Dissolution ⟨711⟩—

Medium: water; 500 mL.

Apparatus 1: 100 rpm.

Time: 60 minutes.

Procedure—Determine the total amount of $C_{12}H_{17}N_2NaO_3$ and $C_{11}H_{17}N_2NaO_3$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 239 nm of filtered portions of the solution under test, suitably diluted with 0.1 N sodium hydroxide, in comparison with a Standard solution having known concentrations of about 7.5 µg each per mL, of USP Secobarbital RS and USP Amobarbital RS in the same medium. An amount of alcohol not to exceed 1% of the total volume of the Standard solution may be used to dissolve the Reference Standards prior to dilution with water and 0.1 N sodium hydroxide.

Tolerances—Not less than 60% *(Q)* of the labeled total amount of $C_{12}H_{17}N_2NaO_3$ and $C_{11}H_{17}N_2NaO_3$ is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements for *Content Uniformity* with respect to secobarbital sodium and to amobarbital sodium.

Assay—

Internal standard solution—Dissolve aprobarbital in chloroform to obtain a solution having a concentration of about 0.75 mg per mL.

Standard preparation—Transfer about 92 mg of USP Secobarbital RS, and about 91 mg of USP Amobarbital RS, both accurately weighed, to a 100-mL volumetric flask, and dissolve in 50 mL of chloroform. Dilute with chloroform to volume, and mix.

Assay preparation—Remove, as completely as possible, the contents of not less than 20 Capsules. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of secobarbital sodium, to a separator, add 20 mL of water, 1 mL of hydrochloric acid, and 100.0 mL of chloroform, and shake for 3 minutes. Remove the chloroform layer, and use as directed in the *Procedure.*

Chromatographic system (see *Chromatography* ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector and contains a 0.6-m × 3.5-mm glass column packed with 3 percent liquid phase G10 on 100- to 120-mesh support S1AB. The column is maintained at about 175°, the injection port at about 235°, the detector block at about 245°, and dry helium is used as the carrier gas at a flow rate of about 55 mL per minute. Chromatograph five replicate injections of the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 2%; the resolution factor between amobarbital and the internal standard is not less than 1.5; the resolution factor between amobarbital and secobarbital is not less than 2.5; and the tailing factor does not exceed 1.5 for any of the three peaks.

Procedure—Mix 5.0 mL of the *Standard preparation* with 5.0 mL of the *Internal standard solution.* Mix 5.0 mL of the *Assay preparation* with 5.0 mL of the *Internal standard solution*. Separately inject equal volumes (about 3 µL) of the resulting solutions into the chromatograph, and record the chromatograms. Measure the responses for the major peaks. The relative retention times with respect to the internal standard are about 1.3 for amobarbital and 1.8 for secobarbital. Calculate the quantity, in mg, of secobarbital sodium ($C_{12}H_{17}N_2NaO_3$) in the portion of Capsules taken by the formula:

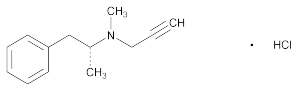
$$(260.27 / 238.28)W(R_U / R_S)$$

in which 260.27 and 238.28 are the molecular weights of secobarbital sodium and secobarbital, respectively, W is the weight, in mg, of USP Secobarbital RS taken for the *Standard preparation*, and R_U and R_S are the ratios of the peak response of secobarbital to that of the internal standard in the *Assay preparation* and the *Standard preparation*, respectively. Similarly calculate the quantity, in mg, of amobarbital sodium ($C_{11}H_{17}N_2NaO_3$) in the portion of Capsules taken by the formula:

$$(248.26 / 226.28)W'(R'_U / R'_S)$$

in which 248.26 and 226.28 are the molecular weights of amobarbital sodium and amobarbital, respectively, W' is the weight, in mg, of USP Amobarbital RS taken for the *Standard preparation*, and R'_U and R'_S are the ratios of the peak response of amobarbital to that of the internal standard obtained from *Assay preparation* and the *Standard preparation*, respectively.

Selegiline Hydrochloride



$C_{13}H_{17}N \cdot HCl$ 223.74

Benzeneethanamine, *N*,α-dimethyl-*N*-2-propynyl-, hydrochloride, (*R*)-.

(–)-(*R*)-*N*,α-Dimethyl-*N*-2-propynylphenethylamine hydrochloride [14611-52-0].

» Selegiline Hydrochloride contains not less than 98.0 percent and not more than 101.0 percent of $C_{13}H_{17}N \cdot HCl$, calculated on the dried basis.

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

USP Reference standards ⟨11⟩—
USP Selegiline Hydrochloride RS
USP Methamphetamine Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 0.5 mg per mL.

Medium: water.

C: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation* obtained as directed in the *Assay*.

D: It responds to the tests for *Chloride* ⟨191⟩.

Melting range ⟨741⟩: not greater than 2°, within the limits of 141° and 145°.

Specific rotation ⟨781S⟩: between –10.0° and –12.0°.

Test solution: 100 mg per mL, in water.

