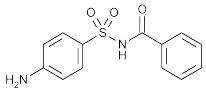
Assay—

Mobile phase, Internal standard solution, and *Standard preparation*—Prepare as directed in the *Assay* under *Triple Sulfa Vaginal Cream*.

Assay preparation—Weigh and finely powder not fewer than 10 Vaginal Inserts. Transfer an accurately weighed portion of the powder, equivalent to about 144 mg of sulfacetamide, 184 mg of sulfabenzamide, and 173 mg of sulfathiazole, to a 250-mL volumetric flask. Add 10.0 mL of water, and shake for 10 minutes. Add 10.0 mL of *Internal standard solution* and 100 mL of acetone, and shake for 30 minutes at low speed on a mechanical shaker. Dilute with acetone to volume, mix, and allow to stand for 30 minutes. Pipet 5 mL of the clear supernatant into a 50-mL volumetric flask, and evaporate on a steam bath with the aid of a gentle stream of nitrogen to dryness. Dissolve the residue in *Mobile phase,* dilute with *Mobile phase* to volume, and mix.

Chromatographic system and *Procedure*—Proceed with the Vaginal Inserts as directed in the *Assay* under *Triple Sulfa Vaginal Cream*.

Sulfabenzamide



$C_{13}H_{12}N_2O_3S$ 276.31
Benzamide, *N*-[(4-aminophenyl)sulfonyl]-.
N-Sulfanilylbenzamide [127-71-9].

» Sulfabenzamide contains not less than 99.0 percent and not more than 100.5 percent of $C_{13}H_{12}N_2O_3S$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩—
USP Sulfabenzamide RS

Clarity and color of solution—Dissolve 2.0 g in 15 mL of 1 N sodium hydroxide, with warming: a colorless to pale yellow solution having not more than a slight turbidity is produced.

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: To about 100 mg, suspended in 2 mL of water, add 100 mg of sodium bicarbonate: it dissolves with effervescence (*distinction from sulfanilamide*, *sulfapyridine*, *sulfathiazole*, *sulfadiazine*, and *sulfaguanidine*).

Melting range, *Class I* ⟨741⟩: between 180° and 184°.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 0.5% of its weight.

Selenium ⟨291⟩: 0.001%, a 300-mg test specimen and 3 mL of *Stock Solution* being used.

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

Ordinary impurities ⟨466⟩—

Test solution: methanol.

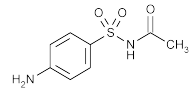
Standard solution: methanol.

Eluant: a mixture of chloroform, methanol, and glacial acetic acid (90:5:5).

Visualization: 1.

Assay—Transfer about 800 mg of Sulfabenzamide, accurately weighed, to a 125-mL conical flask, and dissolve in 25 mL of dimethylformamide. Add 3 drops of thymol blue TS (prepared with methanol), and titrate with 0.1 N sodium methoxide VS to a blue endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N sodium methoxide is equivalent to 27.63 mg of $C_{13}H_{12}N_2O_3S$.

Sulfacetamide



$C_8H_{10}N_2O_3S$ 214.24
Acetamide, *N*-[(4-aminophenyl)sulfonyl]-.
N-Sulfanilylacetamide [144-80-9].

» Sulfacetamide contains not less than 99.0 percent and not more than 100.5 percent of $C_8H_{10}N_2O_3S$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩—
USP Sulfacetamide RS

Clarity and color of solution—Dissolve about 200 mg in 5 mL of 1 N sodium hydroxide: a yellow to faintly yellow solution having not more than a trace of turbidity is produced.

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: Place about 500 mg in a test tube, heat gently until it boils, and cool: an oily liquid, which has the characteristic odor of acetamide, condenses on the walls of the test tube (*distinction from the sublimates of sulfadiazine*, *sulfamerazine*, *sulfamethazine*, *and sulfapyrazine*, *which are solids at room temperature*).

Melting range, *Class I* ⟨741⟩: between 181° and 184°.

Reaction—A solution (1 in 150) is acid to litmus.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Sulfate ⟨221⟩—Digest 1 g with 50 mL of water at about 70° for 5 minutes. Cool immediately to room temperature, and filter. A 25-mL portion of the filtrate so obtained shows no more sulfate than corresponds to 0.2 mL of 0.02 N sulfuric acid (0.04%).

Selenium ⟨291⟩: 0.003%, a 200-mg test specimen being used.

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

Assay—Proceed with Sulfacetamide as directed under *Nitrite Titration* ⟨451⟩. Each mL of 0.1 M sodium nitrite is equivalent to 21.42 mg of $C_8H_{10}N_2O_3S$.

Sulfacetamide Sodium

$C_8H_9N_2NaO_3S \cdot H_2O$ 254.24
Acetamide, *N*-[(4-aminophenyl)sulfonyl]-, monosodium salt, monohydrate.
N-Sulfanilylacetamide monosodium salt monohydrate [6209-17-2].
Anhydrous 236.23 [127-56-0].

» Sulfacetamide Sodium contains not less than 99.0 percent and not more than 100.5 percent of $C_8H_9N_2NaO_3S$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—
USP Sulfacetamide Sodium RS

Identification—

A: Dissolve about 1 g in 25 mL of water, adjust with 6 N acetic acid to a pH of between 4 and 5, and filter. Wash the precipitate with water, and dry at 105° for 2 hours: the sulfacetamide so obtained melts between 180° and 184°.

