earth, and allow to be absorbed for a period of 10 minutes. Elute the column with 60 mL of water-washed ether, evaporate the eluate on a steam bath to dryness, wash the residue with three 20-mL portions of *n*-heptane, and filter. Dry the residue at 105° for 30 minutes: the crystals respond to *Identification* tests *A* and *B* under *Prednisone*.

Dissolution ⟨711⟩**—**

Medium: water; use 500 mL of the *Dissolution Medium* for Tablets labeled to contain 10 mg of prednisone or less, and 900 mL for Tablets labeled to contain more than 10 mg of prednisone.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{21}H_{26}O_5$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 242 nm of 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 Prednisone RS in the same medium. An amount of alcohol not to exceed 5% of the total volume of the Standard solution may be used to bring the prednisone standard into solution prior to dilution with water.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{21}H_{26}O_5$ is dissolved in 30 minutes.

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

Procedure for content uniformity—

Mobile phase, Internal standard solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Prednisone*.

Test preparation—Place 1 Tablet in a volumetric flask of such size that when the contents are diluted to volume the resulting solution has a concentration of about 0.2 mg of prednisone per mL. Add 5 mL of water, swirl, sonicate for 1 minute, add a volume of methanol equal to one-half the volume of the volumetric flask, and sonicate again for 1 minute. Dilute with water to volume, and mix. Transfer 5.0 mL of this solution and 5.0 mL of the *Internal standard solution* to a 50-mL volumetric flask, add dilute methanol (1 in 2) to volume, and mix. Filter through a 5-µm filter, discarding the first 20 mL of the filtrate.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Prednisone*, except to calculate the quantity, in mg, of $C_{21}H_{26}O_5$ in the Tablet taken by the formula:

$$DC(R_U / R_S)$$

in which *D* is the dilution factor for the *Test preparation* and the other terms are as defined therein.

Assay—

Mobile phase, Internal standard solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Prednisone.*

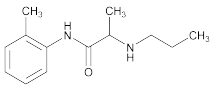
Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 20 mg of prednisone, to a 100-mL volumetric flask. Add 5 mL of water, sonicate for 1 minute, add 50 mL of methanol, and sonicate again for 1 minute. Dilute with water to volume, and mix. Transfer 5.0 mL of this solution and 5.0 mL of the *Internal standard solution* to a 50-mL volumetric flask, add dilute methanol (1 in 2) to volume, and mix. Filter through a 5-µm filter, discarding the first 20 mL of the filtrate.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Prednisone*, except to calculate the quantity, in mg, of $C_{21}H_{26}O_5$ in the portion of Tablets taken by the formula:

$$C(R_U / R_S)$$

in which the terms are as defined therein.

Prilocaine



$C_{13}H_{20}N_2O$ 220.31

Propranamide, *N*-(2-methylphenyl)-2-(propylamino)-.

2-(Propylamino)-*o*-propionotoluidide.

(*RS*)-*N*-(2-methylphenyl)-2-(propylamino)propanamide [721-50-6].

» Prilocaine contains not less than 99.0 percent and not more than 101.0 percent of $C_{13}H_{20}N_2O$, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers, and store below 25°.

USP Reference standards ⟨11⟩**—**

USP Prilocaine RS

USP Prilocaine Related Compound A RS

o-Toluidine hydrochloride.

$CH_3C_6H_4NH_2HCl$ 143.62 [CAS-636-21-5].

USP Prilocaine Related Compound B RS

(*RS*)-*N*-(4-Methylphenyl)-2-(propylamino)propanamide.

$C_{13}H_{20}N_2O$ 220.31

Identification, *Infrared Absorption* ⟨197K⟩—Because of the low melting point of prilocaine, the mortar, pestle, and potassium bromide must be at ambient temperature. Record the IR spectrum using the diffuse reflectance technique.

Melting range, *Class 1a* ⟨741⟩**:** between 36° and 39°, without previous drying.

Water, *Method Ia* ⟨921⟩**:** not more than 0.5%, determined on 1.00 g of sample.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Limit of prilocaine related compound A—

Mobile phase—Prepare as directed under *Related compounds.*

Standard solution—Dissolve an accurately weighed quantity of USP Prilocaine Related Compound A RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 1.3 µg per mL.

Test solution—Transfer about 100 mg of Prilocaine, accurately weighed, to a 10-mL volumetric flask, dissolve and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—Use the system as described under *Related compounds*. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the signal-to-noise ratio of the major peak should be greater than 10.

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 responses for the major peaks: any peak corresponding to prilocaine related compound A (*o*-toluidine) in the *Test solution* is not greater than the response of the major peak in the *Standard solution* (0.01%).

Related compounds—

Buffer—Dilute 1.3 mL of a 1 M monobasic sodium phosphate solution (1.38 g diluted with water to 10 mL) and 32.5 mL of a 0.5 M anhydrous disodium hydrogen phosphate solution (7.1 g diluted with water to 100 mL) with water to 1 L. The pH of this solution is 8.0. Make adjustments as needed.

