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U.S. PHARMACOPEIA
The Standard of Quality℠

Packaging and storage—Preserve in tight containers.

Identification—

A: It meets the requirements of the flame test for *Sodium* ⟨191⟩.

B: Add 2 mL of 15% potassium carbonate TS to 2 mL of Oral Solution, boil, and cool. Add 4 mL of potassium pyroantimonate TS: a dense precipitate is formed *(presence of sodium)*.

C: To 2 mL of a dilution of Oral Solution (1 in 20) add 5 mL of sodium cobaltinitrite TS: a yellow precipitate is not formed immediately *(absence of potassium)*.

D: It meets the requirements of the tests for *Citrate* ⟨191⟩, 3 to 5 drops of Oral Solution and 20 mL of the mixture of pyridine and acetic anhydride being used.

Uniformity of dosage units ⟨905⟩—

FOR ORAL SOLUTION PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

Deliverable volume ⟨698⟩—

FOR ORAL SOLUTION PACKAGED IN MULTIPLE-UNIT CONTAINERS: meets the requirements.

pH ⟨791⟩: between 4.0 and 4.4.

Assay for sodium—

Potassium stock solution, Sodium stock solution, Lithium diluent solution, and *Standard preparation*—Prepare as directed in the *Assay for sodium and potassium* under *Tricitrates Oral Solution*.

Assay preparation—Transfer an accurately measured volume of Oral Solution, equivalent to about 1 g of sodium citrate dihydrate, to a 100-mL volumetric flask, dilute with water to volume, and mix. Transfer 50 µL of this solution to a 10-mL volumetric flask, dilute with *Lithium diluent solution* to volume, and mix.

Procedure—Using a suitable flame photometer, adjusted to read zero with *Lithium diluent solution,* concomitantly determine the sodium flame emission readings for the *Standard preparation* and the *Assay preparation* at the wavelength of maximum emission at about 589 nm. Calculate the quantity, in g, of Na in each mL of Oral Solution taken by the formula:

$$(14.61/25V)(22.99/58.44)(R_{U,Na}/R_{S,Na})$$

in which 14.61 is the weight, in g, of sodium chloride in the *Sodium stock solution; V* is the volume, in mL, of Oral Solution taken, 22.99 is the atomic weight of sodium; 58.44 is the molecular weight of sodium chloride; and $R_{U,Na}$ and $R_{S,Na}$ are the sodium emission readings obtained for the *Assay preparation* and the *Standard preparation,* respectively.

Assay for sodium citrate—

Cation-exchange column—Mix 10 g of styrene-divinylbenzene cation-exchange resin with 50 mL of water in a suitable beaker. Allow the resin to settle, and decant the supernatant until a slurry of resin remains. Pour the slurry into a 15-mm × 30-cm glass chromatographic tube (having a sealed-in, coarse-porosity fritted disk and fitted with a stopcock), and allow to settle as a homogeneous bed. Wash the resin bed with about 100 mL of water, closing the stopcock when the water level is about 2 mm above the resin bed.

Procedure—Transfer an accurately measured volume of Oral Solution, equivalent to about 1 g of sodium citrate dihydrate, to a 100-mL volumetric flask; dilute with water to volume; and mix. Pipet 5 mL of this solution carefully onto the top of the resin bed in the *Cation-exchange column.* Place a 250-mL conical flask below the column, open the stopcock, and allow to flow until the solution has entered the resin bed. Elute the column with 60 mL of water at a flow rate of about 5 mL per minute, collecting about 65 mL of the eluate. Add 5 drops of phenolphthalein TS to the eluate, swirl the flask, and titrate with 0.02 N sodium hydroxide VS. Record the buret reading, and calculate the volume *(B)* of 0.02 N sodium hydroxide consumed. Calculate the quantity, in mg, of sodium citrate dihydrate ($C_6H_5Na_3O_7 \cdot 2H_2O$) in each mL of the Oral Solution taken by the formula:

$$[1.961B(20/V)] - [(294.10/210.14)C]$$

in which 1.961 is the equivalent, in mg, of $C_6H_5Na_3O_7 \cdot 2H_2O$, of each mL of 0.02 N sodium hydroxide; V is the volume, in mL, of Oral Solution taken; 294.10 and 210.14 are the molecular weights of sodium citrate dihydrate and citric acid monohydrate, respectively; and C is the concentration, in mg per mL, of citric acid monohydrate in the Oral Suspension, as obtained in the *Assay for citric acid.*

