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.

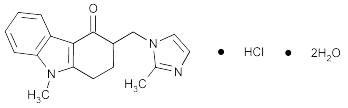
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 216-nm detector and a 4.6-mm 25-cm column that contains packing L10. The flow rate is about 1.5 mL per minute. The column temperature is maintained at 30°. Chromatograph the *Resolution solution,* and record 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,

and stepwise if necessary, with methanol to obtain a solution having a known concentration of 12.5 mg per mL.

Standard solutions—Dissolve an accurately weighed quantity of USP Ondansetron Hydrochloride RS in methanol, and mix to obtain a solution having a known concentration of about 0.25 mg per mL. Quantitatively dilute this solution with methanol to obtain *Standard solutions,* designated below by letter, having the following compositions:

Standard solution	Dilution	Concentration (μg RS per mL)	Percentage (%, for comparison with test specimen)
A	(1 in 5)	50	0.4
B	(1 in 10)	25	0.2
C	(1 in 20)	12.5	0.1

Test solution—Dissolve an accurately weighed quantity of Ondansetron Hydrochloride in methanol to obtain a solution containing 12.5 mg per mL.

Procedure—Separately apply 20 μL of the *Test solution,* 20 μL of each *Standard solution,* and 20 μL of the *Resolution solution* to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Develop the chromatogram in a solvent system consisting of a mixture of chloroform, ethyl acetate, methanol, and ammonium hydroxide (90:50:40:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Examine the plate under short-wavelength UV light: complete resolution of the three components of the *Resolution solution* spot is found. Compare the intensities of any secondary spots observed in the chromatogram of the *Test solution* with those of the principal spots in the chromatograms of the *Standard solutions:* any secondary spot from the chromatogram of the *Test solution* having an R_F value corresponding to that of the uppermost secondary spot of the *Resolution solution* is not larger or more intense than the principal spot obtained from *Standard solution A* (0.4%); and no other secondary spot from the chromatogram of the *Test solution* is larger or more intense than the principal spot obtained from *Standard solution B* (0.2%).

METHOD II—

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

Standard solution—Proceed as directed for *Standard preparation* in the *Assay.*

Test solution—Use the *Assay preparation.*

Procedure—Separately inject equal volumes (about 10 μL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of each impurity in the portion of Ondansetron Hydrochloride taken by the formula:

$$50{,}000(C/W)(1/F)(r_i / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Ondansetron Hydrochloride RS in the *Standard solution; W* is the weight, in mg, of Ondansetron Hydrochloride taken to prepare the *Test solution; F* is the relative response factor of the impurities as described in the accompanying table; r_i is the peak area for each impurity in the *Test solution;* and r_S is the peak area of ondansetron obtained from the *Standard solution:* it meets the requirements given in the accompanying table.

Compound Name	Relative Retention Time	Relative Response Factor	Limit (%)
Ondansetron related compound C	about 0.32	1.2	0.2
Ondansetron related compound D*	about 0.34	—	0.1
Imidazole	about 0.49	0.3	0.2
2-methylimidazole	about 0.54	0.4	0.2
Ondansetron	1.0	—	—
Ondansetron related compound A	about 1.10	0.8	0.2
Unknown	—	1.0	0.1
Total	—	—	0.5

*Quantified in the test for *Limit of ondansetron related compound D.*

Assay—

Mobile phase—Prepare a filtered and degassed mixture of 0.02 M monobasic sodium phosphate (previously adjusted with 1 M sodium hydroxide to a pH of 5.4) and acetonitrile (50:50). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Ondansetron Hydrochloride RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 90 μg per mL.

System suitability solution—Dissolve suitable quantities of USP Ondansetron Hydrochloride RS and USP Ondansetron Related Compound A RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution containing about 90 μg per mL and 20 μg per mL, respectively.

