Uniformity of dosage units ⟨905⟩: meet the requirements.
Water, *Method I* ⟨921⟩: not more than 12.0%.
Assay—

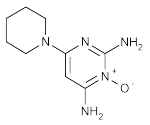
Mobile phase, Standard preparation, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Minocycline Hydrochloride.*

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 50 mg of minocycline ($C_{23}H_{27}N_3O_7$), to a 100-mL volumetric flask, add about 50 mL of water, and shake for about 1 minute. Dilute with water to volume, mix, and filter.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Minocycline Hydrochloride.* Calculate the quantity, in mg, of $C_{23}H_{27}N_3O_7$ in the portion of Tablets taken by the formula:

$$0.1C(r_U / r_S).$$

Minoxidil



$C_9H_{15}N_5O$ 209.25
2,4-Pyrimidinediamine, 6-(1-piperidinyl)-, 3-oxide.
2,4-Diamino-6-piperidinopyrimidine 3-oxide [38304-91-5].

» Minoxidil contains not less than 97.0 percent and not more than 103.0 percent of $C_9H_{15}N_5O$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—
USP Minoxidil RS

Identification, *Infrared Absorption* ⟨197M⟩—Do not dry specimens.

Loss on drying ⟨731⟩—Dry it at 50° and at a pressure not exceeding 5 mm of mercury for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.5%.

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

Chromatographic purity—

Mobile phase and *Chromatographic system*—Prepare as directed in the *Assay*.

Test solution—Prepare a solution of Minoxidil in *Mobile phase* having a concentration of about 0.25 mg per mL.

Procedure—Inject about 10 µL of *Test solution* into the chromatograph, record the chromatogram, and measure the peak response for each component. Calculate the total percentage of impurities taken by the formula:

$$100S / (S + A)$$

in which S is the sum of the areas of the minor component peaks detected, and A is the area of the major component. The total of any impurities detected is not more than 1.5%.

Assay—

Mobile phase—Prepare a solution consisting of a mixture of methanol, water, and glacial acetic acid (700:300:10), add 3.0 g of docusate sodium per L of solution, and mix. Adjust with perchloric acid to a pH of 3.0, filter, and degas.

Internal standard solution—Prepare a solution of medroxyprogesterone acetate in *Mobile phase* having a concentration of about 0.2 mg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Minoxidil RS in *Internal standard solution* to obtain a solution having a known concentration of about 0.25 mg per mL.

Assay preparation—Transfer about 5 mg of Minoxidil, accurately weighed, to a container, add 20.0 mL of *Internal standard solution*, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 25-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph not less than four replicate injections of the *Standard preparation,* and record the peak responses as directed under *Procedure:* the relative standard deviation is not more than 2.0%, and the resolution, *R,* between the internal standard and minoxidil is not less than 2.0.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.8 for the internal standard and 1.0 for minoxidil. Calculate the quantity, in mg, of $C_9H_{15}N_5O$ in the portion of Minoxidil taken by the formula:

$$20C(R_U / R_S)$$

in which C is the concentration, in mg per mL, of USP Minoxidil RS in the *Standard preparation*, and R_U and R_S are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Minoxidil Topical Solution

» Minoxidil Topical Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of minoxidil ($C_9H_{15}N_5O$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Minoxidil RS

Identification—

A: *Infrared Absorption* ⟨197M⟩—

Test specimen—Evaporate 1 mL of the Topical Solution under a stream of nitrogen while heating at 50°.

B: The retention time of the major peak for minoxidil in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation*, as obtained in the *Assay*.

Assay—

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

Assay preparation—Transfer an accurately measured volume of Topical Solution, equivalent to about 100 mg of minoxidil, to a 10-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Transfer 0.5 mL of this solution to a suitable vial, add 20.0 mL of *Internal standard solution*, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Minoxidil.* Calculate the quantity, in mg, of minoxidil

($C_9H_{15}N_5O$) in each mL of the Topical Solution taken by the formula:

$$(400C / V)(R_U / R_S)$$

in which C is the concentration, in mg per mL, of USP Minoxidil RS in the *Standard preparation*, V is the volume, in mL, of the Topical Solution taken for the *Assay preparation*, and R_U and R_S are the ratios of the minoxidil peak to that of the internal standard obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Minoxidil Tablets

» Minoxidil Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of minoxidil ($C_9H_{15}N_5O$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩**—**
USP Minoxidil RS

Identification—Transfer a portion of finely powdered Tablets, equivalent to about 10 mg of minoxidil, to a separator. Add 25 mL of water, and extract with three 15-mL portions of chloroform. Combine the chloroform extracts, and evaporate with the aid of a stream of nitrogen. Wash the inside of the container with about 5 mL of alcohol, add 300 mg of potassium bromide, and evaporate under vacuum at 50° until dry: the IR absorption spectrum of a potassium bromide dispersion prepared from the residue so obtained exhibits maxima at the same wavelengths as that of a similar preparation of USP Minoxidil RS.

