

(ii) *Polymyxin B content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows:

(a) *If the ointment is not water miscible.* 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. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 6. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 6. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

(b) *If the ointment is water miscible.* Place an accurately weighed representative portion of the sample into a high speed glass blender jar containing 1.0 milliliter polysorbate 80 and sufficient 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

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

[42 FR 27234, May 27, 1977, as amended at 55 FR 50173, Dec. 5, 1990]

§ 448.513b Bacitracin zinc-neomycin sulfate ointment.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Bacitracin zinc-neomycin sulfate ointment contains bacitracin zinc and neomycin sulfate in a suitable and harmless ointment base. Each gram contains 500 units of bacitracin and 3.5 milligrams of neomycin. Its bacitracin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of bacitracin that it is represented to contain. Its neomycin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of neomycin that

it is represented to contain. Its moisture content is not more than 0.5 percent. The bacitracin zinc used conforms to the standards prescribed by § 448.13(a)(1). The neomycin sulfate used conforms to the standards prescribed by § 444.42(a)(1) of this chapter.

(2) *Labeling—(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 conforms to the requirements prescribed by § 432.5(a)(3) of this chapter.

(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 complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

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

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

(c) The batch for bacitracin content, neomycin content, and moisture.

(ii) Samples required:

(a) The bacitracin zinc used in making the batch: 10 packages, each containing approximately 1.0 gram.

(b) The neomycin sulfate used in making the batch: 10 packages, each containing approximately 1.0 gram.

(c) The batch: A minimum of six immediate containers.

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

(a) *If the ointment is not water miscible.* 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 0.01*N* hydrochloric acid and shake well. Allow the layers to separate. Remove the acid layer and repeat the extraction procedure with each of

three more 20- to 25-milliliter quantities of 0.01*N* hydrochloric acid. Combine the acid extractives in a suitable volumetric flask and dilute to volume with 0.01*N* hydrochloric acid. (If the bacitracin content is less than 100 units per milliliter in 0.01*N* hydrochloric acid, add sufficient additional hydrochloric acid to each concentration of the standard response line so that each standard solution will have the same amount of acid as the final sample solution.) Remove an aliquot and further dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(b) *If the ointment is water miscible.* Place an accurately weighed representative portion of the sample into a high-speed glass blender jar containing 1.0 milliliter polysorbate 80 and sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot, add sufficient hydrochloric acid so that the amount of acid in the final solution will be the same as in the reference concentration of the working standard and further dilute with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(ii) *Neomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows:

(a) *If the ointment is not water miscible.* 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 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 3. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 3. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(b) *If the ointment is water miscible.* Place an accurately weighed representative portion of the sample into a high-speed glass blender jar containing 1.0 milliliter polysorbate 80 and sufficient 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

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

[42 FR 27234, May 27, 1977, as amended at 50 FR 19920, May 13, 1985]

§ 448.513c Bacitracin zinc-neomycin sulfate-polymyxin B sulfate ointment; bacitracin zinc-neomycin sulfate-polymyxin B sulfate hydrocortisone ointment.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* This drug, in a suitable and harmless ointment base, contains in each gram the following:

(i) 400 units of bacitracin, 3 milligrams of neomycin, and 8,000 units of polymyxin B; or

(ii) 400 units of bacitracin, 3.5 milligrams of neomycin, and 5,000 units of polymyxin B, with or without 10 milligrams of hydrocortisone; or

(iii) 500 units of bacitracin, 3.5 milligrams of neomycin, and 5,000 units of polymyxin B; or

(iv) 500 units of bacitracin, 3.5 milligrams of neomycin, and 10,000 units of polymyxin B.

It may contain a suitable local anesthetic except for combinations in paragraph (a)(1)(ii) of this section that contain hydrocortisone. Its bacitracin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of bacitracin that it is represented to contain. Its neomycin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of neomycin that it is represented to contain. Its polymyxin B content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of polymyxin B that it is represented to contain. Its moisture content is not more