

of each containing approximately 5 grams.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Neomycin content*. Proceed as directed in §444.542a(b)(1)(ii). Its content of neomycin is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of neomycin that it is represented to contain.

(ii) *Polymyxin content*. Proceed as directed in §436.105 of this chapter, except add to each concentration of the polymyxin standards response line a quantity of neomycin to yield the same concentration of neomycin as that present when the sample is diluted to contain 10 units of polymyxin B per milliliter. Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 10 percent potassium phosphate buffer, pH 6.0 (solution 6), and shake well. Remove the buffer layer and repeat the extraction procedure with each of three more 20 to 25 milliliter quantities of solution 6. Combine the extractives in a suitable volumetric flask and fill to volume with solution 6. Further dilute an aliquot with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated). Its content of polymyxin is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of units of polymyxin that it is represented to contain.

§ 444.542f Neomycin sulfate-gramicidin topical ointment; neomycin sulfate-gramicidin-triamcinolone acetone ointment; neomycin sulfate-gramicidin-fludrocortisone acetate ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Each gram of neomycin sulfate-gramicidin topical ointment contains 2.5 milligrams of neomycin and 0.25 milligram of gramicidin. Neomycin sulfate-gramicidin-triamcinolone acetone ointment is an ointment containing, in each gram, 2.5 milligrams of neomycin, 0.25 milligram of gramicidin, and 1.0 milligram of triamcinolone acetone. Neomycin

sulfate-gramicidin-fludrocortisone acetate ointment is an ointment containing, in each gram, 2.5 milligrams of neomycin, 0.25 milligram of gramicidin, and 1.0 milligram of fludrocortisone acetate. If it is intended for ophthalmic use, it is sterile. Their moisture content is not more than 1.0 percent. The neomycin sulfate used conforms to the standards prescribed by §444.42a(a)(1)(i), (v), (vi), and (vii), and in addition if it is used in the preparation of an ophthalmic ointment, paragraph (a)(1) of that section. The gramicidin used conforms to the standards prescribed by §448.25(a)(1)(i), (iii), (iv), (v), and (vi) of this chapter, and in addition if it is used in the preparation of an ophthalmic ointment, paragraph (a)(1) of that section. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Labeling*. If it contains a steroid or it is intended for ophthalmic use, it shall be labeled in accordance with the requirements of §432.5 of this chapter, and its expiration date is 12 months. If it does not contain a steroid or it is not intended for ophthalmic use, each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On the label of the immediate container and on the outside wrapper or container, if any:

(a) The batch mark.

(b) The name and quantity of each active ingredient contained in the drug.

(c) An expiration date that is 12 months after the month during which the batch was certified.

(ii) On the label of the immediate container or other labeling attached to or within the package, adequate directions under which the layman can use the drug safely and efficaciously.

(3) *Requests for certifications; 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 neomycin sulfate used in making the batch for potency, moisture, pH, and identity.

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

(c) The batch for neomycin content, gramicidin content, and moisture, and for sterility if it is intended for ophthalmic use.

(ii) Samples required:

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

(b) The gramicidin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(c) The batch:

(1) For all tests except sterility: A minimum of six immediate containers.

(2) For sterility testing: Twenty immediate containers, collected at regular intervals throughout each filling operation.

(d) In case of an initial request for certification, each other ingredient used in making the batch: One package of each containing approximately 5 grams.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Neomycin content*. Proceed as directed in §444.542a(b)(1). Its content of neomycin 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.

(ii) *Gramicidin content*. Proceed as directed in §448.25(b)(1) of this chapter, except prepare the sample for assay by the following method: Place an accurately weighed representative portion into a separatory funnel. Dissolve the ointment in approximately 50 milliliters of petroleum ether. Extract this solution with four 20-milliliter portions of 80 percent alcohol prepared from alcohol U.S.P. XX. Combine the extractives in a suitable volumetric flask, bring to volume with alcohol U.S.P. XX, and mix well. From this stock solution, dilute an aliquot with alcohol U.S.P. XX to the reference concentration. Its content of gramicidin 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.

(2) *Sterility*. If the ointment is intended for ophthalmic use, proceed as

directed in §436.20 of this chapter, using the method described in paragraph (e)(3) of that section. However, if the ointment is not soluble in isopropyl myristate proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use 100 milligrams in lieu of 300 milligrams of solids.

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

[39 FR 19046, May 30, 1974, as amended at 47 FR 23709, June 1, 1982; 50 FR 19919, May 13, 1985]

§ 444.542g Neomycin sulfate-gramicidin-triamcinolone acetamide cream.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Neomycin sulfate-gramicidin-triamcinolone acetamide cream is a cream containing 2.5 milligrams of neomycin, 0.25 milligram of gramicidin, and 1.0 milligram of triamcinolone acetamide per gram, with one or more suitable and harmless emollients, dispersants, and preservatives in a suitable and harmless cream base. The neomycin sulfate used conforms to the standards prescribed by §444.42a(a)(1) (i), (vi), and (vii). The gramicidin used conforms to the standards prescribed by §448.25(a)(1) (i), (iv), (v), and (vi) of this chapter. Each other substance used, if its name is recognized in the U.S.P. or N.F., shall conform to the standards prescribed therefor by such official compendium.

(2) *Labeling*. It shall be labeled in accordance with the requirements prescribed by §432.5 of this chapter. Its expiration date is 12 months.

(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 neomycin sulfate used in making the batch for potency, pH, and identity.

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

(c) The batch for neomycin content and gramicidin content.

(ii) Samples required: