

if the labeling specifies the amount of vancomycin content in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute with 0.1M potassium phosphate buffer, pH 4.5 (solution 4) to the reference concentration of 10.0 micrograms of vancomycin per milliliter (estimated).

(2) *Chromatographic purity.* Proceed as directed in § 436.366 of this chapter. The relative amount of vancomycin B is not less than 88 percent and the relative amount of any related substance is not more than 4 percent.

(3) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except use sterile distilled water in lieu of diluting fluid A.

(4) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, using a solution containing 5 milligrams of vancomycin per milliliter.

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

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using a solution containing 50 milligrams per milliliter.

(7) *Heavy metals.* Proceed as directed in § 436.208 of this chapter.

(8) *Identity.* Proceed as directed in § 436.211 of this chapter, using the 0.5 percent potassium bromide disc preparation as described in paragraph (b)(1) of that section.

[54 FR 20384, May 11, 1989; 54 FR 22838, May 28, 1989]

§ 455.285c Vancomycin hydrochloride injection.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Vancomycin hydrochloride injection is a frozen, aqueous, iso-osmotic solution of vancomycin hydrochloride and a tonicity adjusting agent. Each milliliter contains vancomycin hydrochloride equivalent to 5 milligrams of vancomycin. Its vancomycin content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of vancomycin that it is represented to contain. It contains not less than 88 percent vancomycin factor B. It contains not more than 4 percent of any individual vancomycin related factor. It is sterile. It contains not

more than 0.33 U.S.P. Endotoxin Unit per milligram of vancomycin hydrochloride. Its pH is not less than 3.0 and not more than 5.0. The vancomycin used conforms to the standards prescribed by § 455.86.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter. In addition, this drug shall be labeled “vancomycin hydrochloride injection.”

(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 vancomycin used in making the batch for vancomycin potency, chromatographic purity, moisture, heavy metals, and identity.

(B) The batch for vancomycin content, chromatographic purity, sterility, bacterial endotoxins, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

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

(B) The batch:

(1) For all tests except sterility: A minimum of 12 immediate containers.

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

(b) *Tests and methods of assay.* Thaw the sample as directed in the labeling. The sample solution used for testing must be at room temperature.

(1) *Vancomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample solution as follows: Using a suitable hypodermic needle and syringe, remove an accurately measured representative portion from each container immediately after thawing and reaching room temperature. Dilute with 0.1M potassium phosphate buffer, pH 4.5 (solution 4), to the reference concentration of 10 micrograms of vancomycin per milliliter (estimated).

(2) *Chromatographic purity.* Proceed as directed in § 436.366 of this chapter. The relative amount of vancomycin B is not less than 88 percent and the relative amount of any related substance is not more than 4 percent.

(3) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in § 436.20(e)(1), except use sterile distilled water in lieu of diluting fluid A.

(4) *Bacterial endotoxins*. Proceed as directed in the U.S.P. bacterial endotoxins test. The specimen under test contains not more than 0.33 U.S.P. Endotoxin Unit per milligram of vancomycin hydrochloride.

(5) *pH*. Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

(6) *Identity*. The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(2) of this section compares qualitatively to that of the vancomycin working standard.

[59 FR 8400, Feb. 22, 1994]

§ 455.290 Vidarabine monohydrate for infusion.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity*. Vidarabine monohydrate for infusion contains in each milliliter vidarabine monohydrate equivalent to 187.4 milligrams of vidarabine in an aqueous suspension containing suitable and harmless buffers and preservatives. 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 is nonpyrogenic. It contains no histamine or histamine-like substances. Its pH is not less than 5.0 and not more than 6.2. 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 for infusion".

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

(b) The batch for vidarabine content, sterility, pyrogens, histamine, and pH.

(ii) 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*. Using a suitable hypodermic needle and syringe, transfer 2 milliliters of the well-shaken suspension to a 500-milliliter volumetric flask. Add approximately 50 milliliters of distilled water and 5 milliliters of glacial acetic acid. Warm on a steam bath for 15 minutes to dissolve the vidarabine. Cool to room temperature and dilute to volume with distilled water. Transfer 4 milliliters to a 25-milliliter volumetric flask and dilute to volume with distilled water.

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

$$\begin{array}{l} \text{Milligrams of} \\ \text{vidarabine} \\ \text{per milliliter} \end{array} = \frac{A \times W_s \times f \times 125}{B \times 1,000 \times 16},$$

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 the standard 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)(2) of that section.

(3) *Pyrogens*. Proceed as directed in § 436.32(a) of this chapter, using a solution containing 10 milligrams of vidarabine per milliliter.

(4) *Histamine*. Proceed as directed in § 436.35 of this chapter. Apply sufficient heat to dissolve the vidarabine.