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Ondansetron Oral Solution

» Ondansetron Oral Solution is a solution of Ondansetron Hydrochloride in a suitable vehicle. It contains 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 well-closed, light-resistant containers.

Change to read:

USP Reference standards ⟨11⟩—

USP Ondansetron Hydrochloride RS

USP Ondansetron Related Compound A RS

▲3-[(Dimethylamino)methyl]-9-methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one hydrochloride.▲ (ERR 1-Apr-2022)

USP Ondansetron Related Compound C RS

▲9-Methyl-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.▲ (ERR 1-Apr-2022)

USP Ondansetron Related Compound D RS

▲9-Methyl-3-methylene-1,2,3,9-tetrahydro-4*H*-carbazol-4-one.▲ (ERR 1-Apr-2022)

Identification—

A: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—

Test solution—Dilute a portion of Oral Solution with a mixture of methanol and water (50:50) to obtain a solution containing about 0.2 mg of ondansetron per mL.

Standard solution: 0.25 mg per mL in methanol.

Developing solvent system: chloroform, ethyl acetate, methanol, and ammonium hydroxide (90:50:40:1).

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.*

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩—It meets the requirements of the tests for absence of *Escherichia coli.* The total aerobic microbial count does not exceed 100 cfu per g, the *Enterobacteriaceae* count does not exceed 10 cfu per g, and the total combined molds and yeasts count does not exceed 50 cfu per g.

Deliverable volume ⟨698⟩**:** meets the requirements.

pH ⟨791⟩**:** between 3.3 and 4.0.

Limit of ondansetron related compound D—

Mobile phase—Proceed as directed in the test for *Limit of ondansetron related compound D* under *Ondansetron Hydrochloride*.

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 containing about 0.5 µg per mL and 2 µg per mL, respectively.

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 0.5 µg per mL.

Test solution—Quantitatively dilute, if necessary, an accurately measured volume of Oral Solution with *Mobile phase* to obtain a solution containing about 0.8 mg of ondansetron per mL.

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 resolution, *R,* between ondansetron related compound D and ondansetron related compound C is not less than 2.0; the tailing factor for ondansetron related compound D is not more than 2.0; and the relative standard deviation for replicate injections is not more than 4.0%.

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

volume of Oral Solution taken by the formula:

$$100D(C_S/C_A)(r_U/r_S)$$

in which D is the dilution factor for the Oral Solution in the *Test solution;* C_S is the concentration, in µg per mL, of USP Ondansetron Related Compound D RS in the *Standard solution;* C_A is the concentration, in µg per mL, of ondansetron in the Oral Solution, as determined in the *Assay;* 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 0.1% is found.

Related compounds—

Mobile phase, System suitability solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Ondansetron Hydrochloride.*

Standard solution—Prepare as directed for the *Standard preparation,* in the *Assay* under *Ondansetron Hydrochloride*.

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 related compound in the volume of Oral Solution taken by the formula:

$$(293.36/329.83)10{,}000(1/F)(1/V)(C_S/C_A)(r_i/r_S)$$

in which 293.36 and 329.83 are the molecular weights of ondansetron and anhydrous ondansetron hydrochloride, respectively; F is the relative response factor for each known and unknown impurity (the values of relative response factors [RRF] and the limits can be obtained from *Table 1*); V is the volume, in mL, of Oral Solution taken; C_S is the concentration, in mg per mL, on the anhydrous basis, of USP Ondansetron Hydrochloride RS in the *Standard solution;* C_A is the concentration, in mg per mL, of ondansetron in the Oral Solution; r_i is the peak response for any related compound obtained from the *Test solution;* and r_S is the peak response for ondansetron obtained from the *Standard solution.*

Table 1

Related Compound	Approx. RRT	RRF	Limit (%)
Ondansetron related compound D*	0.34	—	0.1
Imidazole	0.40	0.46	0.2
2-Methyl imidazole	0.53	0.54	0.2
Des-*C*-methyl ondansetron hydrochloride	0.62	0.76	0.2
N-Desmethyl ondansetron maleate	0.83	0.73	0.2
Ondansetron related compound A	1.2	0.81	0.2
Unknown		1.0	0.2
Total (including ondansetron related compound D)		—	0.5

* Quantified from Limit of related compound D test

Assay—

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

Assay preparation—Transfer an accurately measured volume of Oral Solution, equivalent to about 9 mg of ondansetron, to a 100-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 1.1 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 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. Calculate the quantity, in mg, of ondansetron ($C_{18}H_{19}N_3O$) in each mL of Oral Solution taken by the formula:

$$(293.36/329.83)100(C/V)(r_U/r_S)$$

in which 293.36 and 329.83 are the molecular weights of ondansetron and anhydrous ondansetron hydrochloride, respectively; C is the concentration, in mg per mL, on the anhydrous basis, of USP Ondansetron Hydrochloride RS in the *Standard preparation; V* is the volume, in mL, of Oral Solution taken; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ONDANSETRON ORAL SOLUTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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