

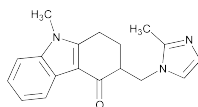
that contains 4- μ m packing L1 may be used.) The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the column efficiency is not less than 2000 theoretical plates; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 μ L) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $C_{34}H_{36}MgN_6O_6S_2$ in the portion of Omeprazole Magnesium taken by the formula:

$$100[(713.12 / (2 \times 345.42))(C_S / C_U)(r_U / r_S)]$$

in which 713.12 and 345.42 are the molecular weights of omeprazole magnesium and omeprazole, respectively; C_S is the concentration, in mg per mL, of omeprazole in the *Standard preparation*; C_U is the concentration, in mg per mL, of omeprazole magnesium in the *Assay preparation*; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Ondansetron



$C_{18}H_{19}N_3O$ 293.36

4H-Carbazol-4-one, 1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1H-imidazol-1-yl)methyl]- (±)-
(±)-2,3-Dihydro-9-methyl-3-[(2-methylimidazol-1-yl)methyl]carbazol-4(1H)-one [99614-02-5].

» Ondansetron contains not less than 98.0 percent and not more than 102.0 percent of $C_{18}H_{19}N_3O$, calculated on the anhydrous basis.

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

USP Reference standards (11)—

USP Ondansetron RS

USP Ondansetron Related Compound C RS
1,2,3,9-Tetrahydro-9-methyl-4H-carbazol-4-one.

USP Ondansetron Related Compound D RS
1,2,3,9-Tetrahydro-9-methyl-3-methylene-4H-carbazol-4-one.

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*.

Water, *Method 1a* (921): not more than 3.0%.

Residue on ignition (281): not more than 0.1%.

Chloride (221)—To 1 g of the substance under test, add 30 to 40 mL of water, and warm gently, if necessary, until no more dissolves. Mix well, and pass through a filter paper that gives a negative test for chloride. Add 1 mL of nitric acid and 1 mL of silver nitrate TS. Dilute with water to 50 mL. Mix well, and allow to stand for 5 minutes protected from direct sunlight: any turbidity formed is not greater than that produced in a similarly treated control solution containing 0.3 mL of 0.020 N hydrochloric acid (0.02%).

Limit of ondansetron related compound D—

Phosphate buffer—Dissolve about 2.72 g of monobasic potassium phosphate in 900 mL of water. Adjust with 1 N sodium

hydroxide or 0.5 N sodium hydroxide to a pH of 5.4, dilute to 1000 mL, and mix.

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

Standard solution—Dissolve an amount of USP Ondansetron Related Compound D RS in *Mobile phase*, and dilute stepwise with *Mobile phase*, to obtain a solution having a known concentration of about 0.4 μ g per mL.

Resolution solution—Prepare a solution of USP Ondansetron Related Compound D RS and USP Ondansetron Related Compound C RS in *Mobile phase* having a known concentration of about 0.6 μ g per mL and 1.0 μ g per mL, respectively.

Test solution—Transfer about 50 mg of Ondansetron, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* (621))—The liquid chromatograph is equipped with a 328-nm detector and a 4.6-mm \times 25-cm column that contains packing L10. The column temperature is maintained at 30°. The flow rate is about 1.5 mL per minute. Chromatograph the *Resolution solution*, and record the peak responses as directed for *Procedure*: the relative retention times are about 0.8 for ondansetron related compound C and 1.0 for ondansetron related compound D; and the resolution, R , between ondansetron related compound C and ondansetron related compound D is not less than 1.5. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure*: the column efficiency is not less than 8000 theoretical plates; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 μ L) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of ondansetron related compound D in the ondansetron taken by the formula:

$$10(C/W)(r_U / r_S)$$

in which C is the concentration, in μ g per mL, of USP Ondansetron Related Compound D RS in the *Standard solution*; W is the weight, in mg, of ondansetron taken to prepare the *Test solution*; and r_U and r_S are the peak responses of ondansetron related compound D obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.10% is found.

Related compounds—

Phosphate buffer, *Mobile phase*, *Resolution solution*, *Standard preparation*, and *Chromatographic system*—Prepare as directed in the *Assay*.

Test solution—Use the *Assay preparation* prepared as directed in the *Assay*.

Procedure—Inject a volume (about 10 μ L) of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of each impurity in the portion of Ondansetron taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak area for each impurity; and r_s is the sum of the areas of all the peaks: not more than 0.1% of any individual impurity is found; and not more than 0.5% of total impurities is found, including ondansetron related compound D. [NOTE—Disregard the peak corresponding to ondansetron related compound D at a relative retention time of about 0.4.]

Assay—

Phosphate buffer—Dissolve about 2.72 g of monobasic potassium phosphate in 900 mL of water. Adjust with 1 N sodium hydroxide or 0.5 N sodium hydroxide to a pH of 5.4, dilute to 1000 mL, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Phosphate buffer* and acetonitrile (52:48). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

Resolution solution—Prepare a solution of USP Ondansetron RS and USP Ondansetron Related Compound A RS in *Mobile phase* having a known concentration of about 0.09 mg per mL and 0.05 mg per mL, respectively.