Mobile phase—Prepare a degassed mixture of *Buffer* and acetonitrile (73:27). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Dissolve accurately weighed quantities of USP Prilocaine RS and USP Prilocaine Related Compound B RS in *Mobile phase,* and dilute quantitatively, and step-

wise if necessary, with *Mobile phase* to obtain a solution having known concentrations of about 2.5 µg per mL and 3.0 µg per mL, respectively.

Test solution—Transfer about 25 mg of Prilocaine, accurately weighed, to a 10-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 240-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.19 for prilocaine related compound B and 1.0 for prilocaine; the resolution, *R,* between prilocaine and prilocaine related compound B is not less than 3.0; and the signal-to-noise ratio for the prilocaine peak is not less than 10.

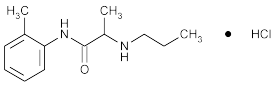
Procedure—Inject a volume (about 20 µL) of the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Run the chromatograms for at least 1.5 times the retention of prilocaine. Check the stability of the baseline by injecting *Mobile phase*. Calculate the percentage of each impurity in the portion of Prilocaine taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the individual peak response of each impurity; and r_s is the sum of the responses of all the peaks: not more than 0.2% of any individual impurity is found; not more than one impurity exceeds 0.1%, and not more than 0.5% of total impurities is found.

Assay—Dissolve 400 mg of Prilocaine, accurately weighed, in 50 mL of glacial acetic acid. Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 perchloric acid is equivalent to 22.03 mg of $C_{13}H_{20}N_2O$.

Prilocaine Hydrochloride



$C_{13}H_{20}N_2O \cdot HCl$ 256.77
Propanamide, *N*-(2-methylphenyl)-2-(propylamino)-, monohydrochloride.
2-(Propylamino)-*o*-propionotoluidide monohydrochloride [1786-81-8].

» Prilocaine Hydrochloride contains not less than 99.0 percent and not more than 101.0 percent of $C_{13}H_{20}N_2O \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

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

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: Dissolve about 300 mg in 5 mL of water, add 4 mL of 6 N ammonium hydroxide, and extract with 50 mL of chloroform. Filter the extract, and evaporate the filtrate on a steam bath with the aid of a current of air. Dissolve about 100 mg of the prilocaine so obtained in 1 mL of alcohol, add 10 drops of cobaltous chloride TS, and shake for 2 minutes: a bright green color develops, and a precipitate is formed.

C: Dissolve about 100 mg in 3 mL of water, render the solution alkaline with 6 N ammonium hydroxide, and filter: the filtrate responds to the tests for *Chloride* ⟨191⟩.

Melting range, *Class I* ⟨741⟩: between 166° and 169°.

Loss on drying ⟨731⟩**—**Dry it at 105° for 4 hours: it loses not more than 0.3% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Heavy metals, *Method I* ⟨231⟩: 0.002%.

Assay—Dissolve about 500 mg of Prilocaine Hydrochloride, accurately weighed, in 50 mL of glacial acetic acid, add 10 mL of mercuric acetate TS and 2 drops of crystal violet TS, and titrate with 0.1 N perchloric acid VS to a blue-green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 25.68 mg of $C_{13}H_{20}N_2O \cdot HCl$.

Prilocaine Hydrochloride Injection

» Prilocaine Hydrochloride Injection is a sterile solution of Prilocaine Hydrochloride in Water for Injection. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_{13}H_{20}N_2O \cdot HCl$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass.

USP Reference standards ⟨11⟩**—**
USP Endotoxin RS
USP Prilocaine Hydrochloride RS

Identification—

A: It meets the requirements under *Identification—Organic Nitrogenous Bases* ⟨181⟩.

B: It responds to *Identification* test *B* under *Prilocaine Hydrochloride*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.9 USP Endotoxin Unit per mg of prilocaine hydrochloride.

pH ⟨791⟩: between 6.0 and 7.0.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Mobile phase—Mix 50 mL of glacial acetic acid and 930 mL of water, and adjust with 1 N sodium hydroxide to a pH of 3.40. Mix about 4 volumes of this solution with 1 volume of acetonitrile, such that the retention time of prilocaine is about 4 to 6 minutes. Filter through a membrane filter (1 µm or finer porosity), and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Prilocaine Hydrochloride RS quantitatively in *Mobile phase* to obtain a solution having a known concentration of about 4 mg per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 200 mg of prilocaine hydrochloride, to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Resolution preparation—Prepare a solution of procainamide hydrochloride in *Mobile phase* containing about 900 µg per mL. Mix 2 mL of this solution and 20 mL of *Standard preparation*.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1, and is operated at a temperature between 20° and 25° maintained at ±1.0° of the selected temperature. The flow rate is about 1.5 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 1.5%. Chromatograph about 10 µL of the *Resolution preparation*, and record the peak responses as directed for *Procedure:*