

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 3.0 and not more than 4.5. The rolitetracycline used conforms to the standards prescribed by § 446.75a(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 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 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 11167, Mar. 17, 1978; 46 FR 46313, Sept. 18, 1981; 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985]

**§ 446.276 Rolitetracycline nitrate injectable dosage forms.**

**§ 446.276a Rolitetracycline nitrate for intravenous use.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Rolitetracycline nitrate for intravenous use is a dry mixture of rolitetracycline nitrate and one or more suitable buffer substances. Its potency is satisfactory if it contains not less than 90 percent 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. It contains no depressor substances. 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, moisture, pH, crystallinity, absorptivity, and identity.

(b) The batch for potency, sterility, pyrogens, depressor substances, 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. 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.

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**§ 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).