Add the following:

■Ondansetron Tablets

» Ondansetron Tablets contain Ondansetron Hydrochloride equivalent to not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ondansetron ($C_{18}H_{19}N_3O$).

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

USP Reference standards ⟨11⟩**—***USP Ondansetron Hydrochloride RS. USP Ondansetron Related Compound A RS.*

Add the following:

•**Labeling—**When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.• (RB 1-Dec-2009)

Identification—

A: *Infrared Absorption* ⟨197K⟩—

Test specimen—Weigh and finely powder a sufficient number of Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of ondansetron hydrochloride, to a suitable conical flask. Add 50 mL of alcohol, and swirl. Pass the liquid through a PTFE filter having a porosity of 0.45 µm into a 50-mL beaker. Evaporate the solvent on a rotary evaporator. Dry the precipitate in an air oven for 1 hour at 105°. Prepare a suitable dispersion of the residue in potassium bromide, and record the spectra of the *Test specimen* and the standard specimen in the spectral range 3800 to 650 cm^{-1}: the *Test specimen* shows strong bands at 1681, 1481, 1281, and 758 cm^{-1}, similar to the potassium bromide dispersion of USP Ondansetron Hydrochloride RS. [NOTE—It is recommended that a solution of USP Ondansetron Hydrochloride RS in alcohol be prepared at a concentration of about 2 mg per mL prior to the evaporation, followed by drying steps.]

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.*

Change to read:

Dissolution ⟨711⟩**—**

•TEST 1—•(RB 1-Dec-2009)

Medium: water; 500 mL, deaerated.

Apparatus 2: 50 rpm.

Time: 15 minutes.

Standard solution—Dissolve an accurately weighed quantity of USP Ondansetron Hydrochloride RS in *Medium,* and dilute quantitatively, and stepwise if necessary, with *Medium* to obtain a solution having a known concentration close to the expected concentration of the *Test solution*.

Test solution—Pass a portion of the solution under test through a suitable filter having a porosity of 0.45 µm, and dilute, if necessary, with *Medium.*

Procedure—Determine the amount of ondansetron dissolved by employing UV absorption at the wavelength of maximum absorbance at about 310 nm on portions of the *Test solution* in comparison with the *Standard solution,* using *Medium* as the blank. Calculate the percentage of ondansetron dissolved by the formula:

$$\frac{A_U \times C_S \times 500 \times 293.36 \times 100}{A_S \times L \times 365.85}$$

in which A_U and A_S are the absorbances obtained from the *Test solution* and *Standard solution,* respectively; C_S is the concentration of ondansetron, in mg per mL, of the *Standard solution;* 500 is the volume, in mL, of *Medium;* 293.36 is the molecular weight of ondansetron; 100 is the conversion factor to percentage; *L* is the Tablet label claim, in mg; and 365.85 is the molecular weight of ondansetron hydrochloride dihydrate.

Tolerances—Not less than 80% (*Q*) of the labeled amount of ondansetron is dissolved in 15 minutes.

•TEST 2—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium, Apparatus 2, Standard solution, Test solution, and *Procedure*—Proceed as directed for *Test 1*.

Time: 30 minutes.

Tolerances—Not less than 80% (*Q*) of the labeled amount of ondansetron is dissolved in 30 minutes.

TEST 3—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.01 N hydrochloric acid; 500 mL, deaerated.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Standard solution—Dissolve an accurately weighed quantity of USP Ondansetron Hydrochloride RS in *Medium,* and dilute quantitatively, and stepwise if necessary, with *Medium* to obtain a solution having a known concentration close to the expected concentration of the *Test solution*.

Test solution—Pass a portion of the solution under test through a suitable filter having a porosity of 0.45 µm, and dilute, if necessary, with *Medium.*

Procedure—Determine the amount of ondansetron dissolved by employing UV absorption at a wavelength of about 248 nm on portions of the *Test solution* in comparison with the *Standard solution,* using *Medium* as the blank. Calculate the percentage of ondansetron dissolved by the formula:

$$\frac{A_U \times C_S \times 500 \times 293.36 \times 100}{A_S \times L \times 365.85}$$

in which A_U and A_S are the absorbances obtained from the *Test solution* and *Standard solution,* respectively; C_S is the concentration of ondansetron, in mg per mL, of the *Standard solution;* 500 is the volume, in mL, of *Medium;* 293.36 is the molecular weight of ondansetron; 100 is the conversion factor to percentage; *L* is the Tablet label claim, in mg; and 365.85 is the molecular weight of ondansetron hydrochloride dihydrate.

Tolerances—Not less than 80% (*Q*) of the labeled amount of ondansetron is dissolved in 30 minutes.• (RB 1-Dec-2009)

•TEST 4—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: 0.1 N hydrochloric acid; 500 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Standard stock solution— Transfer about 45 mg, accurately weighed, of USP Ondansetron Hydrochloride RS to a 100-mL volumetric flask, and dilute with *Medium* to volume.

Standard solution— Dilute the *Standard stock solution* quantitatively and stepwise, if necessary, with *Medium* to obtain a final concentration of about *L*/500 mg/mL, where *L* is the Tablet label claim, in mg.

Sample solution— Pass a portion of the solution under test through a suitable 0.45-µm filter.

