2003

USP

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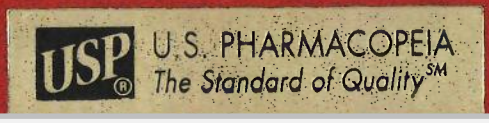
The Official Compendia of Standards



2003

USP 26

THE UNITED STATES PHARMACOPEIA

NF 21

THE NATIONAL FORMULARY

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disperse the specimen using a vortexing mixer. Add 5.0 mL of a solution of methanol in water (45 in 50), insert the stopper securely, shake vigorously for 2 minutes, and centrifuge at 2500 rpm for 3 minutes. Remove the lower, aqueous alcohol phase, and transfer this test solution to a stoppered vial. Apply separately 20 µL of the test solution and 20 µL of a Standard solution of USP Alclometasone Dipropionate RS in methanol containing about 0.25 mg per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture, and dry the applications with the aid of a stream of nitrogen. Position the plate in a saturated, unlined chromatographic chamber, and develop the chromatograms in a solvent system consisting of a mixture of chloroform and acetone (7 : 1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Observe the plate under short-wavelength UV light: the R_f value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

Microbial limits ⟨61⟩—It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Minimum fill ⟨755⟩: meets the requirements.

Assay—

Methanol-water solution—Dilute 450 mL of methanol with water to 500 mL, and mix.

0.05 M Monobasic potassium phosphate—Transfer 3.40 g of monobasic potassium phosphate to a 500-mL volumetric flask, add water to volume, and mix.

Mobile phase—Prepare a filtered and degassed mixture of methanol and *0.05 M Monobasic potassium phosphate* (2 : 1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Transfer about 30 mg of betamethasone dipropionate to a 200-mL volumetric flask, add *Methanol-water solution* to volume, and mix.

Standard preparation—Transfer about 20 mg of USP Alclometasone Dipropionate RS, accurately weighed, to a 200-mL volumetric flask, add *Methanol-water solution* to volume, and mix. Transfer 5.0 mL of this solution to a small stoppered flask, add 5.0 mL of *Internal standard solution*, and mix to obtain a *Standard preparation* having a known concentration of about 0.05 mg of USP Alclometasone Dipropionate RS per mL.

Assay preparation—Transfer an accurately weighed quantity of Ointment, equivalent to about 0.5 mg of alclometasone dipropionate, to a 50-mL centrifuge tube, add 10 mL of 2,2,4-trimethylpentane, insert a stopper securely into the tube, and disperse the specimen using a vortexing mixer. Add 5.0 mL of *Internal standard solution* and 5.0 mL of *Methanol-water solution*, insert the stopper securely, shake vigorously for 2 minutes, and centrifuge at 2500 rpm for 3 minutes. Remove the lower, aqueous alcohol phase, and transfer this *Assay preparation* to a stoppered vial.

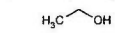
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains packing L1. The flow rate is about 1.2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the resolution, *R*, between the analyte and internal standard peaks is not less than 3.0, and the relative standard deviation for replicate injections is not more than 2%.

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. The relative retention times are about 0.7 for alclometasone dipropionate and 1.0 for betamethasone dipropionate. Calculate the quantity, in mg, of $C_{28}H_{37}ClO_7$ in the portion of Ointment taken by the formula:

$$10C(R_U/R_S),$$

in which *C* is the concentration, in mg per mL, of USP Alclometasone Dipropionate RS in the *Standard preparation*, and R_U and R_S are the peak height ratios obtained from the and the *Standard preparation*, respectively.

Alcohol



C_2H_6O 46.07
Ethanol.
Ethyl alcohol [*64-17-5*].

» Alcohol contains not less than 92.3 percent and not more than 93.8 percent, by weight, corresponding to not less than 94.9 percent and not more than 96.0 percent, by volume, at 15.56°, of C_2H_5OH.

Packaging and storage—Preserve in tight containers, remote from fire.

Identification—

A: Mix 5 drops in a small beaker with 1 mL of potassium permanganate solution (1 in 100) and 5 drops of 2 N sulfuric acid, and cover the beaker immediately with a filter paper moistened with a solution recently prepared by dissolving 0.1 g of sodium nitroferricyanide and 0.25 g of piperazine in 5 mL of water: an intense blue color is produced on the filter paper, the color becoming paler after a few minutes.

B: To 5 mL of a solution (1 in 10) add 1 mL of 1.0 N sodium hydroxide, then slowly (over a period of 3 minutes) add 2 mL of 0.1 N iodine: the odor of iodoform develops, and a yellow precipitate is formed within 30 minutes.

