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Disopyramide Phosphate Extended-Release Capsules

» Disopyramide Phosphate Extended-Release Capsules contain an amount of Disopyramide Phosphate equivalent to not less than 90.0 percent and not more than 110.0 percent of the labeled amount of disopyramide ($C_{21}H_{29}N_3O$).

Packaging and storage—Preserve in well-closed containers.

Labeling—The labeling indicates the *Dissolution Test* with which the product complies.

USP Reference standards ⟨11⟩—
USP Disopyramide Phosphate RS

Identification—Transfer a portion of Capsule contents, equivalent to about 195 mg of disopyramide phosphate, to a 25-mL volumetric flask, add 20 mL of methanol, and shake by mechanical means for 20 minutes. Dilute with methanol to volume, mix, and filter, discarding the first 10 mL of the filtrate. Apply 20 µL each of the subsequent filtrate and of a solution of USP Disopyramide Phosphate RS in methanol containing 7.7 mg per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of toluene, absolute alcohol, and ammonium hydroxide (170:28:2) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by viewing under short-wavelength UV light: the R_F value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

Dissolution ⟨711⟩—

TEST 1—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*.

pH 2.5, 0.1 M Phosphate buffer—Dissolve 272 g of monobasic potassium phosphate in 20 L of water, and adjust with hydrochloric acid to a pH of 2.50 ± 0.04. [NOTE—Do not adjust back to pH 2.50 with base if too much acid is added. It is imperative that the ionic strength of the buffer be controlled.]

Medium: pH 2.5, 0.1 M Phosphate buffer; 1000 mL.

Apparatus 1: 100 rpm.

Times: 1 hour; 2 hours; 5 hours; 12 hours.

Procedure—Filter 10 mL of the solution under test at the required test points. Determine the amount of disopyramide ($C_{21}H_{29}N_3O$) dissolved from UV absorbances at the wavelength of maximum absorbance at about 261 nm of this solution, suitably diluted with *Medium*, if necessary, using *Medium* as the blank, in comparison with a Standard solution having a known concentration of USP Disopyramide Phosphate RS dissolved in *Medium*.

Tolerances—The percentage of the labeled amount of disopyramide ($C_{21}H_{29}N_3O$) dissolved is within the range stated at each of the following times.

Time (hours)	Amount dissolved
1	between 5% and 25%
2	between 17% and 43%
5	between 50% and 80%
12	not less than 85%

TEST 2—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

pH 2.5, *0.1 M Phosphate buffer,* and *Procedure*— Proceed as directed for *Test 1*.

Medium—Prepare as directed for *Test 1;* 900 mL.

Apparatus 2: 100 rpm.

Times and Tolerances:

Time (hours)	Amount dissolved
1	between 5% and 30%
4	between 40% and 65%
8	between 60% and 90%
12	not less than 75%

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

Assay—

Standard preparation—Dissolve an accurately weighed quantity of USP Disopyramide Phosphate RS in 0.1 N sulfuric acid, and dilute quantitatively and stepwise with the same solvent to obtain a solution having a known concentration of about 40 µg per mL.

Assay preparation—Grind the contents of not fewer than 20 Capsules to a powder fine enough to pass through a 40-mesh screen. Transfer an accurately weighed portion of the powder, equivalent to about 650 mg of disopyramide phosphate, to a 500-mL volumetric flask. Add about 400 mL of 0.1 N sulfuric acid, and shake for 30 minutes. Dilute with 0.1 N sulfuric acid to volume, mix, and filter. Dilute an accurately measured portion of the filtrate quantitatively and stepwise with 0.1 N sulfuric acid to obtain a solution having a concentration of about 40 µg per mL.

Procedure—Concomitantly determine the absorbances of the *Assay preparation* and the *Standard preparation* at the wavelength of maximum absorbance at about 261 nm, with a suitable spectrophotometer, using 0.1 N sulfuric acid as the blank. Calculate the quantity, in mg, of $C_{21}H_{29}N_3O$ in the portion of Capsules taken by the formula:

$$16.25(339.48/437.47)C(A_U/A_S)$$

in which 339.48 and 437.47 are the molecular weights of disopyramide and disopyramide phosphate, respectively; C is the concentration, in µg per mL, of USP Disopyramide Phosphate RS in the *Standard preparation;* and A_U and A_S are the absorbances of 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
DISOPYRAMIDE PHOSPHATE EXTENDED-RELEASE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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