Assay for citric acid—Transfer an accurately measured volume of Oral Solution, equivalent to about 0.67 g of citric acid monohydrate, to a 100-mL volumetric flask; dilute with water to volume; and mix. Pipet 5 mL of this solution into a suitable flask, add 25 mL of water and 5 drops of phenolphthalein TS, and titrate with 0.02 N sodium hydroxide VS to a pink endpoint. Record the buret reading, and calculate the volume *(A)* of 0.02 N sodium hydroxide consumed. Calculate the quantity, in mg, of citric acid monohydrate ($C_6H_8O_7 \cdot H_2O$) in each mL of the Oral Solution taken by the formula:

$$1.401A(20/V)$$

in which 1.401 is the equivalent, in mg, of $C_6H_8O_7 \cdot H_2O$, of each mL of 0.02 N sodium hydroxide; and V is the volume, in mL, of Oral Solution taken.

Sodium Fluoride

NaF 41.99

Sodium fluoride.

Sodium fluoride [*7681-49-4*].

» Sodium Fluoride contains not less than 98.0 percent and not more than 102.0 percent of NaF, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Identification—

A: Place 1 g in a platinum crucible *in a well-ventilated hood,* add 15 mL of sulfuric acid, and cover the crucible with a piece of clear, polished glass. Heat the crucible on a steam bath for 1 hour, remove the glass cover, rinse it in water, and wipe dry: the surface of the glass is etched.

B: A solution (1 in 25) responds to the tests for *Sodium* ⟨191⟩.

Acidity or alkalinity—Dissolve 2.0 g in 40 mL of water in a platinum dish, add 10 mL of a saturated solution of potassium nitrate, cool the solution to 0°, and add 3 drops of phenolphthalein TS. If no color appears, a pink color persisting for 15 seconds is produced by not more than 2.0 mL of 0.10 N sodium hydroxide. If the solution is colored pink by the addition of phenolphthalein TS, it is rendered colorless by not more than 0.50 mL of 0.10 N sulfuric acid. Save the neutralized solution for the test for *Fluosilicate.*

Loss on drying ⟨731⟩—Dry it at 150° for 4 hours: it loses not more than 1.0% of its weight.

Fluosilicate—After the solution from the test for *Acidity or alkalinity* has been neutralized, heat to boiling, and titrate while hot with 0.10 N sodium hydroxide until a permanent pink color is obtained: not more than 1.5 mL of 0.10 N sodium hydroxide is required.

Chloride—Dissolve 300 mg in 20 mL of water, and add 200 mg of boric acid, 1 mL of nitric acid, and 1 mL of 0.1 N silver nitrate: any turbidity produced is not greater than that of a blank to which has been added 1.0 mL of 0.0010 N hydrochloric acid (0.012%).

Heavy metals ⟨231⟩—To 1 g, in a platinum dish or crucible, under a hood, add 1 mL of water and 3 mL of sulfuric acid, and heat at as low a temperature as practicable until all of the sulfuric acid has been expelled. Dissolve the residue in 20 mL of water, neutralize the solution to phenolphthalein TS with ammonium hydroxide, add 1 mL of glacial acetic acid, dilute with water to 45 mL, filter, and use 30 mL of the filtrate for the test: the limit is 0.003%.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

(Official until July 1, 2007)

Assay—[NOTE—Store all solutions, except the *Buffer solution,* in plastic containers.]