Standard preparation—Dissolve an accurately weighed quantity of USP Ondansetron RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.090 mg per mL.

Assay preparation—Transfer about 45 mg of Ondansetron, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Pipet 5.0 mL of this solution into a 50-mL volumetric flask. Dilute with *Mobile phase* to volume, and mix.

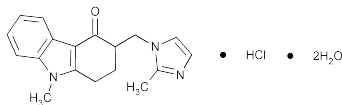
Chromatographic system (see *Chromatography* <621>)—The liquid chromatograph is equipped with a 216-nm detector and a 4.6-mm 25-cm column that contains packing L10. The flow rate is about 1.5 mL per minute. The column temperature is maintained at 30°. Chromatograph the *Resolution solution*, and record the peak responses as directed for *Procedure*: the relative retention times are about 1.1 for ondansetron related compound A and 1.0 for ondansetron; and the resolution, *R*, between ondansetron related compound A and ondansetron is not less than 1.5. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 1.5%.

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 ondansetron peaks. Calculate the quantity, in mg, of $C_{18}H_{19}N_3O$ in the portion of Ondansetron taken by the formula:

$$500C(r_U / r_S)$$

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

Ondansetron Hydrochloride



$C_{18}H_{19}N_3O \cdot HCl \cdot 2H_2O$ 365.86

4*H*-Carbazol-4-one, 1,2,3,9-tetrahydro-9-methyl-3-(2-methyl-1*H*-imidazol-1-yl)methyl-, monohydrochloride, (±)-, dihydrate. (±)-2,3-Dihydro-9-methyl-3-(2-methylimidazol-1-yl)methylcarbazol-4(1*H*)-one monohydrochloride dihydrate [103639-04-9].

» Ondansetron Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{18}H_{19}N_3O \cdot HCl$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight, light-resistant containers. Store at 25°, excursions permitted between 15° and 30°.

USP Reference standards <11>—

USP Ondansetron Hydrochloride RS

USP Ondansetron Related Compound A RS

3[(Dimethylamino)methyl]-1,2,3,9-tetrahydro-9-methyl-4*H*-carbazol-4-one.

USP Ondansetron Resolution Mixture RS

Ondansetron hydrochloride having approximately 0.4% w/w of both ondansetron related compound A and 6,6'-methylene bis-[(1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1*H*-imidazol-1-yl)-methyl]-4*H*-carbazol-4-one)].

USP Ondansetron Related Compound C RS

1,2,3,9-Tetrahydro-9-methyl-4*H*-carbazol-4-one.

USP Ondansetron Related Compound D RS

1,2,3,9-Tetrahydro-9-methyl-3-methylene-4*H*-carbazol-4-one.

Identification—

A: Infrared Absorption <197M>.

B: Dissolve 20 mg in 2 mL of water, add 1 mL of 2 M nitric acid, and filter: the filtrate responds to the test for *Chloride* <191>.

Water, Method Ia <921>: between 9.0% and 10.5%.

Residue on Ignition <281>: not more than 0.1%.

Limit of ondansetron related compound D—

Mobile phase—Prepare a filtered and degassed mixture of 0.02 M monobasic potassium phosphate (previously adjusted with 1 M sodium hydroxide to a pH of 5.4) and acetonitrile (80:20). Make adjustments if necessary (see *System Suitability* under *Chromatography* <621>).

Standard solution—Dissolve an accurately weighed quantity of USP Ondansetron Related Compound D RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.4 µg per mL.

System suitability solution—Dissolve suitable quantities of USP Ondansetron Related Compound D RS and USP Ondansetron Related Compound C RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a concentration of about 0.6 µg per mL and 1 µg per mL, respectively.

Test solution—Transfer about 50 mg of Ondansetron Hydrochloride, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* <621>)—The liquid chromatograph is equipped with a 328-nm detector and a 4.6-mm × 25-cm column that contains packing L10. The flow rate is about 1.5 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure*: the relative retention times are about 0.8 for ondansetron related compound C and 1.0 for ondansetron related compound D; and the resolution, *R*, between ondansetron related compound C and ondansetron related compound D is not less than 1.5. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure*: the column efficiency determined from the analyte peak is not less than 400 theoretical plates; 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 solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of ondansetron related compound D in the portion of Ondansetron Hydrochloride taken by the formula:

$$10,000(C/W)(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Ondansetron Related Compound D RS in the *Standard solution*; *W* is the weight, in mg, of Ondansetron Hydrochloride taken to prepare the *Test solution*; and r_U and r_S are the peak areas obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.10% is found.

Chromatographic purity—

METHOD I—

Resolution solution—Dissolve a quantity of USP Ondansetron Resolution Mixture RS in methanol, and dilute quantitatively,