

of 0.1 microgram of gentamicin per milliliter (estimated).

[39 FR 19046, May 30, 1974, as amended at 46 FR 45332, Sept. 11, 1981; 50 FR 19919, May 13, 1985]

§ 444.540 Neomycin palmitate dermatologic dosage forms.

§ 444.542 Neomycin sulfate dermatologic dosage forms.

§ 444.542a Neomycin sulfate ointment; neomycin sulfate- _____ ointment (the blank being filled in with the established name(s) of the other active ingredient(s) present in accordance with paragraph (a)(1) of this section).

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Neomycin sulfate ointment contains, in each gram, 3.5 milligrams of neomycin in a suitable and harmless water-soluble or oleaginous ointment base, with or without one or more suitable and harmless dispersants, emollients, and preservatives. The following other drugs may be combined with neomycin sulfate ointment in the indicated amounts, per gram:

- (i) If it is for topical use:
 - (a) 0.5 milligram of flurandrenolide; or
 - (b) 0.25 milligram of fluorometholone; or
 - (c) 5.0, 10.0, 15.0, or 25.0 milligrams of hydrocortisone acetate; or
 - (d) 10.0 or 25.0 milligrams of hydrocortisone; or
 - (e) 5.0 milligrams of hydrocortamate hydrochloride; or
 - (f) 1.0, 2.5, or 5.0 milligrams of prednisolone acetate; or
 - (g) 1.0 milligram of triamcinolone acetonide; or
 - (h)-(j) [Reserved]
 - (j) 200 milligrams of benzocaine.
- (ii) If it is for ophthalmic use:
 - (a) 5.0 milligrams or 15.0 milligrams of hydrocortisone acetate; or
 - (b) 2.5 milligrams of sodium prednisolone phosphate; or
 - (c) 0.5 milligram of sodium dexamethasone phosphate.
 - (d) 1.0 milligram of methylprednisolone; or
 - (e) 1.0 milligram of triamcinolone acetonide; or

(f) 2.5 milligrams or 5.0 milligrams of prednisolone acetate; or

(g) 15.0 milligrams of cortisone acetate.

If it is an oleaginous base, its moisture content is not more than 1.0 percent. If it is intended for ophthalmic use, it is sterile. The neomycin sulfate used conforms to the standards prescribed by § 444.42a(a)(1)(i), (vi), and (vii). 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 if it is intended for ophthalmic use, it shall be labeled in accordance with the requirements prescribed by § 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 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 batch for potency and for moisture if the ointment base is oleaginous and for sterility if the ointment 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 batch:

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

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

(c) In the 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) *Extraction*. Proceed as directed in §444.42a(b)(1) of this chapter, except prepare the sample by placing an accurately weighed representative portion of the ointment into a separatory funnel containing 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 25 milliliters of 0.1M potassium phosphate buffer, pH 8.0, and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction with new portions of the buffer at least three times and any additional times necessary to insure complete extraction of the antibiotic. Combine the extractives and adjust to an appropriate volume to give a stock solution of convenient concentration. Further dilute with 0.1M potassium phosphate buffer, pH 8.0, to the proper prescribed reference concentration.

(ii) *Blending*. Proceed as directed in §444.42a(b)(1), except prepare the sample for assay as follows: Transfer an accurately weighed sample into a high-speed glass blender, add 1.0 milliliter of polysorbate 80 and sufficient 0.1M potassium phosphate buffer, pH 8.0, to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute with 0.1M potassium phosphate buffer, pH 8.0, to the proper prescribed reference concentration. The content of neomycin is satisfactory if it is not less than 90 percent and not more than 135 percent of the number of milligrams of neomycin 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 as described in paragraph (e)(3) of that section.

(3) *Moisture*. If the ointment has an oleaginous base, proceed as directed in §436.201 of this chapter.

[39 FR 19045, May 30, 1974, as amended at 39 FR 33666, Sept. 19, 1974; 47 FR 23442, May 28, 1982; 49 FR 34351, Aug. 30, 1984; 50 FR 19919, May 13, 1985; 50 FR 47213, Nov. 15, 1985]

§ 444.542b Neomycin sulfate cream; neomycin sulfate _____ cream (the blank being filled in with the established name(s) of the other active ingredient(s) present in accordance with paragraph (a)(1) of this section).

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Neomycin sulfate cream contains, in each gram, 3.5 milligrams of neomycin in a suitable cream base, with or without one or more suitable and harmless emollients, perfumes, dispersants, and preservatives. The following other drugs may be combined with neomycin sulfate cream in the indicated amounts per gram:

- (i) 2 milligrams of betamethasone; or
- (ii) Dexamethasone sodium phosphate equivalent to 1.0 milligram of dexamethasone phosphate; or
- (iii) 1 milligram of sodium dexamethasone phosphate; or
- (iv) 2.5 milligrams of dichlorisone acetate; or
- (v) 0.25 milligram of fluocinolone acetonide; or
- (vi) 2.5 milligrams, 5 milligrams, or 10 milligrams of methylprednisolone acetate; or
- (vii) 1 milligram of triamcinolone acetonide; or
- (viii) 2.5 milligrams, 5.0 milligrams, or 10.0 milligrams of hydrocortisone; or
- (ix) 10.0 milligrams or 25.0 milligrams of hydrocortisone acetate; or
- (x) 0.5 milligram of flurandrenolide.

The neomycin sulfate used conforms to the standards prescribed by §444.42a(a)(1) (i), (vi), and (vii). 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 corticosteroid, it shall be labeled in accordance with the requirements prescribed by §432.5 of this chapter, and its expiration date is 12 months. If it does not contain a corticosteroid, each