

(ii) *Preparation of working standard, sample, and resolution test solutions*—(A) *Working standard solution.* Accurately weigh approximately 10 milligrams of the loracarbef working reference standard into a 50-milliliter volumetric flask. Dissolve and dilute to volume with mobile phase. Brief sonication may be required to obtain complete dissolution of the material.

(B) *Sample solution.* Accurately weigh approximately 10 milligrams of sample into a 50-milliliter volumetric flask. Dissolve and dilute to volume with mobile phase. Brief sonication may be required to obtain complete dissolution of the material.

(C) *Resolution test solution.* Prepare a resolution test solution containing approximately 0.2 milligram per milliliter each of loracarbef and loracarbef *L*-isomer in the mobile phase.

(iii) *System suitability requirements*—(A) *Asymmetry factor.* The asymmetry factor (A_s) at 5 percent peak height is satisfactory if it is not less than 0.8 and not more than 1.3 for the loracarbef peak.

(B) *Efficiency of the column.* The absolute efficiency (h_r) is satisfactory if it is not more than 20 for the loracarbef peak.

(C) *Resolution factor.* The resolution factor (R) between the peak for loracarbef and the peak for the resolution standard loracarbef *L*-isomer in the resolution test solution is satisfactory if it is not less than 6.0.

(D) *Coefficient of variation (relative standard deviation).* The coefficient of variation (S_R in percent of 5 replicate injections) is satisfactory if it is not more than 2.0 percent.

(E) *Capacity factor (K).* The capacity factor (K) for loracarbef is satisfactory if it is not less than 5 and not more than 8.

If the system suitability parameters have been met, then proceed as described in § 436.216(b) of this chapter.

(iv) *Calculations.* Calculate the micrograms of loracarbef per milligram of sample on an anhydrous basis as follows:

$$\text{Micrograms of loracarbef per milligram} = \frac{A_U \times P_s \times 100}{A_s \times C_U \times (100 - m)}$$

where:

A_U =Area of the loracarbef peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s =Area of the loracarbef peak in the chromatogram of the loracarbef working standard;

P_s =Loracarbef activity in the loracarbef working standard solution in micrograms per milliliter;

C_U =Milligrams of sample per milliliter of sample solution; and

m = Percent moisture content of the sample.

(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 100 milligrams per milliliter.

(4) *Specific rotation.* Dissolve and dilute an accurately weighed sample with sufficient 0.1 *N* HCl to obtain a concentration of approximately 10 milligrams of loracarbef activity per milliliter. Proceed as directed in § 436.210 of this chapter, using a 1.0-decimeter polarimeter tube. Calculate the specific rotation on the anhydrous basis.

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

(6) *Identity.* Proceed as directed in § 436.211 of this chapter, using the 1.0 percent potassium bromide disc prepared as described in § 436.211(b)(1).

Subpart B—Oral Dosage Forms

§ 443.120 Loracarbef oral dosage forms.

§ 443.120a Loracarbef capsules.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Loracarbef capsules are composed of loracarbef and one or more suitable and harmless lubricants and diluents enclosed in a gelatin capsule. Each capsule contains loracarbef equivalent to either 200 milligrams or 400 milligrams of loracarbef. Its loracarbef content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of loracarbef that it is represented to contain. Its moisture content is not more than 8.5 percent. It passes the dissolution test. It passes the identity test. The loracarbef used

conforms to the standards prescribed by § 443.20(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 loracarbef used in making the batch for potency, moisture, pH, specific rotation, crystallinity, and identity.

(B) The batch for content, moisture, dissolution, and identity.

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

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

(B) The batch: A minimum of 100 capsules.

(b) *Tests and methods of assay—(1) Loracarbef content.* Proceed as directed in § 443.20(b)(1), preparing the sample solution and calculating the loracarbef content as follows:

(i) *Preparation of sample solution.* Place one intact capsule in a 200-milliliter volumetric flask containing 150 milliliters of distilled water. Shake the mixture vigorously to aid disruption of the capsule. Sonicate the mixture briefly (5 minutes). Dilute the contents to volume with distilled water. Mix well and immediately transfer a suitable aliquot to a volumetric flask of appropriate size to obtain a solution containing 0.2 milligram per milliliter (estimated) of loracarbef when diluted to volume with mobile phase (described in § 443.20(b)(1)(i)). Filter this solution through a 0.45-micron membrane filter before injecting it into the chromatograph.

(ii) *Calculations.* Calculate the loracarbef content as follows:

$$\text{Milligrams of loracarbef per capsule} = \frac{A_U \times P_s \times d}{A_s \times 1,000}$$

where:

A_U = Area of the loracarbef peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s = Area of the loracarbef peak in the chromatogram of the loracarbef working

standard;

P_s = Loracarbef activity in the loracarbef working standard solution in micrograms per milliliter; and

d = Dilution factor of the sample.

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

(3) *Dissolution test.* Proceed as directed in § 436.215 of this chapter. The quantity Q , the amount of loracarbef activity dissolved, is 75 percent within 30 minutes.

(4) *Identity.* The retention time of the loracarbef response in the high-performance liquid chromatographic procedure described in paragraph (b)(1) of this section as applied to the sample solution compares qualitatively to that of the loracarbef reference standard.

§ 443.120b Loracarbef for oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Loracarbef for oral suspension is loracarbef with one or more suitable and harmless preservatives, sweeteners, suspending agents, colorings, antifoaming agents, and flavorings. When constituted as directed in the labeling, each milliliter contains the equivalent of either 20 or 40 milligrams loracarbef activity. Its loracarbef content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of loracarbef that it is represented to contain. Its moisture content is not more than 2.0 percent. When constituted as described in the labeling, the pH of the suspension is not less than 3.5 and not more than 6.0. It passes the identity test. The loracarbef used conforms to the standards prescribed by § 443.20(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 loracarbef used in making the batch for potency, moisture, pH, specific rotation, crystallinity, and identity.

(B) The batch for content, moisture, pH, and identity.