

(v) It contains no depressor substances.

(vi) Its moisture content is not less than 1.4 nor more than 2.75 percent.

(vii) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 2.0 nor more than 3.0.

(viii) It contains not less than 82 nor more than 90 percent doxycycline on an "as is" basis.

(ix) It gives a positive identity test for doxycycline hyclate.

(x) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this subchapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this subchapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, depressor substances, moisture, pH, doxycycline content, identity, and crystallinity.

(ii) Samples required:

(a) For all tests except sterility: 12 packages, each containing approximately 300 milligrams.

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

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1N hydrochloric acid to obtain a concentration of 1,000 micrograms of doxycycline per milliliter (estimated). Further dilute with sterile distilled water to the reference concentration of 0.100 microgram of doxycycline per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this subchapter, using the method described in paragraph (e)(1) of that section, except use diluting fluid D in lieu of diluting fluid A.

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this subchapter, using a solution containing 7.5 milligrams of doxycycline per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in § 436.35 of this subchapter.

(6) *Moisture.* Proceed as directed in § 436.201 of this subchapter.

(7) *pH.* Proceed as directed in § 436.202 of this subchapter, using an aqueous solution containing the equivalent of 10 milligrams of doxycycline per milliliter.

(8) *Doxycycline content.* Proceed as directed in § 446.20(b)(5).

(9) *Identity.* Proceed as directed in § 436.211 of this subchapter, using the 0.25 potassium bromide mixture described in paragraph (b)(1) of that section.

(10) *Crystallinity.* Proceed as directed in § 436.203(a) of this subchapter.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11155, Mar. 17, 1978; 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985]

§ 446.21 Doxycycline monohydrate.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Doxycycline monohydrate is [4S - (4 α ,4a α ,5 α ,5a α ,6 α ,12a α)] - 4 - (dimethylamino) - 1,4,4a,5,5a,6,11, - 12a - octahydro - 3,5,10,12,12a - pentahydroxy - 6 - methyl - 1,11 - dioxo - 2 - naphtha - cenecarboxamide monohydrate. It is so purified and dried that:

(i) Its potency is not less than 880 micrograms nor more than 980 micrograms of doxycycline per milligram on an "as is" basis.

(ii) [Reserved]

(iii) Its moisture content is not less than 3.6 percent nor more than 4.6 percent.

(iv) Its pH in an aqueous suspension containing the equivalent of 10 milligrams of doxycycline per milliliter is not less than 5.0 nor more than 6.5.

(v) It contains not less than 90 percent nor more than 98 percent doxycycline on an "as is" basis.

(vi) It gives a positive identity test for doxycycline monohydrate.

(vii) It is crystalline.

(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 potency, moisture, pH, doxycycline content, identity, and crystallinity.

(ii) Samples of the batch: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1N hydrochloric acid to obtain a concentration of 1,000 micrograms of doxycycline per milliliter (estimated). Further dilute with sterile distilled water to the reference concentration of 0.100 microgram of doxycycline per milliliter (estimated).

(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 suspension containing the equivalent of 10 milligrams of doxycycline per milliliter.

(5) *Doxycycline content*. Proceed as directed in § 446.20(b)(5).

(6) *Identity*. Proceed as directed in § 436.211 of this chapter, using the 0.25 potassium bromide mixture described in paragraph (b)(1) of that section.

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

[39 FR 19076, May 30, 1974, as amended at 43 FR 11155, Mar. 17, 1978; 45 FR 16476, Mar. 14, 1980; 50 FR 19920, May 13, 1985]

§ 446.42 Meclocycline sulfosalicylate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Meclocycline sulfosalicylate is the sulfosalicylate salt of 7-chloro-4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide. It is so purified and dried that:

(i) Its potency is not less than 620 micrograms of meclocycline per milligram on an “as is” basis.

(ii) Its moisture content is not more than 4.0 percent.

(iii) Its pH is in an aqueous suspension containing 10 milligrams per milliliter is not less than 2.5 and not more than 3.5.

(iv) It is crystalline.

(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 potency, moisture, pH, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Use either of the following methods; however, the results obtained from the high-pressure liquid chromatography method shall be conclusive.

(i) *High-pressure liquid chromatography*. Proceed as directed in § 436.329 of this chapter.

(ii) *Microbiological turbidimetric assay*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient 0.01N methanolic hydrochloric acid (solution 13) to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 0.06 microgram of meclocycline per milliliter (estimated).

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

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

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

[46 FR 3836, Jan. 16, 1981]

§ 446.50 Methacycline hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Methacycline hydrochloride is [4S - (4 α ,4 α ,5 α ,5 α , - 12 α)] - 4 - (dimethylamino) - 1,4,4a,5,5a,6,11,12a - octahydro - 3,5,10,12,12a - pentahydroxy - 6 - methylene - 1,11 - dioxo - 2 - naphthacenecarboxamide monohydrochloride. It is so purified and dried that:

(i) Its potency is not less than 832 micrograms of methacycline per milligram on an “as is” basis.

(ii) [Reserved]

(iii) Its moisture content is not more than 2 percent.