less than 2.0; the column efficiency determined from the butalbital peak is not less than 2000 theoretical plates; and the relative standard deviations of the codeine, caffeine, aspirin, and butalbital responses for replicate injections are not more than 2.0%. Inject 10 µL of the *Salicylic acid solution*, and record the peak response as directed for *Procedure:* the salicylic acid peak has the same retention time as that of the aspirin peak obtained in the chromatogram of the *Standard preparation*. [NOTE—If the retention time of the salicylic acid peak differs from that of the aspirin peak, adjust the pH of the *Mobile phase* with 0.2 N potassium hydroxide or 1 M phosphoric acid so that the salicylic acid peak has the same retention time as that of the aspirin peak. The retention time of the salicylic acid peak decreases about 0.3 minute for each 0.1 pH increase. The retention time of the aspirin peak is essentially unaffected by such pH adjustments.]

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, using the 277-nm detector to record the caffeine and aspirin peak responses and the 210-nm detector to measure the codeine and butalbital responses, and measure the areas for the major peaks. Calculate the quantities, in mg, of caffeine ($C_8H_{10}N_4O_2$), aspirin ($C_9H_8O_4$), and butalbital ($C_{11}H_{16}N_2O_3$) in the portion of Capsules taken by the same formula:

$$200C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of the appropriate USP Reference Standard in the *Standard preparation;* and r_U and r_S are the peak responses of the corresponding analyte obtained from the *Assay preparation* and the *Standard preparation*, respectively. Calculate the quantity, in mg, of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$) in the portion of Capsules taken by the formula:

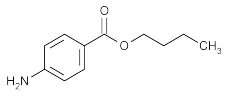
$$(406.37 / 397.37)(200C)(r_U / r_S)$$

in which 406.37 and 397.37 are the molecular weights of codeine phosphate hemihydrate and anhydrous codeine phosphate, respectively; C is the concentration, in mg per mL, of USP Codeine Phosphate RS in the *Standard preparation;* and r_U and r_S are the codeine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively. Correct the amount of aspirin obtained for the amount of salicylic acid present by the formula:

$$A - (0.01FA)$$

in which A is the quantity, in mg, of aspirin in the portion of Capsules taken to prepare the *Assay preparation;* and F is the percentage of salicylic acid obtained in the test for *Limit of free salicylic acid.*

Butamben



$C_{11}H_{15}NO_2$ 193.24
Benzoic acid, 4-amino-, butyl ester.
Butyl *p*-aminobenzoate [94-25-7].

» Butamben, dried over phosphorus pentoxide for 3 hours, contains not less than 98.0 per cent and not more than 101.0 per cent of $C_{11}H_{15}NO_2$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—
USP Butamben RS

Completeness and color of solution—One g dissolves completely in 30 mL of alcohol and in 30 mL of ether, and the solutions are colorless.

Identification, *Infrared Absorption* ⟨197K⟩.

Melting range, *Class I* ⟨741⟩: between 57° and 59°.

Reaction—Dissolve 1 g in 10 mL of neutralized alcohol: a clear solution results. Dilute this solution with 10 mL of water, and add 2 drops of phenolphthalein TS and 1 drop of 0.1 N sodium hydroxide: a red color is produced.

Loss on drying ⟨731⟩—Dry it over phosphorus pentoxide for 3 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Chloride—To a solution of 200 mg in 10 mL of alcohol add 1 mL of 2 N nitric acid and a few drops of silver nitrate TS: no opalescence is produced.

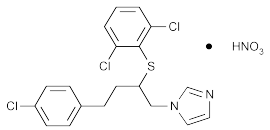
Heavy metals, *Method I* ⟨231⟩—Dissolve 2 g in 2 mL of 1 N acetic acid and sufficient alcohol to make 25 mL: the limit is 0.001%.

Assay—

Ferrocyphen indicator solution—Dissolve, without warming, 0.5 g of ferrocyphen in 50 mL of sulfuric acid.

Procedure—Dissolve about 400 mg of Butamben, previously dried and accurately weighed, in a mixture of 100 mL of water and 20 mL of hydrochloric acid. Add 1 mL of *Ferrocyphen indicator solution*. Cool the solution in an ice bath to about 10 °, and titrate with 0.1 M sodium nitrite VS to a violet endpoint that is stable for not less than three minutes. Per form a blank determination, and make any necessar y correction. Each mL of 0.1 M sodium nitrite is equivalent to 19.32 mg of $C_{11}H_{15}NO_2$.

Butoconazole Nitrate



$C_{19}H_{17}Cl_3N_2S \cdot HNO_3$ 474.79
1*H*-Imidazole, 1-[4-(4-chlorophenyl)-2-[(2,6-dichlorophenyl)thio] butyl-, mononitrate, (±)-.
(±)-1-[4-(*p*-Chlorophenyl)-2-[(2,6-dichlorophenyl)-thio]butyl]imidazole mononitrate [64872-77-1].

» Butoconazole Nitrate contains not less than 98.0 percent and not more than 102.0 per cent of $C_{19}H_{17}Cl_3N_2S \cdot HNO_3$, calculated on the dried basis.

