

BRIEFING

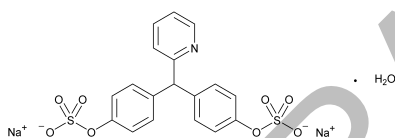
**Sodium Picosulfate.** On the basis of validated methods of analysis, a new *USP* Pending Standards monograph for this drug substance is proposed. The liquid chromatographic procedure in the test for *Related compounds* is based on analyses performed with the Restek Pinnacle ODS brand of L1 column. The typical retention time for the sodium picosulfate peak is 9 to 11 minutes.

(MD-GRE: E. Gonikberg)     RTS—C55188

**Add the following:**

■ **Sodium Picosulfate**

Draft 1.0



$C_{18}H_{13}NNa_2O_8S_2 \cdot H_2O$      499.42

4,4'-(2-Pyridylmethylene)diphenyl bis(hydrogen sulfate) disodium salt, monohydrate.

Sodium 4,4'-(pyridin-2-ylmethylene)bis(4,1-phenylene) disulfate, monohydrate.

4,4'-(Pyridin-2-ylmethylene)bisphenyl bis (sodium sulfate), monohydrate.

Anhydrous     [10040-45-6].

» Sodium Picosulfate contains not less than 98.5 percent and not more than 100.5 percent of  $C_{18}H_{13}NNa_2O_8S_2$ , calculated on the anhydrous basis.

**Packaging and storage**—Preserve in tight, light-resistant containers. Store at room temperature.

**USP Reference standards** <11>—*USP Sodium Picosulfate RS*. *USP Sodium Picosulfate Related Compound A RS*.

**Color of solution** <631>—

*Reference solution*—Mix 0.75 mL of Matching Fluid O with 99.25 mL of dilute hydrochloric acid (10 g per 1000 mL).

*Test solution*—Dissolve 2.5 g of Sodium Picosulfate in 50 mL of water. [NOTE—Retain the remaining portion of the *Test solution* for the test for *Acidity and Alkalinity*.]

*Procedure*—Proceed as directed under *Color and Achromicity* <631>: the *Test solution* is not more intensely colored than the *Reference solution*.

**Identification**—

**A:** *Infrared Absorption* <197K>.

**B:** It meets the requirements of the pyroantimonate precipitate test for *Sodium* <191>.

**Acidity and Alkalinity**—To 10 mL of the *Test solution* retained from the test for *Color of solution* add a drop of phenolphthalein TS. The solution is colorless: not more than 0.25 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to pink.

**Water, Method Ia** (921): between 3.0% and 5.0%.

**Chloride** <221>—A 1.0-g portion shows no more chloride than corresponds to 0.30 mL of 0.020 N hydrochloric acid: not more than 0.02%.

**Sulfate** <221>—A 500-mg portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid: not more than 0.04%.

**Heavy metals, Method I** <231>: 0.001%.

**Related substances**—

*Phosphate buffer pH 7.5*—Transfer 2.3 g of dibasic sodium phosphate dihydrate to a 1-L flask, and dissolve in water. Add 200 mg of cetyltrimethylammonium bromide. Adjust with phosphoric acid to a pH of 7.5, and dilute with water to volume.

*Mobile phase*—Prepare a mixture of *Phosphate buffer pH 7.5* and acetonitrile (60 : 40).

*Diluent*—Prepare a mixture of *Phosphate buffer pH 7.5* and acetonitrile (1 : 1).

2 / Sodium Picosulfate

*Impurity solution*—Prepare a solution in *Diluent* containing 0.25 mg of USP Sodium Picosulfate Related Compound A RS per mL.

*System suitability solution*—Transfer about 2 mg of Sodium Picosulfate to a 100-mL volumetric flask, and dissolve in a small amount of water. Add 2.0 mL of the *Impurity solution*, dilute with water to volume, and mix.

*Test solution*—Transfer about 50.0 mg of Sodium Picosulfate to a 100-mL volumetric flask. Dissolve in, dilute with water to volume, and mix well. Transfer 10.0 mL to a 50-mL volumetric flask, dilute with water to volume, and mix.

*Chromatographic system* (see *Chromatography* <621>)—The liquid chromatograph is equipped with a 263-nm detector and a 4.6-mm × 15-cm column that contains 5-μm packing L1. The flow rate is about 1.0 mL per minute. The column temperature is maintained at 40°. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure*: the resolution between sodium picosulfate related compound A and sodium picosulfate is not less than 10.

*Procedure*—Inject about 40 μL of the *Test solution* into the chromatograph, record the chromatogram, identify the impurities listed in *Table 1*, and measure the peak areas. Calculate the percentage of each impurity in the portion of Sodium Picosulfate taken by the formula:

$$100(r_i/r_s)$$

in which  $r_i$  is the area of each individual impurity peak in the *Test solution*; and  $r_s$  is the sum of the areas of all peaks in the chromatogram of the *Test solution*.

**Assay**—Dissolve about 400 mg of Sodium Picosulfate, accurately weighed, in 80 mL of methanol. Titrate with 0.1 N perchloric acid VS and determine the endpoint potentiometrically. Each mL of 0.1 N perchloric acid is equivalent to 48.14 mg of C<sub>18</sub>H<sub>13</sub>NNa<sub>2</sub>O<sub>8</sub>S<sub>2</sub>.

Table 1

Name	Relative Retention Time	Limit (%)
4,4'-[(Pyridin-2-yl)methylene]bisphenol	0.3	0.2
4-[(Pyridin-2-yl)(4-hydroxyphenyl)methyl]phenyl sodium sulfate*	0.5	0.2
Sodium picosulfate	1.0	n/a
2,4'-[(Pyridin-2-yl)methylene]bisphenyl bis(sodium sulfate)	1.4	0.10
Any other individual impurity	—	0.10
Total impurities	—	0.5

\* USP Sodium Picosulfate Related Compound A RS.