Specific gravity ⟨841⟩: between 0.812 and 0.816 at 15.56°, indicating between 92.3% and 93.8%, by weight, or between 94.9% and 96.0%, by volume, of C_2H_5OH.

Acidity—To 50 mL, in a glass-stoppered flask, add 50 mL of recently boiled water. Add phenolphthalein TS, and titrate with 0.020 N sodium hydroxide to a pink color that persists for 30 seconds: not more than 0.90 mL of 0.020 N sodium hydroxide is required for neutralization.

Limit of nonvolatile residue—Evaporate 40 mL in a tared dish on a water bath, and dry at 105° for 1 hour: the weight of the residue does not exceed 1 mg.

Water-insoluble substances—Dilute it with an equal volume of water: the mixture is clear and remains clear for 30 minutes after cooling to 10°.

Aldehydes and other foreign organic substances—Place 20 mL in a glass-stoppered cylinder that has been thoroughly cleaned with hydrochloric acid, then rinsed with water and finally with the Alcohol to be tested. Cool the contents to approximately 15°, and add, by means of a carefully cleaned pipet, 0.10 mL of 0.10 N potassium permanganate, noting accurately the time of addition. Mix at once by inverting the stoppered cylinder, and allow it to stand at 15° for 5 minutes: the pink color does not entirely disappear.

Amyl alcohol and nonvolatile, carbonizable substances—Allow 25 mL to evaporate spontaneously from a porcelain dish, carefully protected from dust, until the surface of the dish is barely moist: no red or brown color is produced immediately upon the addition of a few drops of sulfuric acid.

Limit of acetone and isopropyl alcohol—To 1.0 mL add 1.0 mL of water, 1.0 mL of a saturated solution of dibasic sodium phosphate, and 3.0 mL of a saturated solution of potassium permanganate. Warm the mixture to 45° to 50°, and allow to stand until the permanganate color is discharged. Add 3.0 mL of 2.5 N sodium hydroxide, and filter, without washing, through a sintered-glass filter. Prepare a control by mixing 1.0 mL of the saturated solution of dibasic sodium phosphate, 3.0 mL of 2.5 N sodium hydroxide, 80 µg of acetone, and 5.0 mL of water. To each solution add 1 mL of furfural solution (1 in 100), allow to stand for 10 minutes, then to 1.0 mL of each solution add 3 mL of hydrochloric acid: any pink color produced in the test solution is not more intense than that in the control.

Methanol—To 1 drop add 1 drop of water, 1 drop of dilute phosphoric acid (1 in 20), and 1 drop of potassium permanganate solution (1 in 20). Mix, allow to stand for 1 minute, and add sodium metabisulfite solution (1 in 20), dropwise, until the permanganate color is dis-

tropic acid TS, and heat on a water bath at 60° for 10 minutes: any violet color should not exceed that produced by 0.04 mg of methanol in 1 mL of water, treated in the same way as the sample.

Dehydrated Alcohol

C_2H_6O 46.07
Ethanol.
Ethyl alcohol [*64-17-5*].

» Dehydrated Alcohol contains not less than 99.2 percent, by weight, corresponding to not less than 99.5 percent, by volume, at 15.56°, of C_2H_5OH.

Packaging and storage—Preserve in tight containers, remote from fire.

Identification—

A: Mix 5 drops in a small beaker with 1 mL of potassium permanganate solution (1 in 100) and 5 drops of 2 N sulfuric acid, and cover the beaker immediately with a filter paper moistened with a solution recently prepared by dissolving 0.1 g of sodium nitroferricyanide and 0.25 g of piperazine in 5 mL of water: an intense blue color is produced on the filter paper, the color becoming paler after a few minutes.

B: To 5 mL of a solution (1 in 10) add 1 mL of 1.0 N sodium hydroxide, then slowly (over a period of 3 minutes) add 2 mL of 0.1 N iodine: the odor of iodoform develops, and a yellow precipitate is formed within 30 minutes.

Specific gravity ⟨841⟩: not more than 0.7962 at 15.56°, indicating not less than 99.2% of C_2H_5OH by weight.

Acidity—To 50 mL, in a glass-stoppered flask, add 50 mL of recently boiled water. Add phenolphthalein TS, and titrate with 0.020 N sodium hydroxide to a pink color that persists for 30 seconds: not more than 0.90 mL of 0.020 N sodium hydroxide is required for neutralization.

Limit of nonvolatile residue—Evaporate 40 mL in a tared dish on a water bath, and dry at 105° for 1 hour: the weight of the residue does not exceed 1 mg.