Buffer solution and *Standard preparations*—Prepare as directed in the *Assay* under *Sodium Fluoride Oral Solution.*

Assay preparation—Transfer about 100 mg of Sodium Fluoride, accurately weighed, to a 250-mL volumetric flask. Add 50 mL of water, mix for 5 minutes, dilute with water to volume, and mix. Transfer 10.0 mL of this solution to a 50-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Sodium Fluoride Oral Solution*. Calculate the quantity, in mg, of NaF in the portion of Sodium Fluoride taken by the formula:

$$(41.99 / 18.998)(1.25C)$$

in which 41.99 is the molecular weight of sodium fluoride; 18.998 is the atomic weight of fluorine; and C is the determined concentration of fluoride, in µg per mL, in the *Assay preparation*.

Sodium Fluoride Oral Solution

» Sodium Fluoride Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of NaF.

Packaging and storage—Preserve in tight containers, plastic containers being used for Oral Solution having a pH below 7.5.

Labeling—Label Oral Solution in terms of the content of sodium fluoride (NaF) and in terms of the content of fluoride ion.

USP Reference standards ⟨11⟩—*USP Sodium Fluoride RS.*

Identification—

A: Transfer 0.1 mL of Oral Solution to a small test tube, and add 0.1 mL of a freshly prepared mixture (1 : 1) of sodium alizarinsulfonate solution (1 in 1000) and zirconyl nitrate solution (1 in 1000) in 7 N hydrochloric acid: a yellow color is produced.

B: If necessary, reduce the volume of a portion of it by heating on a steam bath to a reduced volume containing about 10 mg of sodium per mL: the solution so obtained responds to the tests for *Sodium* ⟨191⟩.

Assay—[NOTE—Store all solutions, except *Buffer solution*, in plastic containers.]

Buffer solution—Dissolve 57 mL of glacial acetic acid, 58 g of sodium chloride, and 4 g of (1,2-cyclohexylenedinitrilo)tetraacetic acid in 500 mL of water. Adjust with 5 N sodium hydroxide to a pH of 5.25 ± 0.25, dilute with water to 1000 mL, and mix.

Standard preparations—Dissolve an accurately weighed quantity of USP Sodium Fluoride RS quantitatively in water to obtain a solution containing 420 µg per mL. Each mL of this solution (*Standard preparation A*) contains 190 µg of fluoride ion (10^{-2} M). Transfer 25.0 mL of *Standard preparation A* to a 250-mL volumetric flask, dilute with water to volume, and mix. This solution (*Standard preparation B*) contains 19 µg of fluoride ion per mL (10^{-3} M). Transfer 25.0 mL of *Standard preparation B* to a 250-mL volumetric flask, dilute with water to volume, and mix. This solution (*Standard preparation C*) contains 1.9 µg of fluoride ion per mL (10^{-4} M).

Assay preparation—Transfer an accurately measured volume of Oral Solution, equivalent to about 10 mg of fluoride, to a 500-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Pipet 20 mL of each *Standard preparation* and of the *Assay preparation* into separate plastic beakers each containing a plastic-coated stirring bar. Pipet 20 mL of *Buffer solution* into each beaker. Concomitantly measure the potentials (see *pH* ⟨791⟩), in mV, of the solutions from the *Standard preparations* and of the solution from the *Assay preparation*, with a pH meter capable of a minimum reproducibility of ±0.2 mV and equipped with a fluoride-specific ion-indicating electrode and a calomel reference electrode. [NOTE—When taking measurements, immerse the electrodes in the solution, stir on a magnetic stirrer having an insulated top until equilibrium is attained (1 to 2 minutes), and record the potential. Rinse and dry the electrodes between measurements, taking care to avoid damaging the crystal of the specific-ion electrode.] Plot the logarithms of the fluoride-ion concentrations, in µg per mL, of the *Standard preparations* versus potential, in mV. From the measured potential of the *Assay preparation* and the standard response line, determine the concentration, C, in µg per mL, of fluoride ion in the *Assay preparation*. Calculate the quantity, in mg, of fluoride ion in each mL of the Oral Solution taken by the formula:

$$0.5(C / V)$$

in which C is the determined concentration of fluoride, in µg per mL, in the *Assay preparation*, and V is the volume, in mL, of Oral Solution taken. Multiply the quantity of fluoride ion by 2.21 to obtain the quantity of NaF.

