

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

§ 449.550b Nystatin-iodochlorhydroxyquin ointment.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Nystatin-iodochlorhydroxyquin ointment is composed of nystatin and iodochlorhydroxyquin in a suitable and harmless ointment base. Each gram contains 100,000 units of nystatin and 10 milligrams of iodochlorhydroxyquin. Its nystatin content is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of units of nystatin that it is represented to contain. Its iodochlorhydroxyquin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of iodochlorhydroxyquin that it is represented to contain. It passes the identity test for iodochlorhydroxyquin. Its moisture content is not more than 0.5 percent. The nystatin used conforms to the standards prescribed by § 449.50(a)(1). The iodochlorhydroxyquin used conforms to the standards prescribed by U.S.P. XVIII.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The nystatin used in making the batch for potency, loss on drying, pH, and identity.

(b) The iodochlorhydroxyquin used in making the batch for all U.S.P. XVIII specifications.

(c) The batch for nystatin content, iodochlorhydroxyquin content, iodochlorhydroxyquin identity, and moisture.

(ii) Samples required:

(a) The nystatin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of seven immediate containers.

(b) *Tests and methods of assay—(1) Nystatin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an

accurately weighed representative portion of the sample into a high-speed glass blender jar containing sufficient dimethylformamide to give a convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and dilute with sufficient dimethylformamide to yield a stock solution containing 400 units of nystatin per milliliter (estimated). Further dilute an aliquot of the stock solution with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

(2) *Iodochlorhydroxyquin content—(i) Reagents.* (a) Ferric chloride reagent. Dissolve 1.0 gram of ferric chloride ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$) in a mixture of 1.0 milliliter of concentrated hydrochloric acid and sufficient distilled water to make 1 liter.

(b) Acetone, reagent grade.

(c) 2-Methoxyethanol, reagent grade.

(ii) *Preparation of standard solution.* Dissolve an accurately weighed portion of iodochlorhydroxyquin U.S.P. reference standard in sufficient 2-methoxyethanol to make a solution containing 1.0 milligram of iodochlorhydroxyquin per milliliter. Transfer 5.0 milliliters of this standard solution to a 50-milliliter volumetric flask.

(iii) *Preparation of sample solution.* Accurately weigh a portion of the sample equivalent to 50 milligrams of iodochlorhydroxyquin into a 125-milliliter Erlenmeyer flask. Add 50 milliliters of acetone, warm on a steam bath, and shake gently. Cool to room temperature and filter contents through a pledget of glass wool into a 100-milliliter volumetric flask. Wash the Erlenmeyer flask with two 20-milliliter portions of acetone and filter the washings into the volumetric flask. Dilute to volume with acetone and mix thoroughly. Transfer a 10-milliliter aliquot of the acetone solution to a 50-milliliter volumetric flask and evaporate on a steam bath. To the residue, add 20 milliliters of 2-methoxyethanol and swirl to dissolve the iodochlorhydroxyquin.

(iv) *Procedure.* To each flask containing standard solution and sample solution, respectively, add 2.0 milliliters of ferric chloride reagent and dilute to

volume with 2-methoxyethanol. Mix thoroughly. Using a suitable spectrophotometer equipped with 1.0-centimeter cells and a blank prepared by diluting 2.0 milliliters of ferric chloride reagent to 50 milliliters with 2-methoxyethanol, determine the absorbance of the sample and standard solutions at 650 nanometers. Set the instrument to 100-percent transmission with the blank.

(v) *Calculation.*

Milligrams of iodochlorhydroxyquin per gram of sample = $(\text{Absorbance of sample} \times 50) / (\text{Absorbance of standard} \times \text{Weight of sample in grams})$

(3) *Iodochlorhydroxyquin identity.* Proceed as directed in § 436.400 of this chapter, preparing the sample solution as follows: Accurately weigh a portion of the sample equivalent to 50 milligrams of iodochlorhydroxyquin into a 125-milliliter Erlenmeyer flask. Add 50 milliliters of acetone, warm on a steam bath, and shake gently. Cool to room temperature and filter contents through a pledget of glass wool into a 100-milliliter volumetric flask. Wash the Erlenmeyer flask with two 20-milliliter portions of acetone and filter the washings into the volumetric flask. Dilute to volume with acetone and mix thoroughly.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter.

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§ 449.550c Nystatin-neomycin sulfate-gramicidin-triamcinolone acetone ointment; nystatin-neomycin sulfate-gramicidin-fludrocortisone acetate ointment.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* The drug is nystatin, neomycin sulfate, gramicidin, and either triamcinolone acetonide or fludrocortisone acetate in a suitable ointment base. Each gram contains 100,000 units of nystatin, 2.5 milligrams of neomycin, 0.25 milligram of gramicidin, and either 1.0 milligram of triamcinolone acetonide or 1.0 milligram of fludrocortisone acetate. Its nystatin content is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of units of nystatin that it is represented to

contain. Its neomycin content is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of milligrams of neomycin that it is represented to contain. Its gramicidin content is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of milligrams of gramicidin that it is represented to contain. Its moisture content is not more than 0.5 percent. The nystatin used conforms to the standards prescribed by § 449.50(a)(1) (i), (iii), (iv), and (v). The neomycin sulfate used conforms to the standards prescribed by § 444.42a(a)(1) of this chapter. The gramicidin used conforms to the standards prescribed by § 448.25(a)(1) (i), (iii), (iv), (v), and (vi) of this chapter.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The nystatin used in making the batch for potency, loss on drying, pH, and identity.

(b) The neomycin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(c) The gramicidin used in making the batch for potency, loss on drying, residue on ignition, melting point, crystallinity, and identity.

(d) The batch for potency and moisture.

(ii) Samples required:

(a) The nystatin used in making the batch: 10 packages, each consisting of 300 milligrams.

(b) The neomycin sulfate used in making the batch: 10 packages, each consisting of 300 milligrams.

(c) The gramicidin used in making the batch: 10 packages, each consisting of 500 milligrams.

(d) The batch: A minimum of seven immediate containers.

(b) *Tests and methods of assay—(1) Potency—(i) Nystatin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Blend an accurately weighed representative portion in a high-speed glass blender for 3 to 5 minutes with sufficient dimethylformamide to give a