B: Place about 500 mg of the sulfacetamide obtained in *Identification* test *A* in a test tube, and heat gently until it boils: an oily liquid, which has the characteristic odor of acetamide, condenses on the walls of the test tube (*distinction from the sublimates of sulfadiazine, sulfamerazine, and sulfamethazine, which are solids at room temperature*).

C: The filtrate obtained in *Identification* test *A* responds to the tests for *Sodium* ⟨191⟩.

D: Dissolve about 100 mg in 5 mL of water, and add 5 drops of cupric sulfate TS: a light bluish green precipitate is formed, and it remains unchanged on standing.

E: Dissolve about 500 mg in 10 mL of dilute hydrochloric acid (1 in 10). To about one-half of the solution add 2 mL of trinitrophenol TS: a very heavy flocculent or almost gelatinous precipitate is formed. To the remainder of the solution add 3 drops of formaldehyde TS: a white precipitate is formed, and it changes to orange on standing (*distinction from sulfamethoxypyridazine*).

pH ⟨791⟩: between 8.0 and 9.5, in a solution (1 in 20).

Water, *Method I* ⟨921⟩: not more than 8.1%.

Selenium ⟨291⟩: 0.003%, a 200-mg test specimen being used.

Heavy metals—Dissolve 1.0 g in 25 mL of water, and add 5 drops of freshly prepared sodium sulfide TS: any color produced is not darker than that of a control made with 25 mL of water, 2.0 mL of *Standard Lead Solution* (see *Heavy Metals* ⟨231⟩), and 5 drops of sodium sulfide TS (0.002%).

Ordinary impurities ⟨466⟩—

Test solution: methanol.

Standard solution: methanol.

Eluant: a mixture of ethyl acetate, methanol, and ammonium hydroxide (17:6:5).

Visualization: 1.

Assay—Proceed with Sulfacetamide Sodium as directed under *Nitrite Titration* ⟨451⟩. Each mL of 0.1 M sodium nitrite is equivalent to 23.62 mg of $C_8H_9N_2NaO_3S$.

Sulfacetamide Sodium Ophthalmic Ointment

» Sulfacetamide Sodium Ophthalmic Ointment contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_8H_9N_2NaO_3S \cdot H_2O$. It is sterile.

Packaging and storage—Preserve in collapsible ophthalmic ointment tubes.

USP Reference standards ⟨11⟩—
USP Sulfacetamide Sodium RS

Identification—Dissolve a quantity of Ophthalmic Ointment, equivalent to about 1 g of sulfacetamide sodium, in 100 mL of ether in a separator, and extract the mixture with 25 mL of water. Wash the extract with 25 mL of ether, and warm the water extract on a steam bath to remove the last traces of ether. Adjust with 6 N acetic acid to a pH of between 4 and 5, and filter. Wash the precipitate with water, and dry at 105° for 2 hours: the sulfacetamide so obtained melts between 180° and 184°, and responds to *Identification* tests *B*, *D*, and *E* under *Sulfacetamide Sodium.*

Sterility ⟨71⟩: meets the requirements.

Metal particles—It meets the requirements of the test for *Metal Particles in Ophthalmic Ointments* ⟨751⟩.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of water, methanol, and glacial acetic acid (89:10:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Transfer about 50 mg of USP Sulfacetamide Sodium RS, accurately weighed, to a 40-mL centrifuge tube. Add 10.0 mL of dilute methanol (1 in 5), insert the stopper, and mix, using a vortex mixer, for about 3 minutes to dissolve the Reference Standard. Add 7.5 mL of heptane, insert the stopper, and mix, using a vortex mixer, for another 3 minutes. Centrifuge to effect separation of the phases. Withdraw and discard the upper heptane layer. Transfer 3.0 mL of the bottom layer to a 500-mL volumetric flask, add dilute methanol (1 in 5) to volume, and mix.

Assay preparation—Transfer an accurately weighed quantity of Ophthalmic Ointment, equivalent to about 100 mg of sulfacetamide sodium, to a 40-mL centrifuge tube. Add 15.0 mL of heptane, insert the stopper, and mix, using a vortex mixer, for about 3 minutes to dissolve the Ophthalmic Ointment. Add 20.0 mL of dilute methanol (1 in 5), insert the stopper, and mix, using a vortex mixer, for 3 minutes. Centrifuge to effect separation of the phases. Withdraw and discard the upper heptane layer. Transfer 3.0 mL of the bottom layer to a 500-mL volumetric flask, add dilute methanol (1 in 5) to volume, and mix.

System suitability preparation—Dissolve 3 mg of sulfanilamide in 100 mL of the *Standard preparation*, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation* and the *System suitability preparation*, and record the peak responses as directed for *Procedure:* the column efficiency determined from the analyte peak is not less than 1500 theoretical plates, the resolution, *R,* between the sulfacetamide and sulfanilamide peaks is not less than 3, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 90 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_8H_9N_2NaO_3S \cdot H_2O$ sulfacetamide sodium in the portion of Ophthalmic Ointment taken by the formula:

$$3.33(254.24 / 236.23)C(r_U / r_S)$$

in which 254.24 and 236.23 are the molecular weights of sulfacetamide sodium monohydrate and anhydrous sulfacetamide sodium, respectively, *C* is the concentration, in µg per mL, of sulfacetamide sodium, calculated on the anhydrous basis, in the *Standard preparation*, and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Sulfacetamide Sodium Ophthalmic Solution

» Sulfacetamide Sodium Ophthalmic Solution is a sterile solution containing not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_8H_9N_2NaO_3S \cdot H_2O$. It may contain suitable buffers, stabilizers, and antimicrobial agents.