Sodium Fluoride Tablets

» Sodium Fluoride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of NaF.

Packaging and storage—Preserve in tight containers.

Labeling—Label the Tablets in terms of the content of sodium fluoride (NaF) and in terms of the content of fluoride ion. The Tablets that are to be chewed may be labeled as Sodium Fluoride Chewable Tablets.

USP Reference standards ⟨11⟩—*USP Sodium Fluoride RS.*

Identification—

A: Disperse 20 finely powdered Tablets in 25 mL of water, shake, and filter: a portion of the filtrate responds to the tests for *Sodium* ⟨191⟩.

B: Evaporate a 10-mL portion of the filtrate obtained in *Identification* test *A* to dryness. To the residue add a mixture of 0.1 mL of freshly prepared sodium alizarinsulfonate solution (1 in 1000) and 0.1 mL of a 1 in 1000 solution of zirconyl nitrate in 7 N hydrochloric acid: a yellow color is produced.

Disintegration ⟨701⟩: 15 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—[NOTE—Store all solutions, except *Buffer solution*, in plastic containers.]

Buffer solution and *Standard preparations*—Prepare as directed in the *Assay* under *Sodium Fluoride Oral Solution*.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 10 mg of fluoride, to a plastic 500-mL conical flask containing 400 mL of water. Heat on a steam bath for 25 minutes with occasional shaking, cool to room temperature, transfer to a 500-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Sodium Fluoride Oral Solution*. Calculate the quantity, in mg, of fluoride ion in the portion of Tablets taken by the formula:

$$0.5C$$

in which C is the determined concentration, in µg per mL, of fluoride ion in the *Assay preparation*. Multiply the quantity of fluoride ion by 2.21 to obtain the quantity of NaF.

Sodium Fluoride and Acidulated Phosphate Topical Solution

» Sodium Fluoride and Acidulated Phosphate Topical Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of fluoride ion.

Packaging and storage—Preserve in tight plastic containers.

Labeling—Label Topical Solution in terms of the content of sodium fluoride (NaF) and in terms of the content of fluoride ion.

USP Reference standards ⟨11⟩—*USP Sodium Fluoride RS.*

pH ⟨791⟩—Place about 40 mL in a plastic beaker, add about 250 mg of quinhydrone, and stir for 1 minute, leaving some of the quinhydrone undissolved. Determine the pH using a hydrofluoric acid frit-junction calomel reference electrode and a hydrofluoric acid-resistant metallic electrode: the pH is between 3.0 and 4.5.

Other requirements—It responds to the *Identification* tests under *Sodium Fluoride and Phosphoric Acid Gel.*

Assay—

Buffer solution and *Standard preparations*—Prepare as directed in the *Assay* under *Sodium Fluoride Oral Solution.*

Assay preparation—Transfer an accurately measured volume of Topical Solution, equivalent to about 20 mg of fluoride ion, to a 1000-mL volumetric flask, add water to dissolve, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Sodium Fluoride Oral Solution.* Calculate the quantity, in mg, of fluoride ion in each mL of the Topical Solution taken by the formula:

$$C/V$$

in which C is the determined concentration of fluoride ion, in µg per mL, in the *Assay preparation*, and V is the volume, in mL, of Topical Solution taken.

Sodium Fluoride and Phosphoric Acid Gel

» Sodium Fluoride and Phosphoric Acid Gel contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of fluoride ion, in an aqueous medium containing a suitable viscosity-inducing agent.

Packaging and storage—Preserve in tight, plastic containers.

Labeling—Label Gel in terms of the content of sodium fluoride (NaF) and in terms of the content of fluoride ion.