Loss on drying ⟨731⟩—Dry it in vacuum at 60° for 3 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Heavy metals, *Method II* ⟨231⟩: not more than 0.002%.

Chromatographic purity—

Buffer solution, Mobile phase, and *System suitability solution*—Proceed as directed in the *Assay*.

Standard solution—Transfer 10.0 mL of the *System suitability solution* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Transfer 10.0 mL of this solution to a 50 mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Test solution—Transfer 50 mg of Selegiline Hydrochloride to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system—Proceed as directed in the *Assay*. Inject about 20 µL of the *Standard solution*, and record the peak responses as directed in the *Procedure:* the resolution, *R,* between the methamphetamine and selegiline peaks is not less than 3, and the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, and allow the *Test solution* to elute for not less than three times the retention time of selegiline. Record the chromatograms, and measure the peak responses. Calculate the percentage of each impurity in the portion of Selegiline Hydrochloride taken by the formula:

$$5000(C / W)(r_i / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Selegiline Hydrochloride RS in the *Standard solution*, *W* is the weight, in mg, of Selegiline Hydrochloride taken to prepare the *Test solution*, r_i is the peak response for each impurity in the chromatogram of the *Test solution*, and r_S is the peak response for selegiline in the chromatogram of the *Standard solution*. Not more than 0.2% of any individual impurity is found, and the sum of all impurities is not more than 1.0%.

Assay—

Buffer solution—Prepare a solution of 0.1 M monobasic ammonium phosphate, adjust with phosphoric acid to a pH of 3.1, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (80:20). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Selegiline Hydrochloride RS, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.1 mg per mL.

System suitability solution—Dissolve accurately weighed quantities of USP Methamphetamine Hydrochloride RS and USP Selegiline Hydrochloride RS in *Mobile phase* to obtain a solution containing 0.1 mg per mL of each Reference Standard.

Assay preparation—Transfer an accurately weighed quantity, about 50 mg of Selegiline Hydrochloride, to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 205-nm detector and a 3.9-mm × 30-cm column that contains 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 resolution, *R,* between the methamphetamine and selegiline peaks is not less than 3, and 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 for the major peaks. Calculate the quantity, in mg, of $C_{13}H_{17}N \cdot HCl$ in the portion of Selegiline Hydrochloride taken by the formula:

$$500C(r_U / r_S)$$

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

Selegiline Hydrochloride Tablets

» Selegiline Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{13}H_{17}N \cdot HCl$.

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

USP Reference standards ⟨11⟩**—**
USP Selegiline Hydrochloride RS
USP Methamphetamine Hydrochloride 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: water; 500 mL.

Apparatus 1: 50 rpm.

Time: 20 minutes.

Determine the amount of $C_{13}H_{17}N \cdot HCl$ dissolved using the following method.

Monobasic ammonium phosphate solution—Dissolve 11.5 g of monobasic ammonium phosphate in 1000 mL of water. Adjust with 85% phosphoric acid to a pH of 3.1.

Mobile phase—Prepare a filtered and degassed mixture of *Monobasic ammonium phosphate solution* and acetonitrile (4:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Transfer 25.0 mg, accurately weighed, of USP Selegiline Hydrochloride RS to a 50-mL volumetric flask. Dissolve in and dilute with water to volume, and mix. Pipet 2.0 mL of this solution into a 100-mL volumetric flask, dilute with water to volume, and mix.

Test solution—At 20 minutes withdraw a 10-mL portion of the solution under test and centrifuge for 10 minutes at 3500 rpm.

Chromatographic system—The liquid chromatograph is equipped with a 205-nm detector and a 3.9-mm × 30-cm column that contains packing L1. Chromatograph the *Standard solution*, and record the peak responses. The relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 15 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the amount of $C_{13}H_{17}N \cdot HCl$ dissolved.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{13}H_{17}N \cdot HCl$ is dissolved in 20 minutes.

Chromatographic purity—

Buffer solution, *Mobile phase, System suitability solution*, and *Chromatographic system*—Proceed as directed in the test for *Chromatographic purity* under *Selegiline Hydrochloride*.

Standard solution—Transfer 10.0 mL of the *System suitability solution* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Transfer 10.0 mL of this solution to a 20-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Test solution—Use a portion of the supernatant obtained from the *Assay preparation*.

Procedure—Proceed as directed in the test for *Chromatographic purity* under *Selegiline Hydrochloride*. Calculate the percentage of each impurity, excluding methamphetamine hydrochloride, in the portion of Tablets taken by the formula:

$$5000(C / W)(r_i / r_s)$$

in which *W* is the weight, in mg, of the labeled content of selegiline hydrochloride in the portion of Tablets taken to prepare the *Test solution*, and the other terms are as defined therein. Not more than 0.5% of any individual impurity is found, and the sum of all impurities, excluding methamphetamine hydrochloride, is not more than 2.0%.

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

Limit of methamphetamine hydrochloride—

Buffer solution, *Mobile phase, System suitability solution*, *Test solution*, and *Chromatographic system*—Proceed as directed in the test for *Chromatographic purity* under *Selegiline Hydrochloride*.