

(v) The statement "Expiration date _____", the blank being filled in with the date that is 12 months after the month during which the batch was certified, unless use of a longer dating period has been approved in accordance with the provisions of §432.5(a)(3) of this chapter.

(vi) The statement, "The potency of this drug cannot be assured for longer than 60 days after the container is first opened for compounding a prescription".

(vii) The statements, "For use only in extemporaneous prescription compounding. Not for manufacturing use".

(4) *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 the batch for potency, loss on drying, pH, zinc content, and identity.

(ii) Samples required: A 0.5-gram portion for each 5,000 packages in the batch, but in no case less than 10 such portions. Each such portion shall be collected at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample (usually 25 to 35 milligrams) in sufficient 0.01*N* hydrochloric acid to give a bacitracin concentration of 100 units per milliliter (estimated). Further dilute an aliquot with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

NOTE: The final sample solution must contain the same amount of hydrochloric acid as the reference concentration of the working standard.

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in §436.200(b) of this chapter.

(4) *pH.* Proceed as directed in §436.202 of this chapter, using a saturated solution (approximately 100 milligrams of the sample per milliliter).

(5) *Zinc content.* Proceed as directed in §436.312 of this chapter.

(6) *Identity.* Proceed as directed in §436.319 of this chapter.

[42 FR 27238, May 27, 1977, as amended at 50 FR 19920, May 13, 1985]

§ 448.930 Polymyxin B sulfate in certain other dosage forms.

§ 448.930a Polymyxin B sulfate for prescription compounding.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Polymyxin B sulfate for prescription compounding is the sulfate salt of a kind of polymyxin or a mixture of two or more such salts intended for use in the extemporaneous compounding of prescriptions by practicing pharmacists. It is a white to buff-colored powder. It is so purified and dried that:

(i) Its potency is not less than 6,000 units of polymyxin B per milligram, on an anhydrous basis.

(ii) [Reserved]

(iii) Its loss on drying is not more than 7.0 percent.

(iv) Its pH in an aqueous solution containing 5 milligrams per milliliter is not less than 5.0 and not more than 7.5.

(v) Its residue on ignition is not more than 5 percent.

(vi) It gives positive color identity tests for polymyxin.

(2) *Packaging.* The immediate container shall be of colorless, transparent glass and it shall be a tight container as defined by the U.S.P. It shall be so sealed that the contents cannot be used without destroying such seal. Each such container shall contain 100 million units of polymyxin B.

(3) *Labeling.* In addition to the requirements of §432.5(a)(3) of this chapter, each package shall bear on its outside wrapper or container and on the immediate container the following:

(i) The statement "Caution: Federal law prohibits dispensing without prescription".

(ii) The statement "Not sterile".

(iii) The batch mark.

(iv) The number of units of polymyxin B activity in each milligram of the polymyxin B sulfate and the number of grams of polymyxin B sulfate in the immediate container.

(v) The statement, "The potency of this drug cannot be assured for longer than 60 days after the container is first opened for compounding a prescription".

(vi) The statements, "For use only in extemporaneous prescription compounding. Not for manufacturing use".

(4) *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 the batch for potency, loss on drying, pH, residue on ignition, and identity.

(ii) Samples required: A 0.5-gram portion for each 5,000 packages in the batch, but in no case less than 10 such portions. Each such portion shall be collected at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in 2 milliliters of sterile distilled water for each 5 milligrams of weighed sample. Further dilute an aliquot with sufficient 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in §436.200(b) of this chapter.

(4) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 5 milligrams per milliliter.

(5) *Residue on ignition.* Proceed as directed in §436.207(a) of this chapter.

(6) *Identity.* (i) To a solution of 2 milligrams of polymyxin B sulfate in 5 milliliters of water, add 0.5 milliliter of triketohydrindene solution (1:1,000) and 2 drops of pyridine, boil for 1 minute, and cool; a blue color develops; and

(ii) To a solution of 2 milligrams of polymyxin B sulfate in 5 milliliters of water, add 5 milliliters of sodium hydroxide solution (1:10), mix well, and add, dropwise, 5 drops of a cupric sul-

fate solution (1:100) mixing after the addition of each drop; a reddish-violet color is produced.

[39 FR 19115, May 30, 1974, as amended at 46 FR 16684, Mar. 13, 1981; 50 FR 19920, May 13, 1985]

§ 448.930b Sterile polymyxin B sulfate-benzalkonium chloride urethral lubricant.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Sterile polymyxin B sulfate-benzalkonium chloride urethral lubricant is polymyxin B sulfate and benzalkonium chloride, with one or more suitable and harmless suspending agents, in a suitable and harmless base. It contains, in each gram, 5,000 units of polymyxin B and 330 micrograms of benzalkonium chloride. Its content of polymyxin B is satisfactory if it contains 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. It is sterile. Its pH is not less than 4.0 and not more than 5.5. The polymyxin B sulfate used conforms to the standards prescribed by §448.30a(a)(1), except sterility, pyrogens, and heavy metals.

(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 polymyxin B sulfate used in making the batch for potency, pH, loss on drying, residue on ignition, and identity.

(b) The batch for potency, sterility, and pH.

(ii) Samples required:

(a) The polymyxin B 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: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in §436.105 of