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Clorazepate Dipotassium Tablets

» Clorazepate Dipotassium Tablets contain not less than 90.0 percent and not more than 110.0 percent of clorazepate dipotassium ($C_{16}H_{11}ClK_2N_2O_4$).

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—

USP 2-Amino-5-chlorobenzophenone RS $C_{13}H_{10}ClNO$ 231.68

USP Nordazepam RS

7-Chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one.

$C_{15}H_{11}ClN_2O$ 270.72

USP Clorazepate Dipotassium RS

Identification—The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Dissolution ⟨711⟩—

Medium: 0.01 N hydrochloric acid; 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{16}H_{11}ClK_2N_2O_4$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 240 nm on filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Clorazepate Dipotassium RS in the same *Medium*.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{16}H_{11}ClK_2N_2O_4$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

PROCEDURE FOR CONTENT UNIFORMITY—

Standard solution—Dissolve an accurately weighed quantity of USP Clorazepate Dipotassium RS in 0.01 M sodium hydroxide, and dilute quantitatively, and stepwise if necessary, with 0.01 M sodium hydroxide to obtain a solution having a known concentration of about 7.6 µg per mL.

Test solution—Transfer 1 Tablet to a suitable container, add 200 mL of 0.01 M sodium hydroxide, and homogenize for not less than 3 minutes. Centrifuge a portion of this solution for 15 minutes, and filter the supernatant, discarding the first 20 mL. Dilute an accurately measured portion of the filtrate with 0.01 M sodium hydroxide to obtain a solution having a known concentration of about 7.6 µg per mL.

Procedure—Concomitantly determine the absorbances of the *Standard solution* and the *Test solution* in 1-cm cells at the wavelength of maximum absorbance at about 231 nm, with a suitable spectrophotometer, using 0.01 M sodium hydroxide as the blank.

Related compounds—

METHOD I—

Phosphate buffer solution—Dissolve about 13.8 g of monobasic sodium phosphate in 500 mL of water, adjust with 1 N sodium hydroxide to a pH of 8.0, and mix.

Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, and *Phosphate buffer solution* (5:4:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Dissolve an accurately weighed quantity of USP Nordazepam RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, with acetonitrile to obtain a solution having a known concentration of about 66 µg per mL. Transfer 4.0 mL of this solution to a 25-mL volumetric flask, add 5.0 mL of 0.7 M potassium carbonate and 3.0 mL of acetonitrile, dilute with water to volume, mix, and filter.

Test solution—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 15 mg of clorazepate dipotassium, to a suitable container. Add 5 mL of acetonitrile, 5 mL of 0.7 M potassium carbonate, and 15 mL of water, stir for 10 minutes, and filter. [Note—Prepare fresh before each injection, and use within 3 minutes.]

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Chromatographic system—The liquid chromatograph is equipped with a 232-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms for not less than twice the retention time of nordazepam, and measure the peak responses. Calculate the quantity, in mg, of each impurity in the portion of Tablets taken by the formula:

$$25C(r_i/r_S)$$

in which C is the concentration, in mg per mL, of USP Nordazepam RS in the *Standard solution;* r_i is the peak response of each impurity obtained from the *Test solution;* and r_S is the peak response for nordazepam obtained from the *Standard solution:* not more than 2.0% of nordazepam is found.

METHOD II—

Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, and a 1 M solution of tetrabutylammonium hydroxide in methanol (110:90:1), adjust with phosphoric acid to a pH of 7.7, and mix. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard solution—Dissolve an accurately weighed quantity of USP 2-Amino-5-chlorobenzophenone RS in acetonitrile to obtain a solution having a known concentration of about 0.50 mg per mL. Dilute with water to obtain a solution having a known concentration of about 0.25 mg per mL. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with a mixture of 0.1 mM sodium hydroxide and acetonitrile (7:3) to volume, and mix. Transfer 15 mL of this solution to a 50-mL volumetric flask, dilute with a mixture of 0.1 mM sodium hydroxide and acetonitrile (7:3) to volume, and mix.

Test solution—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 15 mg of clorazepate dipotassium, to a suitable container, add 10 mL of a mixture of 0.1 mM sodium hydroxide and acetonitrile (7:3), mix, shake by mechanical means for 10 minutes, and filter.

Chromatographic system—The liquid chromatograph is equipped with a 238-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the quantity, in mg, of each impurity in the portion of Tablets taken by the formula:

$$10C(r_i/r_S)$$

in which C is the concentration, in mg per mL, of USP 2-Amino-5-chlorobenzophenone RS in the *Standard solution;* r_i is the peak response of each impurity obtained from the *Test solution;* and r_S is the response of the 2-amino-5-chlorobenzophenone peak obtained from the *Standard solution:* the sum of all impurities, other than nordazepam, found in *Method I* and *Method II* is not more than 0.5%.

Assay—

Buffer solution—Transfer 5.0 mL of 1 M tetrabutylammonium hydroxide in methanol to a 1-L volumetric flask, dilute with water to volume, adjust with phosphoric acid to a pH of 7.5, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (7:3). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Clorazepate Dipotassium RS in 0.01 M sodium hydroxide, and dilute quantitatively, and stepwise if necessary, with 0.01 M sodium hydroxide to obtain a solution having a known concentration of about 60 µg per mL. Shake by mechanical means for 15 minutes, and filter.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 75 mg of clorazepate dipotassium, to a suitable container, add 200 mL of 0.01 M sodium hydroxide, and homogenize for not less than 3 minutes. Transfer 15 mL of this solution to a 100-mL volumetric flask, dilute with 0.01 M sodium hydroxide to volume, mix, and filter.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 230-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses of the major peaks. Calculate the quantity, in mg, of clorazepate dipotassium

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($C_{16}H_{11}ClK_2N_2O_4$) in the portion of Tablets taken by the formula:

$$1333C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Clorazepate Dipotassium RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
CLORAZEPATE DIPOTASSIUM TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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