

Determine by inspection of the recorded spectrum the exact wavelengths of minimum absorption at approximately 11.3 and 12.65 microns. Also determine by inspection the exact wavelengths of maximum absorption at approximately 11.65 and 11.86 microns. In the following subdivision, references to these four nominal wavelengths are to the exact wavelengths observed on the particular instrument being used.

(b) *Standard containing 10 percent of polymorph A.* Draw a straight baseline between the minima occurring at 11.3 and 12.65 microns. Draw straight lines at 11.65 and 11.86 microns intersecting both the recorded spectrum and the baseline. Obtain the corrected absorbances at 11.65 and 11.86 microns and calculate the absorbance ratios as follows:

$$\text{Absorbance ratio} = \frac{S_{11.65} - B_{11.65}}{S_{11.86} - B_{11.86}}$$

where:

$S_{11.65}$ = Absorbance value of recorded spectrum at 11.65 microns;

$B_{11.65}$ = Absorbance value at point of intersection of the 11.65-micron line with the baseline;

$S_{11.86}$ = Absorbance value of recorded spectrum at 11.86 microns;

$B_{11.86}$ = Absorbance value at point of intersection of the 11.86-micron line with the baseline.

(c) *Sample.* Proceed as described in paragraph (b)(3)(iv)(b) of this section.

(v) *Calculation.* The absorbance ratio of the sample must be greater than the absorbance ratio of the standard containing 10 percent of polymorph A.

[39 FR 19166, May 30, 1974, as amended at 49 FR 6093, Feb. 17, 1984; 50 FR 19921, May 13, 1985]

§ 455.120 Cycloserine capsules.

(a) *Requirements for certification—(1) Standards of identity, quality, and purity.* Cycloserine capsules are capsules composed of crystalline cycloserine, with or without one or more suitable and harmless buffer substances, diluents, binders, and lubricants. Each capsule contains 250 milligrams of cycloserine. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cycloserine that it is rep-

resented to contain. The loss on drying is not more than 1.0 percent. The cycloserine used conforms to the standards prescribed by § 455.20(a)(1).

(2) *Labeling.* In addition to the labeling prescribed by § 432.5 of this chapter, the labeling of each package shall bear a warning to the effect that the drug is to be used in patients with tuberculosis who fail to respond to treatment with isoniazid, streptomycin, paraaminosalicylic acid, viomycin, pyrazinamide, or combinations of these drugs, and that the drug may cause serious reactions such as convulsive seizures and mental disturbances.

(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) Cycloserine used in making the batch for potency, loss on drying, pH, residue on ignition, crystallinity, and identity.

(b) The batch for cycloserine content and loss on drying.

(ii) Samples required:

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

(b) The batch: Minimum of 30 capsules.

(b) *Tests and methods of assay—(1) Potency.* Using the cycloserine working standard as the standard of comparison, assay for potency by either of the following methods; however, the results obtained from the microbiological turbidimetric assay shall be conclusive.

(i) *Chemical colorimetric assay—(a) Reagents.* (1) Acetic acid—1.0*N* solution.

(2) Sodium hydroxide—4.0*N* and 0.1*N* solutions.

(3) Sodium nitroprusside—4.0 percent solution: Dissolve 4.0 grams in sufficient distilled water to make 100.0 milliliters. Mix well. Store in amber bottle.

(4) Oxidized nitroprusside reagent—Mix equal parts of the 4.0 percent sodium nitroprusside solution and 4.0*N* sodium hydroxide, and let stand for 1 hour before using. Prepare daily and store in amber bottle.

(5) Cycloserine standard solution—dilute an appropriate-sized aliquot of the

stock standard solution, prepared as directed in § 455.20(b)(1)(i)(a), in 0.1*N* sodium hydroxide to obtain a working standard solution containing 100 micrograms of cycloserine per milliliter.

(b) *Procedure.* Transfer the contents of 10 capsules into a 1,000-milliliter volumetric flask. Add 0.1*N* sodium hydroxide to dissolve the sample, and add sufficient 0.1*N* sodium hydroxide to measure 1,000 milliliters. Mix well and filter. Dilute an aliquot of the filtrate with sufficient 0.1*N* sodium hydroxide to give a concentration of 0.1 milligram per milliliter (estimated) and mix

well. Pipette exactly 1.0 milliliter of the working standard solution and 1.0 milliliter of the sample solution into separate test tubes. Add exactly 3.0 milliliters of 1.0*N* acetic acid and exactly 1.0 milliliter of oxidized nitroprusside reagent to each of the test tubes; then mix thoroughly. Allow the tubes to stand at room temperature for 10 to 15 minutes, in order that maximum color intensity may develop. Using a reagent blank, determine the absorbance of the solutions at 625 nanometers in a suitable spectrophotometer.

Calculation:

$$\text{Milligrams of cycloserine per capsule} = \frac{\text{Sample absorbance}}{\text{Standard absorbance}} \times \text{Labeled potency per capsule in milligrams}$$

(ii) *Microbiological turbidimetric assay.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules in a high-speed glass blender with sufficient sterile distilled water to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute the stock solution with sterile distilled water to the reference concentration of 50 micrograms of cycloserine per milliliter (estimated).

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

[39 FR 19166, May 30, 1974, as amended at 50 FR 19921, May 13, 1985]

§ 455.150 Calcium novobiocin oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Calcium novobiocin oral suspension is a suspension containing calcium novobiocin and one or more suitable and harmless diluents, preservatives, suspending agents, surfactants, flavorings, and colorings in purified water. Each milliliter contains 25 milligrams of novobiocin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of novobiocin that it is represented to contain. The pH is not less than 6.0 and

not more than 7.5. The calcium novobiocin used conforms to the standards prescribed by § 455.50(a)(1) (i), (iv), (v), (vi), and (vii). If sodium novobiocin is reacted with a suitable calcium salt to form calcium novobiocin, the sodium novobiocin used conforms to the standards prescribed by § 455.51(a)(1) (i), (iv), (v), (vi), (vii), and (viii).

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

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

(i) Results of tests and assays on:

(a) The calcium novobiocin used in making the batch for potency, pH, crystallinity, identity, and specific rotation. If sodium novobiocin is used in making the batch: Potency, pH, residue on ignition, specific rotation, identity, and crystallinity.

(b) The batch for potency and pH.

(ii) Samples required:

(a) The calcium novobiocin or the sodium novobiocin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch: Minimum of 5 immediate containers.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Remove a representative sample of the sirup with a suitable