Dissolution ⟨711⟩**—**

Medium: pH 7.2 phosphate buffer (see under *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 900 mL.

Apparatus 1: 75 rpm.

Time: 15 minutes.

Procedure—Determine the amount of $C_9H_{15}N_5O$ dissolved from UV absorbances at the wavelength of maximum absorbance 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 Minoxidil RS in the same medium. For Tablets containing up to 10 mg of minoxidil, measurement is made at about 231 nm; for Tablets containing more than 10 mg, the wavelength used is about 287 nm.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_9H_{15}N_5O$ is dissolved in 15 minutes.

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

Assay—

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

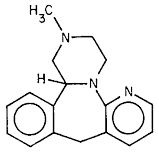
Assay preparation—Weigh and finely powder not less than 10 Tablets. To an accurately weighed portion of the powder, equivalent to about 5 mg of minoxidil, add 20.0 mL of *Internal standard solution*, shake for 5 minutes, and centrifuge.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Minoxidil*. Calculate the quantity, in mg, of minoxidil ($C_9H_{15}N_5O$) in the portion of Tablets taken by the formula:

$$20C(R_U / R_S)$$

in which the terms are as defined therein.

Mirtazapine



$C_{17}H_{19}N_3$ 265.35
Pyrazino[2,1-*a*]pyrido[2,3-*c*][2]benzazepine,1,2,3,4,10,14b-hexahydro-2-methyl-.
1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-*a*]pyrido[2,3-*c*][2]-benzazepine [85650-52-8].

» Mirtazapine contains not less than 98.0 percent and not more than 102.0 percent of $C_{17}H_{19}N_3$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers, and store at controlled room temperature.

Labeling—Label it to indicate whether it is anhydrous or hemihydrate.

USP Reference standards ⟨11⟩**—**
USP Mirtazapine RS
USP Mirtazapine Resolution Mixture RS
This resolution mixture contains approximately 0.1% w/w each of the following:
Impurity A: 14b*RS*-2-methyl-1,2,3,4,10,14b-hexahydropyrazino[2,1-*a*]pyrido[2,3-*c*]benzazepine 2-oxide.
Impurity B: [2-[(2*RS*)-4-methyl-2-phenylpiperazin-1-yl]pyridin-3-yl]methanol.
Impurity C: (14b*RS*)-2-methyl-3,4,10,14b-tetrahydropyrazinol[2,1-*a*]pyridol[2,3-*c*][2]benzazepin-1(2*H*)-one.
Impurity F: (14b*RS*)-2-methyl-1,3,4,14b-tetrahydropyrazino-[2,1-*a*]pyrido[2,3-*c*]benzazepin-10(2*H*)-one.
Impurity E: 0.2% w/w of (2*RS*)-4-methyl-1-(3-methylpyridin-2-yl)-2-phenylpiperazine.
Impurity D: 0.5% w/w of (14b*RS*)-1,2,3,4,10,14b-hexahydropyrazino[2,1-*a*]pyrido[2,3-*c*][2]benzazepine.

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: 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.*

Specific rotation ⟨781S⟩**:** between +2° and –2°.

Test solution: 10 mg per mL, in denatured alcohol.

Water, *Method I* ⟨921⟩**:** not more than 3.5%.

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

Heavy metals, *Method II* ⟨231⟩**:** 0.001%.

Related compounds—

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

System suitability solution—Dissolve a suitable quantity of USP Mirtazapine Resolution Mixture RS in *Diluent* to obtain a solution with a final concentration of about 1.5 mg per mL.

Standard solution—Dilute quantitatively a suitable volume of the *Standard preparation,* as prepared in the *Assay,* with *Diluent* to obtain a solution having a known concentration of about 0.0015 mg per mL (1.5 µg per mL).

Test solution—Proceed as directed for the *Assay stock preparation,* as prepared in the *Assay*.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 240-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. The column temperature is maintained at 40°. Chromatograph the *System suitability solution.* Identify the impurity peaks using the relative retention