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 in (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
Column temperature: 30°C
[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:

\[
\text{Result} = \left( \frac{r_0}{r_1} \right) \times \left( \frac{C_1}{C_0} \right) \times 100
\]

\(r_0\) = peak response of formic acid from the Sample solution
\(r_1\) = peak response of formic acid from the Standard solution
\(C_1\) = concentration of formic acid in the Standard solution (mg/mL)
\(C_0\) = 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>
<thead>
<tr>
<th>Nominal K-value</th>
<th>Quantity (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18</td>
<td>5.00</td>
</tr>
<tr>
<td>&gt; 18 to &lt; 95</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt; 95</td>
<td>0.10</td>
</tr>
</tbody>
</table>

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°C. Calculate the K-value of Povidone:

\[
\text{Result} = \left( \frac{300c \log z + (c - 1.5c \log z)^2}{1.15c \log z - c} \right) \times 0.003c + 1
\]

\(c\) = 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

B: NMT 20% for Povidone having a nominal K-value of 30 or less; NMT 4.0% for Povidone having a nominal K-value of 4.0–7.0

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

(C₆H₉NO)₂ · x I
2-Pyrrolidinone, 1-ethenyl-, homopolymer, compd. with iodine. 1-Vinyl-2-pyrrolidinone polymer, compound with iodine [23655-41-8].

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°C 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
utain the percentage of iodide ion. Not more than 6.6%, cal-
culated 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 dis-
solve 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 thio-
sulfate is equivalent to 12.69 mg of I.

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**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 30 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 pro-
cedures.) 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, equiva-
 lent 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 elec-
trode 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).

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**Povidone-Iodine Cleansing Solution**

» Povidone-Iodine Cleansing Solution is a solu-
ton 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 con-
tain 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 C2H5OH.

**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, deter-
mining 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.

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**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 C2H5OH.