

and purity. Chloramphenicol-hydrocortisone acetate for ophthalmic suspension contains 12.5 milligrams of chloramphenicol and 25 milligrams of hydrocortisone acetate with one or more suitable and harmless buffer substances, preservatives, and diluents. When reconstituted as directed in the labeling, its potency is not less than 90 percent and not more than 130 percent of the number of milligrams of chloramphenicol that it is represented to contain. It is sterile. Its pH is not less than 7.1 and not more than 7.5. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1).

(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 chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

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

(ii) Samples required:

(a) The chloramphenicol 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.* Use either of the following methods:

(i) *Microbiological turbidimetric assay.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Dilute an accurately measured representative aliquot of the sample with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(ii) *Spectrophotometric assay.* Reconstitute the sample as directed in the labeling and dilute a 1.0-milliliter aliquot in sufficient distilled water to obtain a solution containing 20 micrograms of chloramphenicol per milliliter. Dissolve an accurately weighed portion of the working standard in sufficient distilled water to obtain a solution containing 20 micrograms per milliliter. Using a suitable spectrophotometer and distilled water as the blank, determine the absorbance of the sample and standard solutions at 278 nanometers. Calculate the potency of the sample as follows:

Milligrams of chloramphenicol per milliliter = Absorbance of sample X labeled potency per milliliter in milligrams / Absorbance of standard.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

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

[49 FR 6093, Feb. 17, 1984]

§ 455.390 Vidarabine monohydrate ophthalmic ointment.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Vidarabine monohydrate ophthalmic ointment contains in each gram vidarabine monohydrate equivalent to 28.11 milligrams of vidarabine in a suitable and harmless base. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of vidarabine that it is represented to contain. It is sterile. It passes the test for metal particles. The vidarabine monohydrate used conforms to the standards prescribed by § 455.90a(a)(1).

(2) *Labeling.* In addition to the labeling requirements prescribed by § 432.5 of this chapter, this drug shall be labeled "vidarabine ophthalmic ointment".

(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:k

(a) The vidarabine monohydrate used in making the batch for vidarabine content sterility, loss on drying, specific rotation, and identity.

(b) The batch for vidarabine content, sterility, and metal particles.

(i) Samples required:

(a) The vidarabine monohydrate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 16 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Vidarabine content*. Proceed as directed in § 436.325 of this chapter, except prepare the sample solution and calculate the vidarabine content as follows:

(i) *Preparation of sample solution*. Accurately weigh a portion of the sample containing the equivalent of approximately 12 milligrams of vidarabine (estimated) into a 100-milliliter volumetric flask. Add approximately 80 milliliters of distilled water and heat for 15 minutes on a steam bath. Shake to dissolve the vidarabine and, while the solution is still hot, add 10 milliliters of heptane to dissolve the ointment base. Swirl gently until the ointment base is dissolved. Cool to room temperature and dilute the aqueous phase to volume with distilled water. Discard the heptane phase and mix the solution.

(ii) *Calculations*. Calculate the vidarabine content as follows:

$$\text{Percent vidarabine} = \frac{A \times W_s \times f}{(B \times W_u \times 10)}$$

where:

A=Area of the vidarabine sample peak (at a retention time equal to that observed for the standard);

B=Area of the standard peak;

W_s =Weight of standard in milligrams;

W_u =Weight of sample in milligrams; and

f =Potency of standard in micrograms per milligram.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(3) of that section.

(3) *Metal particles*. Proceed as directed in § 436.206 of this chapter.

[42 FR 44224, Sept. 2, 1977, as amended at 44 FR 30335, May 25, 1979; 50 FR 19921, May 13, 1985]

Subpart E—Otic Dosage Forms

§ 455.410 Chloramphenicol otic.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Chloramphenicol otic is a solution of chloramphenicol in a suitable and harmless vehicle. Each milliliter contains 5.0 milligrams of chloramphenicol. Its potency is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of chloramphenicol that it is represented to contain. It is sterile. Its moisture content is not more than 2 percent. Its pH is not less than 4 and not more than 8. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1).

(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 the following:

(i) Results of tests and assays on—

(a) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity; and

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

(ii) Samples required:

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

(b) The batch:

(1) For all tests except sterility: A minimum of 20 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 § 436.106 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the sample with distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of