Assay preparation—Transfer about 45 mg of Ondansetron Hydrochloride, 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. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for ondansetron and 1.1 for ondansetron related compound A; 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 major peaks. Calculate the quantity, in mg, of $C_{18}H_{19}N_3O \cdot HCl$ in the portion of Ondansetron Hydrochloride taken by the formula:

$$500C(r_U / r_S)$$

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

Ondansetron Hydrochloride Oral Suspension

» Ondansetron Hydrochloride Oral Suspension is a suspension of Ondansetron Hydrochloride. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$), calculated on the anhydrous basis. Prepare Ondansetron Hydrochloride Oral Suspension 1.0 mg of Ondansetron Hydrochloride (dihydrate) equivalent to 0.8 mg of Ondansetron per mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩):

Ondansetron (as Hydrochloride dihydrate)	80 mg
Vehicle: a mixture of Vehicle for Oral Suspension, *NF,* and Vehicle for Oral Solution, (regular or sugar-free), *NF* (1:1), a sufficient quantity to make	100 mL

If using Tablets, place the Tablets in a suitable glass mortar, and comminute well, or add Ondansetron Hydrochloride powder. Add 50 mL of the mixed Vehicle in 5-mL portions, and mix well with each addition. Transfer the contents of the mortar, stepwise and quantitatively, to a calibrated bottle. Add sufficient Vehicle to bring the preparation to final volume, and mix well.

Packaging and storage—Preserve in tight, light-resistant containers. Store at controlled room temperature, or in a cold place.

Labeling—Label it to state that it is to be well shaken before use, and to state the beyond-use date. Label content as: Each mL of Ondansetron Hydrochloride Oral Suspension contains 1 mg of Ondansetron Hydrochloride (dihydrate) equivalent to 0.8 mg Ondansetron.

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

pH ⟨791⟩**:** between 3.6 and 4.6.

Beyond-use date: 42 days after the day on which it was compounded.

Assay—

Mobile phase—Prepare a filtered and degassed solution of 43 mM monobasic potassium phosphate buffer adjusted with a mixture of 1 N sodium hydroxide and acetonitrile (85:15) to a pH of 5.4. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

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

Assay preparation—After each amber plastic vial containing Oral Suspension that is stored at 4° is brought to room temperature, pipet 500 µL of Oral Suspension from each bottle into a 100-mL volumetric flask, and dilute with *Mobile phase* to volume. Pass through a 0.45-µm filter, and keep frozen at –70° until assayed.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 216-nm detector, a 3.9-mm × 20-mm guard column that contains 4-µm packing L10, and a 4.6-mm × 25-cm analytical column that contains 5-µm packing L10. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the retention time is about 30 minutes for ondansetron hydrochloride; and the relative standard deviation for replicate injections is not more than 1.6%.

Procedure—Separately inject equal volumes (about 80 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 ondansetron hydrochloride ($C_{18}H_{19}N_3O \cdot HCl \cdot 2H_2O$) in the volume of Oral Suspension taken by the formula:

$$200(C/V)(r_U / r_S)$$

in which C is the concentration, in µg per mL, of USP Ondansetron Hydrochloride RS in the *Standard preparation; V* is the volume, in mL, of Oral Suspension taken; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Ondansetron Injection

» Ondansetron Injection is a sterile solution of Ondansetron Hydrochloride in Water for Injection or of Ondansetron in Water for Injection prepared with the aid of Hydrochloric Acid. It may contain suitable buffers and/or tonicity adjusting agents. It contains an amount of Ondansetron Hydrochloride equivalent to not less than 95.0 percent and not more than 105.0 percent of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$).

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, at a temperature between 2° and 30°, protected from light.

USP Reference standards ⟨11⟩**—**
USP Endotoxin RS
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 Related Compound B RS
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—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*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 9.9 USP Endotoxin Units per mg of ondansetron hydrochloride.

pH ⟨791⟩: between 3.3 and 4.0.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

Limit of ondansetron related compound D—

Mobile phase, *Standard solution*, *System suitability solution*, and *Chromatographic system*—Proceed as directed in the test for *Limit of ondansetron related compound D* under *Ondansetron Hydrochloride*.

Test solution—Transfer an accurately measured volume of Injection, equivalent to about 10 mg of ondansetron, to a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.