Procedure—Determine the amount of ondansetron dissolved by employing UV absorption at a wavelength of about 249 nm on portions of the *Sample solution* in comparison with the *Standard solution,* using *Medium* as the blank and a 1-cm cell for Tablets labeled to contain 4 mg or 8 mg, or a 0.2-cm cell for Tablets labeled to contain 16 mg or 24 mg. Calculate the percentage of ondansetron dissolved by the formula:

$$\frac{A_U \times C_S \times 500 \times 293.36 \times 100}{A_S \times L \times 365.85}$$

in which A_U and A_S are the absorbances obtained from the *Sample solution* and *Standard solution,* respectively; C_S is the concentration of ondansetron, in mg per mL, of the *Standard solution;* 500 is the volume, in mL, of *Medium;* 293.36 is the molecular weight of ondansetron; 100 is the conversion factor to percentage; L is the Tablet label claim, in mg; and 365.85 is the molecular weight of ondansetron hydrochloride dihydrate.

Tolerances—Not less than 80% (Q) of the labeled amount of ondansetron is dissolved in 30 minutes.• (RB 1-Mar-2010)

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

Related compounds—

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

Standard solution—Dilute the *Standard preparation* from the *Assay* with *Mobile phase* to obtain a known concentration of about 1.5 µg per mL of ondansetron.

System suitability solution—Prepare a solution containing USP Ondansetron Related Compound A RS and USP Ondansetron Hydrochloride RS in *Mobile phase* to obtain final concentrations of about 0.05 mg per mL and 0.1 mg per mL, respectively.

Test solution—Weigh and crush not fewer than 20 Tablets. Transfer an accurately weighed quantity of powder, equivalent to 50 mg of ondansetron, to a 100-mL volumetric flask. Add about 70 mL of *Mobile phase,* and sonicate for about 20 minutes. Dilute with *Mobile phase* to volume, and mix. Centrifuge the solution. Pass a portion of the solution through a suitable nylon filter having a porosity of 0.45 µm, and use the filtrate.

Chromatographic system (see *Chromatography* ⟨621⟩)—Prepare as directed in the *Assay.* Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between ondansetron related compound A and ondansetron is not less than 2.0. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation of the ondansetron peak for replicate injections is not more than 5.0%.

Procedure—Separately inject a volume (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph. Run the chromatograph for at least 45 minutes for the *Test solution,* and measure the peak responses. Calculate the percentage of each impurity in the portion of Tablets taken by the formula:

$$100(C_S / C_T)(1 / F)(r_i / r_S)$$

where C_S is the concentration, in mg per mL, of ondansetron in the *Standard solution;* C_T is the concentration, in mg per mL, of ondansetron in the *Test solution;* r_i is the peak area of any impurity in the *Test solution;* r_S is the peak area of ondansetron in the *Standard solution;* and F is the relative response factor of any impurity, as shown in *Table 1*.

Table 1

Impurity	Relative Retention Time	Relative Response Factor (F)	Limit (%, w/w)
2-Methyl imidazole[a]	0.22	0.53	NMT 0.2
Ondansetron related compound C[b]	0.40	1.2	NMT 0.2
Ondansetron related compound D[c]	0.47	1.3	NMT 0.1
Ondansetron related compound A[d]	0.87	0.90	NMT 0.2
Desmethylondansetron[a, e]	0.90	0.91	NMT 0.2
Ondansetron	1.0	—	—
Any other individual unspecified degradation product	—	1.0	NMT 0.2
Total	—	—	NMT 1.0

[a]Not to be included in total impurities.
[b]1,2,3,9-Tetrahydro-9-methyl-4*H*-carbazol-4-one.
[c]1,2,3,9-Tetrahydro-9-methyl-3-methylene-4*H*-carbazol-4-one.
[d]3[(Dimethylamino)methyl]-1,2,3,9-tetrahydro-9-methyl-4*H*-carbazol-4-one.
[e]1,2,3,9-Tetrahydro-9-methyl-3-[1*H*-imidazol-1-yl)methyl]-4*H*-carbazol-4-one.

Assay—

Buffer solution—Accurately transfer about 2.7 g of monobasic potassium hydrogen phosphate (KH_2PO_4) to a 1000-mL volumetric flask. Dissolve in and dilute with water to volume, and mix. Adjust with 1 N sodium hydroxide to a pH of 5.4.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (80 : 20).

Diluent: a mixture of *Buffer solution* and acetonitrile (50 : 50).

Standard preparation—Dissolve an accurately weighed quantity of USP Ondansetron Hydrochloride RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.05 mg per mL of ondansetron (free base).

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 50 mg of ondansetron, based on the label claim, to a 100-mL volumetric flask. Add about 70 mL of *Diluent,* and sonicate for about 20 minutes. Dilute with *Diluent* to volume, and mix. Centrifuge a portion of the solution. Quantitatively dilute the supernatant with *Diluent* to obtain a solution having a nominal concentration of 0.05 mg per mL of ondansetron, based on the label claim. Pass through a suitable nylon filter having a porosity of 0.45 µm, and use the filtrate.

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 5-µm packing L10. The flow rate is about 1.5 mL per minute. The column is maintained at ambient temperature. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor for the ondansetron peak is not more than 2.0; and the relative standard deviation for replicate injections is not more 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 area responses for the major peaks. Calculate the percentage of the label claim of ondansetron ($C_{18}H_{19}N_3O$) in the portion of Tablets taken by the formula:

$$100(C_S / C_U)(1 / L)(r_U / r_S)$$

in which C_S is the concentration, in mg per mL, of ondansetron (free base) in the *Standard preparation;* C_U is the nominal concentration, in fractional number of Tablets per mL, of the *Assay prepa-*

ration; L is the label claim, in mg per Tablet; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.■2S *(USP32)*

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