than 1 hour to dissolve as completely as possible. Titrate immediately with 0.1 N sodium thiosulfate VS, adding 3 mL of starch TS as the endpoint is approached. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N sodium thiosulfate is equivalent to 12.69 mg of I.

Povidone-Iodine Topical Aerosol

» Povidone-Iodine Topical Aerosol is a solution of Povidone-Iodine under nitrogen in a pressurized container. It contains not less than 85.0 percent and not more than 120.0 percent of the labeled amount of iodine (I).

Packaging and storage—Preserve in pressurized containers, and avoid exposure to excessive heat.

Identification—Spray Topical Aerosol into a beaker or flask until about 50 mL has been collected, and allow to stand for 5 minutes to allow the entrapped propellant to escape. (Retain portions of the solution so obtained for the *pH* and *Assay* procedures.) The solution meets the requirements of the following tests.

A: Add 1 mL of a dilution containing about 0.05% of iodine to a mixture of 1 mL of starch TS and 9 mL of water: a deep blue color is produced.

B: Transfer 10 mL to a 50-mL conical flask, avoiding contact with the neck of the flask. Cover the mouth of the flask with a small disk of filter paper, and wet it with 1 drop of starch TS: no blue color appears within 60 seconds.

pH ⟨791⟩**—**The pH of the solution prepared for the *Identification* tests is not more than 6.0.

Other requirements—It meets the requirements for *Pressure Test*, *Minimum Fill*, and *Leakage Test* under *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩.

Assay—Transfer an accurately measured volume of the solution of Topical Aerosol prepared for the *Identification* tests, equivalent to about 50 mg of iodine, to a 100-mL beaker, and dilute with water to a total volume of not less than 30 mL. Titrate immediately with 0.02 N sodium thiosulfate VS, determining the endpoint potentiometrically, using a platinum-calomel electrode system. Perform a blank determination, and make any necessary correction. Each mL of 0.02 N sodium thiosulfate is equivalent to 2.538 mg of iodine (I).

Povidone-Iodine Ointment

» Povidone-Iodine Ointment is an emulsion, solution, or suspension of Povidone-Iodine in a suitable water-soluble ointment base. It contains not less than 85.0 percent and not more than 120.0 percent of the labeled amount of iodine (I).

Packaging and storage—Preserve in tight containers.

Identification—

A: Add 1 mL of an alcohol dilution of it containing about 0.05% of iodine to a mixture of 1 mL of starch TS and 9 mL of water: a deep blue color is produced.

B: Place 10 g in a 50-mL beaker, avoiding contact with the walls of the beaker. Cover the mouth of the beaker with a disk of filter paper, and wet it with 1 drop of starch TS: no blue color appears within 60 seconds.

Minimum fill ⟨755⟩**:** meets the requirements.

pH ⟨791⟩**:** between 1.5 and 6.5, determined in a solution (1 in 20).

Assay—Transfer an accurately weighed quantity of Ointment, equivalent to about 50 mg of iodine, to a 100-mL beaker, add water to make a total volume of not less than 30 mL, and stir until the ointment is dissolved. Titrate immediately with 0.02 N sodium thiosulfate VS, determining the endpoint potentiometrically, using a platinum-calomel electrode system. Perform a blank determination, and make any necessary correction. Each mL of 0.02 N sodium thiosulfate is equivalent to 2.538 mg of I.

Povidone-Iodine Cleansing Solution

» Povidone-Iodine Cleansing Solution is a solution of Povidone-Iodine with one or more suitable surface-active agents. It contains not less than 85.0 percent and not more than 120.0 percent of the labeled amount of iodine (I). It may contain a small amount of alcohol.

Packaging and storage—Preserve in tight containers.

Identification—

A: It responds to *Identification* tests *A* and *B* under *Povidone-Iodine Topical Aerosol*.

B: To 2 mL of it in a glass-stoppered test tube add 1 mL of peanut oil and 4 mL of water, and shake vigorously for 10 seconds. Allow to stand for 3 minutes: a stable emulsion is formed.

pH ⟨791⟩**:** between 1.5 and 6.5.

Alcohol content (*if present*) ⟨611⟩**:** between 90.0% and 110.0% of the labeled amount of C_2H_5OH.

Assay—Transfer to a 100-mL beaker an accurately measured volume of Solution, equivalent to about 50 mg of iodine, and add water to make a total volume of not less than 30 mL. Titrate immediately with 0.02 N sodium thiosulfate VS, determining the endpoint potentiometrically, using a platinum-calomel electrode system. Perform a blank determination, and make any necessary correction. Each mL of 0.02 N sodium thiosulfate is equivalent to 2.538 mg of I.

Povidone-Iodine Topical Solution

» Povidone-Iodine Topical Solution is a solution of Povidone-Iodine. It contains not less than 85.0 percent and not more than 120.0 percent of the labeled amount of iodine (I). It may contain a small amount of alcohol.

Packaging and storage—Preserve in tight containers.

Identification—It responds to *Identification* tests *A* and *B* under *Povidone-Iodine Topical Aerosol*.

pH ⟨791⟩**:** between 1.5 and 6.5.

Alcohol content (*if present*) ⟨611⟩**:** between 90.0% and 110.0% of the labeled amount of C_2H_5OH.