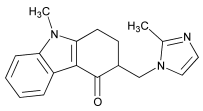
Ondansetron



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

4*H*-Carbazol-4-one, 1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1*H*-imidazol-1-yl)methyl]- (±)-.

(±)-2,3-Dihydro-9-methyl-3-[(2-methylimidazol-1-yl)methyl] carbazol-4(1*H*)-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. USP Ondansetron Related Compound D RS.*

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 Ia* ⟨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 I 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 µg 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 µg per mL and 1.0 µg 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 × 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 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 ondansetron taken by the formula:

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

in which C is the concentration, in µg 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 µL) 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.]

Organic volatile impurities ⟨467⟩**:** meets the requirements.
(Official until July 1, 2008)

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.