$C_{19}H_{21}NO \cdot HCl$ in the portion of Doxepin Hydrochloride taken by the formula:

$$0.5C[(r_{U(Z)} + r_{U(E)}) / (r_{S(Z)} + r_{S(E)})]$$

in which C is the concentration, in µg per mL, of USP Doxepin Hydrochloride RS in the *Standard preparation*, and $r_{U(Z)}$ and $r_{U(E)}$ are the respective peak responses of the (*Z*)- and (*E*)-isomers obtained from the *Assay preparation*, and $r_{S(Z)}$ and $r_{S(E)}$ are the respective peak responses of the (*Z*)- and (*E*)-isomers obtained from the *Standard preparation*. Calculate the percentage of the (*Z*)-isomer in the *Assay preparation* taken by the formula:

$$(r_{U(Z)} / r_{S(Z)})(W_S / W_T)(P_Z)$$

in which W_S is the weight, in mg, of USP Doxepin Hydrochloride RS in the *Standard preparation*, W_T is the weight, in mg, in the portion of Doxepin Hydrochloride taken, and P_Z is the labeled percentage of (*Z*)-isomer in USP Doxepin Hydrochloride RS. Similarly calculate the percentage of (*E*)-isomer in the *Assay preparation* taken by the formula:

$$(r_{U(E)} / r_{S(E)})(W_S / W_T)(P_E)$$

in which P_E is the labeled percentage of (*E*)-isomer in USP Doxepin Hydrochloride RS.

Doxepin Hydrochloride Capsules

» Doxepin Hydrochloride Capsules contain not less than 90.0 per cent and not more than 110.0 percent of the labeled amount of doxepin ($C_{19}H_{21}NO$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Doxepin Hydrochloride RS

Identification—The retention times of the major peaks for *(E)*- and *(Z)*-isomers in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩**—**

Medium: water; 900 mL.

Apparatus 1: 50 rpm.

Time: 30 minutes.

*Procedure—*Determine the amount of $C_{19}H_{21}NO$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 292 nm on filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Doxepin Hydrochloride RS in the same *Medium.*

*Tolerances—*Not less than 80% *(Q)* of the labeled amount of $C_{19}H_{21}NO$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements, the following procedure being used where the test for *Content Uniformity* is required.

*Diluting solution—*Prepare a mixture containing 500 mL of methanol and 500 mL of 0.05 M monobasic sodium phosphate, and filter. Adjust with 2 N sodium hydroxide to a pH of 6.7.

*Standard preparation—*Transfer 20 mg of USP Doxepin Hydrochloride RS, accurately weighed, to a 200-mL volumetric flask, dissolve in and dilute with *Diluting solution* to volume, and filter.

*Test preparation—*Transfer the contents of 1 Capsule into an appropriate volumetric flask, add *Diluting solution* to about 80% of the volume of the flask, and shake the flask by mechanical means for about 30 minutes. Dilute with *Diluting solution* to volume. Make further dilutions, if necessary, to obtain a solution having a known concentration of 0.1 mg per mL of doxepin hydrochloride. Individually test 9 more Capsules using the above procedure.

*Procedure—*Determine the amount of active ingredient in each unit of the *Test preparation* from UV absorbances at the wavelength of maximum absorbance at about 292 nm using 0.5-cm cells in comparison with the *Standard preparation.*

Water, *Method I* ⟨921⟩**:** not more than 9.0%, determined on the contents of 1 Capsule.

Assay—

Mobile phase, Standard preparation, and *Chromatographic system—*Proceed as directed in the *Assay* under *Doxepin Hydrochloride.*

*Assay preparation—*Remove, as completely as possible, the contents of not fewer than 20 Capsules. Weigh the contents and determine the average weight per Capsule. Mix the combined contents, and transfer an accurately weighed quantity of the powder, equivalent to about 50 mg of doxepin hydrochloride, to a 100-mL volumetric flask. Add about 70 mL of *Mobile phase,* and shake by mechanical means for 30 minutes. Dilute with *Mobile phase* to volume, mix, and filter. Pipet 10.0 mL of this solution into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

*Procedure—*Proceed as directed for *Procedure* in the *Assay* under *Doxepin Hydrochloride.* Calculate the quantity, in mg, of $C_{19}H_{21}NO \cdot HCl$ in the portion of Capsules taken by the formula:

$$0.5C[(r_{U(Z)} + r_{U(E)}) / (r_{S(Z)} + r_{S(E)})]$$

in which the terms are as defined therein.

Doxepin Hydrochloride Oral Solution

» Doxepin Hydrochloride Oral Solution contains not less than 90.0 per cent and not more than 110.0 percent of the labeled amount of doxepin ($C_{19}H_{21}NO$).

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

Labeling—Label it to indicate that each dose is to be diluted with water or other suitable fluid to approximately 120 mL, just prior to administration.

USP Reference standards ⟨11⟩**—**
USP Doxepin Hydrochloride RS

Identification—

*Mobile phase—*Add 0.2 mL of diethylamine to a solution containing 250 mL of chloroform and 750 mL of acetonitrile in a vacuum flask. Prior to use, degas the contents of the flask by stirring vigorously with a magnetic stirrer, while applying vacuum, for 10 minutes.

*Procedure—*Transfer 5.0 mL of the Oral Solution to a 60-mL separator, add 1 mL of sodium hydroxide solution (1 in 25), 1 g of sodium chloride, and 5.0 mL of ethyl acetate, and shake the mixture vigorously for 1 minute. Allow the phases to separate, transfer 1.0 mL of the clear upper phase to a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Transfer about 22 mg of USP Doxepin Hydrochloride RS to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Inject 4-µL portions of both solutions into a high-pressure liquid chromatograph (see *Chromatography* ⟨621⟩) fitted with a 50-cm × 2-mm column packed with silica microspheres and equipped with an UV detector capable of monitoring absorption at 254 nm and a suitable recorder. Adjust the operating parameters to obtain a flow rate of about 24 mL per hour. The chromatogram of the test solution exhibits two peaks having retention times