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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 436 and 442

[Docket No. 94N–0352]

Antibiotic Drugs; Cefuroxime Axetil for Oral Suspension

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the antibiotic drug regulations to include the accepted standards for cefuroxime axetil for its use in a new dosage form of cefuroxime axetil, cefuroxime axetil for oral suspension. The manufacturer has supplied sufficient data and information to establish its safety and efficacy.

DATES: Effective June 22, 1995; written comments, notice of participation, and requests for a hearing by June 22, 1995; data, information, and analyses to justify a hearing by July 24, 1995.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: James Timper, Center for Drug Evaluation and Research (HFD–520), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–6714.

SUPPLEMENTARY INFORMATION: FDA has evaluated data submitted in accordance with regulations promulgated under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357), as amended, with respect to a request for approval of a new dosage form of cefuroxime axetil, cefuroxime axetil for oral suspension. The agency has concluded that the data supplied by the manufacturer concerning this antibiotic drug are adequate to establish its safety and efficacy when used as directed in the labeling and that the regulations should be amended in parts 436 and 442 (21 CFR parts 436 and 442) to include the accepted standards for this product.

Environmental Impact

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Submitting Comments and Filing Objections

This final rule announces standards that FDA has accepted in a request for approval of an antibiotic drug. Because this final rule is not controversial and because, when effective, it provides notice of accepted standards, FDA finds that notice and comment procedure is unnecessary and not in the public interest. This final rule, therefore, is effective June 22, 1995. However interested persons may, on or before June 22, 1995, submit written comments to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Any person who will be adversely affected by this final rule may file objections to it and request a hearing. Reasonable grounds for the hearing must be shown. Any person who decides to seek a hearing must file (1) on or before June 22, 1995, a written notice of participation and request for a hearing, and (2) on or before July 24, 1995, the data, information, and analyses on which the person relies to justify a hearing, as specified in 21 CFR 314.300. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for a hearing that no genuine and substantial issue of fact precludes the action taken by this order, or if a request for a hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who request(s) the hearing, making findings and conclusions and denying a hearing. All submissions must be filed in three copies, identified with the docket number appearing in the heading of this document and filed with the Dockets Management Branch.

The procedures and requirements governing this order, a notice of participation and request for a hearing, a submission of data, information, and analyses to justify a hearing, other comments, and grant or denial of a hearing are contained in 21 CFR 314.300.

All submissions under this order, except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Parts 436 and 442

Antibiotics.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 436 and 442 are amended as follows:

PART 436—TESTS AND METHODS OF ASSAY OF ANTIBIOTIC AND ANTIBIOTIC-CONTAINING DRUGS

1. The authority citation for 21 CFR part 436 continues to read as follows:

Authority: Sec. 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357).

2. Section 436.215 is amended by alphabetically adding a new entry to the table in paragraph (b) and by revising paragraph (c)(9) to read as follows:

§ 436.215 Dissolution test.

* * * * *

(b) * * *

Dosage form	Dissolution medium	Rotation rate [1]	Sampling time(s)	Apparatus
* *	*	*	*	* *
Cefuroxime axetil for oral suspension.	900 mL Sorenson's Modified Phosphate Buffer, pH 7.0.	50	30 min	2
* *	*	*	*	* *

[1] Rotation rate of basket or paddle stirring element (revolutions per minute).

(c) * * *

(9) *Cefuroxime axetil tablets and powder for oral suspension*—(i) *Preparation of working standard solution*—(*a*) *Cefuroxime axetil tablets.* Accurately weigh approximately 60 milligrams of cefuroxime axetil working standard into a suitable-sized volumetric flask. Dissolve in 5 milliliters of methanol and dilute to volume with 0.07*N* hydrochloric acid to obtain a known concentration equivalent to 0.01 to 0.02 milligram of cefuroxime activity per milliliter.

(*b*) *Cefuroxime axetil for oral suspension.* Accurately weigh approximately 15 milligrams of cefuroxime axetil working standard into a 100-milliliter volumetric flask. Dissolve in 5 milliliters of methanol and dilute to volume with Sorenson's Modified Phosphate Buffer, pH 7.0 (4.2 grams of sodium dihydrogen orthophosphate dihydrate and 14.3 grams of hydrogen disodium orthophosphate dodecahydrate per liter of water).

(ii) *Preparation of sample solution*—(*a*) *Cefuroxime axetil tablets.* Filter through a 0.45-micron filter and dilute an accurately measured portion of the filtrate with sufficient 0.07*N* hydrochloric acid to obtain a concentration equivalent to 0.01 to 0.02 milligram of cefuroxime activity per milliliter (estimated).