Water-insoluble substances—Dilute it with an equal volume of water: the mixture is clear and remains clear for 30 minutes after cooling to 10°.

Aldehydes and other foreign organic substances—Place 20 mL in a glass-stoppered cylinder that has been thoroughly cleaned with hydrochloric acid, then rinsed with water and finally with the Dehydrated Alcohol to be tested. Cool the contents to approximately 15°, and add, by means of a carefully cleaned pipet, 0.10 mL of 0.10 N potassium permanganate, noting accurately the time of addition. Mix at once by inverting the stoppered cylinder, and allow it to stand at 15° for 5 minutes: the pink color does not entirely disappear.

Amyl alcohol and nonvolatile, carbonizable substances—Allow 25 mL to evaporate spontaneously from a porcelain dish, carefully protected from dust, until the surface of the dish is barely moist: no red or brown color is produced immediately upon the addition of a few drops of sulfuric acid.

Ultraviolet absorbance—Record the UV absorption spectrum between 340 nm and 235 nm in a 1-cm cell, with water in a matched cell in the reference beam: the absorbance is not more than 0.08 at 240 nm, and 0.02 between 270 nm and 340 nm, and the curve drawn through these points is smooth.

Limit of acetone and isopropyl alcohol—To 1.0 mL add 1 mL of water, 1 mL of a saturated solution of dibasic sodium phosphate, and 3 mL of a saturated solution of potassium permanganate. Warm the mixture to 45° to 50°, and allow to stand until the permanganate color is discharged. Add 3 mL of 2.5 N sodium hydroxide, and 80 µg of acetone in 9 mL. To each solution add 1 mL of furfural solution (1 in 100), and allow to stand for 10 minutes, then to 1.0 mL of each solution add 3 mL of hydrochloric acid: any pink color produced in the test solution is not more intense than that in the control.

Methanol—To 1 drop add 1 drop of water, 1 drop of dilute phosphoric acid (1 in 20), and 1 drop of potassium permanganate solution (1 in 20). Mix, allow to stand for 1 minute, and add sodium metabisulfite solution (1 in 20), dropwise, until the permanganate color is discharged. If a brown color remains, add 1 drop of the dilute phosphoric acid. To the colorless solution add 5 mL of freshly prepared chromotropic acid TS, and heat on a water bath at 60° for 10 minutes: no violet color appears.

Dehydrated Alcohol Injection

» Dehydrated Alcohol Injection is Dehydrated Alcohol suitable for parenteral use.

Packaging and storage—Preserve in single-dose containers, preferably of Type I glass. The container may contain an inert gas in the headspace.

Specific gravity ⟨841⟩: not more than 0.8035 at 15.56°, indicating not less than 96.8%, by weight, of C_2H_5OH.

Acidity—To 50 mL, in a glass-stoppered flask, add 50 mL of recently boiled water. Add phenolphthalein TS, and titrate with 0.020 N sodium hydroxide to a pink color that persists for 30 seconds: not more than 10.0 mL of 0.020 N sodium hydroxide is required for neutralization.

Other requirements—It meets the requirements for *Identification*, *Limit of nonvolatile residue*, *Water-insoluble substances*, *Aldehydes and other foreign organic substances*, *Amyl alcohol and nonvolatile, carbonizable substances*, *Ultraviolet absorbance*, *Limit of acetone and isopropyl alcohol*, and *Methanol* under *Dehydrated Alcohol*, and meets the requirements under *Injections* ⟨1⟩.

Rubbing Alcohol

» Rubbing Alcohol and all preparations under the classification of Rubbing Alcohols are manufactured in accordance with the requirements of the U.S. Treasury Department, Bureau of Alcohol, Tobacco, and Firearms, Formula 23-H (8 parts by volume of acetone, 1.5 parts by volume of methyl isobutyl ketone, and 100 parts by volume of ethyl alcohol) being used. It contains not less than 68.5 percent and not more than 71.5 percent by volume of dehydrated alcohol, the remainder consisting of water and the denaturants, with or without color additives, and perfume oils. Rubbing Alcohol contains, in each 100 mL, not less than 355 mg of sucrose octaacetate or not less than 1.40 mg of denatonium benzoate. The preparation may be colored with one or more color additives, listed by the FDA for use in drugs. A suitable stabilizer may be added. Rubbing Alcohol complies with the requirements of the Bureau of Alcohol, Tobacco, and Firearms of the U.S. Treasury Department.

NOTE—Rubbing Alcohol is packaged, labeled, and sold in accordance with the regulations issued by the U.S. Treasury Department, Bureau of Alcohol, Tobacco, and Firearms.