

§ 453.21 Clindamycin palmitate hydrochloride.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Clindamycin palmitate hydrochloride is the white to off-white amorphous powder of the hydrochloride salt of the palmitic acid ester of clindamycin. It is freely soluble in water, ethanol, chloroform, and ether. It is so purified and dried that:

- (i) It contains not less than 540 micrograms of clindamycin per milligram.
- (ii) [Reserved]
- (iii) Its moisture content is not more than 3.0 percent.
- (iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 2.8 and not more than 3.8.
- (v) It passes the identity test for clindamycin palmitate hydrochloride.

(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 the batch for clindamycin content, moisture, pH, and identity.
- (ii) Samples required: 10 packages, nine containing not less than 300 milligrams and one package containing not less than 2 grams.

(b) *Tests and methods of assay—(1) Clindamycin content.* Proceed as directed in § 436.303 of this chapter.

(2) [Reserved]

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

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Identity.* Proceed as directed in § 436.211 of this chapter, using the sample preparation method described in paragraph (b)(2) of that section.

[39 FR 19161, May 30, 1974, as amended at 50 FR 19921, May 13, 1985]

§ 453.22 Clindamycin phosphate.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Clindamycin phosphate is a water-soluble ester of clindamycin and

phosphoric acid. It occurs as a white to off-white powder. It is so purified and dried that:

(i) Its clindamycin content is not less than 758 micrograms of clindamycin per milligram calculated on an anhydrous basis.

(ii) Its microbiological activity is not less than 758 micrograms of clindamycin per milligram calculated on an anhydrous basis.

(iii) [Reserved]

(iv) Its moisture content is not more than 6.0 percent.

(v) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 3.5 and not more than 4.5.

(vi) It is crystalline.

(vii) It passes the identity test for clindamycin phosphate.

(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 the batch for clindamycin content, microbiological activity, moisture, pH, crystallinity, and identity.

(ii) Samples required: 10 packages, nine containing approximately 300 milligrams and one containing 1.5 grams.

(b) *Tests and methods of assay—(1) Clindamycin content (vapor phase chromatography).* Proceed as directed in § 436.304 of this chapter.

(2) *Microbiological activity (microbiological agar diffusion assay).* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Accurately weigh approximately 12 milligrams of the clindamycin phosphate sample into a 50-milliliter glass-stoppered centrifuge tube. Pipet 25 milliliters of the pH 9.0 borate buffer into the centrifuge tube. Add 10 milliliters of chloroform and shake vigorously for 15 minutes. Centrifuge the resulting mixture and pipet a 20-milliliter aliquot of the aqueous phase into a 35-milliliter centrifuge tube. Add a weighed amount of intestinal alkaline phosphatase equivalent to 50 units of

activity¹ and allow the solution to stand until the enzyme has completely dissolved. Place the tube into a water bath at 37° C ±2° C for 2.5 hours. After the 2.5-hours hydrolysis, allow the solution to cool. Further dilute an aliquot of the solution with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 1.0 microgram of clindamycin per milliliter (estimated).

(3) [Reserved]

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

(5) *pH*. Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(6) *Crystallinity*. Proceed as directed in §436.203(a) of this chapter.

(7) *Identity*. Proceed as directed in §436.211 of this chapter, using the sample preparation method described in paragraph (b)(2) of that section, except dry the sample for 2 hours at 100° C and allow to equilibrate with the atmosphere for 1 hour.

[46 FR 2996, Jan. 13, 1981, as amended at 50 FR 19921, May 13, 1985]

§ 453.22a Sterile clindamycin phosphate.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity*. Sterile clindamycin phosphate is a water-soluble ester of clindamycin and phosphoric acid. It occurs as a white to off-white powder. It is so purified and dried that:

(i) Its clindamycin content is not less than 758 micrograms of clindamycin per milligram calculated on an anhydrous basis.

(ii) Its microbiological activity is not less than 758 micrograms of clindamycin per milligram calculated on an anhydrous basis.

(iii) It is sterile.

(iv) It is nonpyrogenic.

(v) [Reserved]

(vi) It contains no depressor substances.

(vii) Its moisture content is not more than 6 percent.

¹Defined such that 50 units hydrolyzes at least 20 micromoles of a clindamycin phosphate authentic sample under the assay conditions described in this section.

(viii) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 3.5 and not more than 4.5.

(ix) It is crystalline.

(x) It passes the identity test for clindamycin phosphate.

(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 the batch for clindamycin content, microbiological activity, sterility, pyrogens, depressor substances, moisture, pH, crystallinity, and identity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, nine containing approximately 300 milligrams and one containing 1.5 grams.

(b) For sterility testing: 20 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay—(1) Clindamycin content (vapor phase chromatography)*. Proceed as directed in §436.304 of this chapter.

(2) *Microbiological activity (microbiological agar diffusion assay)*. Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Accurately weigh approximately 12 milligrams of the clindamycin phosphate sample into a 50-milliliter glass-stoppered centrifuge tube. Pipet 25 milliliters of the pH 9.0 borate buffer into the centrifuge tube. Add 10 milliliters of chloroform and shake vigorously for 15 minutes. Centrifuge the resulting mixture and pipet a 20-milliliter aliquot of the aqueous phase into a 35-milliliter centrifuge tube. Add a weighed amount of intestinal alkaline phosphatase equivalent to 50 units of activity¹ and allow the solution to stand until the enzyme has completely dissolved. Place the tube into a water bath at 37° C.±2° C. for 2.5 hours. After the 2.5-hour hydrolysis, allow the solution to cool. Further dilute an aliquot of the solution with

¹Defined such that 50 units hydrolyzes at least 20 micromoles of a clindamycin phosphate authentic sample under the assay conditions described in this section.