(*b*) *Cefuroxime axetil for oral suspension.* Filter the sample through an 8-micron filter. A coarse prefilter may be used to prevent clogging. Use the filtrate solution without further dilution.

(iii) *Procedure*—(*a*) *Cefuroxime axetil tablets.* Using a suitable spectrophotometer and 0.07*N* hydrochloric acid as the blank, determine the absorbance of each standard and sample solution at the absorbance peak at approximately 280 nanometers. Determine the exact position of the absorption peak for the particular instrument used.

(*b*) *Cefuroxime axetil for oral suspension.* Using a suitable spectrophotometer and Sorenson's Modified Phosphate Buffer, pH 7.0 (4.2 grams of sodium dihydrogen orthophosphate dihydrate and 14.3 grams of hydrogen disodium orthophosphate dodecahydrate per liter of water) as the blank, determine the absorbance of each standard and sample solution at the absorbance peak at approximately 280 nanometers. Determine the exact position of the absorption peak for the particular instrument used.

(iv) *Calculations.* Determine the total amount of cefuroxime activity dissolved as follows:

$$T = \frac{A_U \times {}_C \times d \times 900}{A_s}$$

where:
T = Total milligrams of cefuroxime activity dissolved;
A_U = Absorbance of sample;
c = Cefuroxime activity of working standard solution in milligrams per milliliter;
d = Dilution factor of sample filtrate; and
A_s = Absorbance of standard.

* * * * *

PART 442—CEPHA ANTIBIOTIC DRUGS

3. The authority citation for 21 CFR part 442 continues to read as follows:

Authority: Sec. 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357).

§ 442.119a [Redesignated from § 442.119]

4. Section 442.119 is redesignated as § 442.119a and new §§ 442.119 and 442.119b are added to subpart B to read as follows:

§ 442.119 Cefuroxime axetil oral dosage forms.

§ 442.119b Cefuroxime axetil for oral suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefuroxime axetil for oral suspension is cefuroxime axetil with one or more suitable and harmless diluents, suspending and sweetening agents, and flavorings. When reconstituted as directed in the labeling, it contains cefuroxime axetil equivalent to 25 milligrams of cefuroxime per millimeter. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cefuroxime that it is represented to contain. It passes the dissolution test. Its moisture content is not more than 0.2 percent. When reconstituted as directed in the labeling, its pH is not less than 3.5 and not more than 5.5. It passes the identity test. The cefuroxime axetil used conforms to the standards prescribed by § 442.19(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 cefuroxime axetil used in making the batch for potency, isomer A ratio, moisture, crystallinity, and identity.

(B) The batch for cefuroxime potency, dissolution, moisture, pH of constituted suspension, and identity.

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

(A) The cefuroxime axetil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 12 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 442.19(b)(1). Working standard and sample solutions and calculations are as follows:

(i) *Preparation of working standard solution.* Dissolve approximately 15 milligrams of the cefuroxime axetil working standard, accurately weighed, in 20.0 milliliters of methanol in a 50-milliliter volumetric flask. Dilute to volume with deionized water, and swirl to mix. Store for no more than 8 hours under refrigeration and protected from light.

(ii) *Preparation of sample solution.* Reconstitute the sample as directed in

the labeling. Transfer an accurately measured representative portion of the suspension equivalent to one dose into a 200-milliliter volumetric flask. Add 10 milliliters of methanol and disperse the sample. Dilute to volume with methanol. Dilute 20.0 milliliters of this solution to volume in a 50-milliliter volumetric flask with deionized water, swirl to mix, and allow to stand for 10 minutes. (Note: A white turbidity is formed.) Filter this solution via a suitable disposable filter unit, discarding the first 5 milliliters. Store for no more than 8 hours under refrigeration and protect from light.

(iii) *Calculations*. Calculate the milligrams of cefuroxime per dose (5 milliliters) as follows:

$$\text{Milligrams of cefuroxime per 5 milliliters of sample} = \frac{A_U \times P_S \times d}{A_S \times 1{,}000}$$

where:

A_U = Sum of the areas of the cefuroxime axetil sample isomer A and isomer B peaks;

A_S = Sum of the peak areas of the cefuroxime axetil working standard isomer A and isomer B peaks;

P_S = Cefuroxime activity in the cefuroxime axetil working standard solution in micrograms per milliliter; and

d = Dilution factor of the sample.