USP Reference standards ⟨11⟩—*USP Sodium Fluoride RS.*

Identification—

A: Place a quantity of Gel, equivalent to about 500 mg of fluoride ion, in a platinum crucible in a well-ventilated hood, and add 15 mL of sulfuric acid. Cover the crucible with a piece of clear, polished glass, and heat on a steam bath for 1 hour. Remove the glass cover, rinse it in water, and dry: the glass surface exposed to vapors from the crucible is etched.

B: It responds to the tests for *Phosphate* ⟨191⟩.

Viscosity ⟨911⟩—Place a quantity of Gel in a suitable plastic container, insert the stopper securely, and allow to stand until the gel is free from air bubbles. Place it in a water bath maintained at a temperature of 25 ± 0.5° until it adjusts to the temperature of the water bath (30 minutes or longer). Do not stir the gel while it is in the bath. Remove the sample from the bath, stir the gel gently for 5 seconds, and without delay, using a rotational viscosimeter, determine the viscosity using the appropriate spindle to obtain a scale reading between 10% and 90% of full scale at a speed of 60 rpm or of 30 rpm. Calculate the viscosity, in centipoises, by multiplying the scale reading by the constant for the spindle and speed used: the viscosity is between 7000 and 20,000 centipoises.

pH ⟨791⟩—Place about 40 mL in a plastic beaker, add about 250 mg of quinhydrone, and stir for 1 minute, leaving some of the quinhydrone undissolved. Determine the pH using a hydrofluoric acid frit-junction calomel reference electrode and a platinum electrode: the pH is between 3.0 and 4.0.

Assay—[NOTE—Store all solutions, except *Buffer solution*, in plastic containers.]

Buffer solution and *Standard preparations*—Prepare as directed in the *Assay* under *Sodium Fluoride Oral Solution.*

Assay preparation—Transfer a quantity of Gel, equivalent to about 20 mg of fluoride ion, accurately weighed, to a 1000-mL volumetric flask, add water to dissolve, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Sodium Fluoride Oral Solution.* The quantity, in mg, of fluoride ion in the portion of Gel taken is equivalent to C, the determined concentration of fluoride ion, in µg per mL, in the *Assay preparation.*

Sodium Fluoride and Phosphoric Acid Topical Solution

» Sodium Fluoride and Phosphoric Acid Topical Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of fluoride ion.

Packaging and storage—Preserve in tight, plastic containers.

Labeling—Label Topical Solution in terms of the content of sodium fluoride (NaF) and in terms of the content of fluoride ion.

USP Reference standards ⟨11⟩—*USP Sodium Fluoride RS.*

pH ⟨791⟩—Using 40 mL of Topical Solution, proceed as directed in the test for *pH* under *Sodium Fluoride and Phosphoric Acid Gel:* the pH is between 3.0 and 4.5.

Other requirements—It responds to the *Identification* tests under *Sodium Fluoride and Phosphoric Acid Gel.*

Assay—[NOTE—Store all solutions, except *Buffer solution*, in plastic containers.]

Buffer solution and *Standard preparations*— Prepare as directed in the *Assay* under *Sodium Fluoride Oral Solution.*

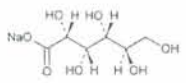
Assay preparation—Transfer an accurately measured volume of Topical Solution, equivalent to about 20 mg of fluoride ion, to a 1000-mL volumetric flask, add water to dissolve, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Sodium Fluoride Oral Solution.* Calculate the quantity, in mg, of fluoride ion in each mL of the Topical Solution taken by the formula:

$$C/V$$

in which C is the determined concentration of fluoride ion, in µg per mL, in the *Assay preparation*, and V is the volume, in mL, of Topical Solution taken.

Sodium Gluconate



$C_6H_{11}NaO_7$ 218.14

D-Gluconic acid, monosodium salt.

Monosodium D-gluconate [*527-07-1*].

» Sodium Gluconate contains not less than 98.0 percent and not more than 102.0 percent of $C_6H_{11}NaO_7$.