

(1) For all tests except sterility: A minimum of 10 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 subchapter, preparing the sample for assay as follows: Reconstitute the sample as directed in the labeling. Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is [represented as a single dose container; or if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the sample thus obtained 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 0.24 microgram of rolitetracycline 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(b) of this subchapter, using a solution containing 5.0 milligrams of rolitetracycline per milliliter.

(4) [Reserved]

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

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

(7) *pH*. Proceed as directed in § 436.202 of this subchapter, using a solution prepared as directed in the labeling.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11168, Mar. 17, 1978; 43 FR 34457, Aug. 4, 1978; 46 FR 46313, Sept. 18, 1981; 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985]

§ 446.276b Rolitetracycline nitrate for intramuscular use.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Rolitetracycline nitrate for intramuscular use is a dry mixture of rolitetracycline nitrate, one or more suitable buffer substances, and lidocaine hydrochloride. Its potency is satisfactory if it is not less than 90 per-

cent and not more than 115 percent of the number of milligrams of rolitetracycline that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 5 percent. When reconstituted as directed in the labeling, its pH is not less than 2.5 nor more than 4.0. The rolitetracycline nitrate used conforms to the standards prescribed by § 446.76a(a)(1).

(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:

(a) The rolitetracycline nitrate used in making the batch for potency, depressor substances, moisture, pH, crystallinity, absorptivity, and identity.

(b) The batch for potency, sterility, pyrogens, loss on drying, and pH.

(ii) Samples required:

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

(b) The batch:

(1) For all tests except sterility: A minimum of 10 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 subchapter, preparing the sample for assay as follows: Reconstitute the sample as directed in the labeling. Then using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the sample thus obtained 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 0.24 microgram of rolitetracycline 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(b) of this subchapter, using a solution containing 5.0 milligrams of rolitetracycline per milliliter.

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

(5) *pH*. Proceed as directed in § 436.202 of this subchapter, using a solution prepared as directed in the labeling.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11168, Mar. 30, 1978; 46 FR 46313, Sept. 18, 1981; 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985]

§ 446.281 Tetracycline hydrochloride injectable dosage forms.

§ 446.281a Sterile tetracycline hydrochloride.

The requirements for certification and the tests and methods of assay for sterile tetracycline hydrochloride packaged for dispensing are described in § 446.81a.

§ 446.281c Tetracycline hydrochloride for intramuscular use.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Tetracycline hydrochloride for intramuscular use is a dry mixture of tetracycline hydrochloride, magnesium chloride, or magnesium ascorbate and one or more suitable buffer substances, with or without one or more suitable preservatives and anesthetic agents, and with or without one or more suitable solubilizers and stabilizers. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of tetracycline hydrochloride that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 5.0 percent. Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 2.0 and not more than 3.0. Its 4-epianhydrotetracycline content is not more than 3.0 percent. The tetracycline hydrochloride used conforms to the standards prescribed by § 446.81a(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 tetracycline hydrochloride used in making the batch for potency, depressor substances, loss on drying, pH, absorptivity, 4-epianhydrotetracycline content, crystallinity, and identity.

(b) The batch for potency, sterility, pyrogens, loss on drying, pH, and 4-epianhydrotetracycline content.

(ii) Samples required:

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

(b) The batch: A minimum of 10 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Reconstitute the sample as directed in the labeling. Then, using a suitable hypodermic needle and syringe, remove all the withdrawable contents if it is represented as a single dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the sample thus obtained with sufficient 0.1N hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of tetracycline hydrochloride per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, 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(b) of this chapter, using a solution containing 5.0 milligrams of tetracycline hydrochloride per milliliter.

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