(2) *Dissolution*. Proceed as directed in § 436.215 of this chapter. The quantity Q (the amount of cefuroxime activity dissolved) is 60 percent at 30 minutes.

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

(4) *pH*. Reconstitute as directed in the labeling and proceed as directed in § 436.202 of this chapter.

(5) *Identity*. The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefuroxime axetil working standard.

Dated: May 9, 1995.

Murray M. Lumpkin,

Deputy Director, Center for Drug Evaluation and Research.

[FR Doc. 95–12604 Filed 5–22–95; 8:45 am]

BILLING CODE 4160–01–F

21 CFR Part 522

[Docket No. 95N–0096]

Implantation or Injectable Dosage Form New Animal Drugs; Guaifenesin

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the animal drug regulations to reflect the change of the animal drug name from glyceryl guaiacolate to guaifenesin. This amendment is an administrative change to redesignate glyceryl guaiacolate products as guaifenesin products.

EFFECTIVE DATE: May 23, 1995.

FOR FURTHER INFORMATION CONTACT: Mohammad I. Sharar, Center for Veterinary Medicine (HFV–216), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–1722.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 30, 1972 (37 FR 12936) and November 5, 1976 (41 FR 48732), FDA published final rules which reflected approval of injectable glyceryl guaiacolate products. In the **Federal Register** of December 10, 1984 (49 FR 48038), FDA published a final rule which reflected approval of a guaifenesin powder for injection. Guaifenesin is the newer chemical name for glyceryl guaiacolate. At the time of the December 10, 1984, approval, the prior approvals were not amended to reflect the newer chemical name. FDA is amending the regulations in part 522 (21 CFR part 522) to reflect the newer chemical name by removing §§ 522.1060, 522.1060a, and 522.1060b; by adding a new sponsor to § 522.1085; and by adding new § 522.1086 *Guaifenesin injection*.

FDA has determined under 21 CFR 25.24(a)(9) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 522

Animal drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs and redelegated to the Center for Veterinary Medicine, 21 CFR part 522 is amended as follows:

PART 522—IMPLANTATION OR INJECTABLE DOSAGE FORM NEW ANIMAL DRUGS

1. The authority citation for 21 CFR part 522 continues to read as follows:

Authority: Sec. 512 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b).

§ 522.1060 [Removed]

2. Section 522.1060 *Glyceryl guaiacolate implantation or injectable dosage forms* is removed.

§ 522.1060a [Removed]

3. Section 522.1060a *Glyceryl guaiacolate sterile powder* is removed.

§ 522.1060b [Removed]

4. Section 522.1060b *Glyceryl guaiacolate injection* is removed.

§ 522.1085 [Amended]

5. Section 522.1085 *Guaifenesin sterile powder* is amended in paragraph (b) by removing ''000031'' and adding in its place the phrase ''000031 and 037990''.

6. New § 522.1086 is added to read as follows:

§ 522.1086 Guaifenesin injection.

(a) *Specifications*. Each milliliter of sterile aqueous solution contains 50 milligrams of guaifenesin and 50 milligrams of dextrose.

(b) *Sponsor*. See No. 037990 in § 510.600(c) of this chapter.

(c) *Conditions of use*. (1) The drug is used intravenously in horses as a skeletal muscle relaxant.

(2) Administer rapidly at a dosage of 1 milliliter per pound of body weight.

(3) No to be used in horses intended for food.

(4) Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Dated: May 5, 1995.

Stephen F. Sundlof,

Director, Center for Veterinary Medicine.

[FR Doc. 95–12506 Filed 5–22–95; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF EDUCATION

34 CFR Parts 78, 208, 215, 230, 232, 233, 234, 236, 238, 241, 245, 246, 247, 250, 251, 252, 253, 254, 255, 256, 257, 258, 282, 298, 346, 347, 354, 362, 372, 374, 405, 407, 408, 409, 414, 416, 417, 418, 419, 422, 423, 424, 445, 462, 463, 471, 473, 474, 475, 476, 500, 501, 520, 524, 525, 526, 537, 538, 548, 555, 561, 573, 574, 581, 629, 665, 671, 673, 691, 698, 700, 706, 707, 708, 722, 750, 755, 757, 758, 760, 761, 762, 763, 768, 773, 778, 779, and 790

Removal of Regulations

AGENCY: Department of Education.

ACTION: Final regulations.

SUMMARY: The Secretary amends the Code of Federal Regulations (CFR) to remove unnecessary and obsolete regulations. As a result of new legislation, absence of funding, and review in accordance with the President's regulatory reinvention initiative, the Secretary has determined