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

USP Reference standards ⟨11⟩—
USP Butoconazole Nitrate RS

Identification, *Infrared Absorption* ⟨197K⟩.

Loss on drying ⟨731⟩—Dry it in vacuum at 60 ° for 3 hours: it loses not more than 1.0% of its weight.

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

Ordinary impurities ⟨466⟩—

Test solution: a mixture of methylene chloride and methanol (2:1).

Standard solutions: a mixture of methylene chloride and methanol (2:1).

Adsorbent: a 0.25-mm layer of chromatographic silica gel.

Eluant: a mixture of chloroform, tetrahydrofuran, cyclohexane, and ammonium hydroxide (18:18:13:1).

Visualization: 22.

Assay—

Phosphate buffer—Dissolve 2.18 g of monobasic potassium phosphate and 4.18 g of dibasic potassium phosphate in 900 mL of water, dilute with water to 1000 mL, and mix.

Mobile phase—Prepare a filtered and degassed mixture of methanol and *Phosphate buffer* (3:1), making adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Butoconazole Nitrate RS in *Mobile phase*, and quantitatively dilute with *Mobile phase* to obtain a solution having a known concentration of about 0.2 mg per mL.

Assay preparation—Transfer about 20 mg of Butoconazole Nitrate, accurately weighed, to a 100-mL volumetric flask, and dissolve in *Mobile phase*. Dilute with *Mobile phase* to volume, mix, and filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 229-nm detector and a 4.6-mm × 25-cm column that contains packing L1 and is maintained at 40°. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the column efficiency determined from the analyte peak is not less than 2800 theoretical plates; the tailing factor for the analyte peak is not more than 1.5; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 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 $C_{19}H_{17}Cl_3N_2S \cdot HNO_3$ in the portion of Butoconazole Nitrate taken by the formula:

$$100C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Butoconazole Nitrate RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Butoconazole Nitrate Vaginal Cream

» Butoconazole Nitrate Vaginal Cream is Butoconazole Nitrate in a suitable cream base. It contains not less than 90.0 per cent and not more than 110.0 per cent of the labeled amount of butoconazole nitrate ($C_{19}H_{17}Cl_3N_2S \cdot HNO_3$).

Packaging and storage—Preserve in collapsible tubes or tight containers. Avoid excessive heat and avoid freezing.

USP Reference standards ⟨11⟩—
USP Butoconazole Nitrate RS

Identification—Prepare a mixture of the *Standard preparation* and the *Assay preparation* (1:1), prepared as directed in the *Assay*, and chromatograph as directed in the *Assay:* the chromatogram so obtained exhibits two main peaks, corresponding to butoconazole nitrate and the internal standard.

Minimum fill ⟨755⟩: meets the requirements.

Assay—

Acetate buffer—Dissolve 1.4 g of potassium acetate in 980 mL of water, adjust with about 2 mL of glacial acetic acid to a pH of 4.3 ± 0.1, dilute with water to 1000 mL, and mix. Adjust the buffer molarity (0.018-0.072 M) as necessary to obtain suitable chromatographic performance. Increased retention time may be achieved by a decrease in the buffer molarity.

Mobile phase—Prepare a filtered and degassed mixture of methanol and *Acetate buffer* (65:35). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of methanol and *Acetate buffer* (6:4).

Internal standard solution—Dissolve 1-benzylimidazole in methanol to obtain a solution containing about 1.6 mg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Butoconazole Nitrate RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to obtain a stock solution having a known concentration of about 400 µg per mL. Transfer 2.0 mL of this stock solution and 3.0 mL of *Internal standard solution* to a 50-mL flask, add 35.0 mL of *Diluent*, and mix.

Assay preparation—Place about 200 mL of methanol in a 250-mL volumetric flask. Transfer to the flask an accurately weighed quantity of Vaginal Cream, equivalent to about 100 mg of butoconazole nitrate, and sonicate until the Vaginal Cream is dissolved completely. Cool to room temperature, dilute with methanol to volume, and mix. Transfer 2.0 mL of this solution to a 50-mL flask, add 3.0 mL of *Internal standard solution* and 35.0 mL of *Diluent*, and mix. Allow the precipitated excipients which form to rise to the top of the solution, remove them by aspiration, and discard. Centrifuge or filter the remaining solution.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 225-nm detector and a 4.6-mm × 25-cm column that contains packing L9 which has been converted to the potassium form by the use of 0.555 M potassium acetate solution. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.6 for butoconazole nitrate and 1.0 for 1-benzylimidazole; the resolution, *R*, between the analyte and internal standard peaks is not less than 4.0; the column efficiency determined from the analyte peak is not less than 1100 theoretical plates; the tailing factor for the analyte peak is not more than 2.1; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 20 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 butoconazole nitrate ($C_{19}H_{17}Cl_3N_2S \cdot HNO_3$) in the portion of Vaginal Cream taken by the formula:

$$0.25C(R_U / R_S)$$

in which C is the concentration, in µg per mL, of USP Butoconazole Nitrate RS in the stock solution used to prepare the *Standard preparation;* and R_U and R_S are the peak response ratios of butoconazole nitrate to the internal standard obtained from the *Assay preparation* and the *Standard preparation*, respectively.