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Add the following:

▲Alosetron Tablets

DEFINITION

Alosetron Tablets contains an amount of Alosetron Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of alosetron ($C_{17}H_{18}N_4O$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020) [Note—The UV spectra of the major peaks of the *Sample solution* and the *Standard solution* as obtained in the *Assay* may also be used to meet the *Acceptance criteria*.]

Standard stock solution: 0.115 mg/mL of USP Alosetron Hydrochloride RS in water

Standard solution: 2.3 µg/mL of USP Alosetron Hydrochloride RS in water, from the *Standard stock solution*

Sample solution: Transfer a number of Tablets, nominally equivalent to 1 mg of alosetron, to a 250-mL volumetric flask. Fill the flask to about ¾ full with water and shake for 30 min. Dilute with water to volume, mix, and pass through a PVDF filter or other suitable filter of 0.45-µm pore size, discarding at least 15 mL of the filtrate.

Wavelength range: 200–400 nm

Cell: 1 cm

Blank: Water

Acceptance criteria: The spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the *Standard solution*, concomitantly measured.

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure** Protect solutions containing alosetron hydrochloride from light.

Buffer: 0.02 M monobasic sodium phosphate. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: *Buffer* and acetonitrile (80:20)

Diluent: Mix 1 mL of phosphoric acid with 1000 mL of water.

Standard stock solution: 0.115 mg/mL of USP Alosetron Hydrochloride RS in *Diluent*

Standard solution: 0.0115 mg/mL of USP Alosetron Hydrochloride RS in *Diluent*, from the *Standard stock solution*

Sample solution: Nominally 0.01 mg/mL of alosetron prepared as follows. Transfer 10 Tablets to a suitable volumetric flask. Fill the flask to about ¾ full with *Diluent*, shake for 10 min, and then sonicate for another 10 min. Dilute with *Diluent* to volume, mix, let the solids settle, and pass through a PVDF filter or other suitable filter of 0.45-µm pore size, discarding at least 6 mL of the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 7.5-cm; 3-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 15 µL

Autosampler temperature: 5°

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of alosetron ($C_{17}H_{18}N_4O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Alosetron Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of alosetron in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of alosetron, 294.36

M_{r2} = molecular weight of alosetron hydrochloride, 330.82

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Protect solutions containing alosetron hydrochloride from light.

Medium: Water (deaerated); 500 mL

Apparatus 2: 75 rpm

Time: 20 min

Mobile phase: Prepare as directed in the *Assay*.

Sample solution: Pass a portion of the solution under test through a PVDF filter or other suitable filter of 0.45-µm pore size, discarding at least 15 mL of the filtrate.

Standard stock solution: 0.115 mg/mL of USP Alosetron Hydrochloride RS in *Medium*

Standard solution: 2.3 µg/mL of USP Alosetron Hydrochloride RS in water, from the *Standard stock solution*. Further dilute with *Medium*, if needed, to a concentration that is similar to that of the *Sample solution*.

Chromatographic system: Proceed as directed in the *Assay*, except for *Injection volume*.

Injection volume: 75 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of the labeled amount of alosetron ($C_{17}H_{18}N_4O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of alosetron from the *Sample solution*

r_S = peak response of alosetron from the *Standard solution*

C_S = concentration of USP Alosetron Hydrochloride RS in the *Standard solution* (mg/mL)

L = labeled amount of alosetron (mg/Tablet)

V = volume of *Medium*, 500 mL

M_{r1} = molecular weight of alosetron, 294.36

M_{r2} = molecular weight of alosetron hydrochloride, 330.82

Tolerances: NLT 80% (*Q*) of the labeled amount of alosetron ($C_{17}H_{18}N_4O$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Protect solutions containing alosetron hydrochloride from light.

Buffer: Prepare as directed in the *Assay*.

Solution A: *Buffer*

Solution B: Acetonitrile

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system for at least 10 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
5	90	10
20	50	50
25	50	50

Diluent: *Buffer* and acetonitrile (90:10)

System suitability solution: 200 µg/mL of USP Alosetron Hydrochloride RS and 0.5 µg/mL of USP Alosetron Related Compound A RS in *Diluent*

Standard stock solution: 0.115 mg/mL of USP Alosetron Hydrochloride RS in *Diluent*

Standard solution: 0.46 µg/mL of USP Alosetron Hydrochloride RS in *Diluent*, from the *Standard stock solution*

Sample solution: Nominally 200 µg/mL of alosetron prepared as follows. Transfer a number of Tablets, equivalent to 5 mg of alosetron, to a suitable container. Add 25 mL of *Diluent*, shake for 10 min, and then sonicate for another 20 min. Mix, let the solids settle, and pass through a PVDF filter or other suitable filter of 0.45-µm pore size, discarding at least 6 mL of the filtrate.

Chromatographic system: Proceed as directed in the *Assay*, except for *Injection volume*.

Injection volume: 5 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 7 between alosetron and alosetron related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of alosetron from the *Standard solution*

C_S = concentration of USP Alosetron Hydrochloride RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of alosetron in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 2*)

M_{r1} = molecular weight of alosetron, 294.36

M_{r2} = molecular weight of alosetron hydrochloride, 330.82

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Alosetron	1.0	—	—
Alosetron related compound A	1.1	1.3	0.3
Any other individual impurity	—	1.0	0.5
Total impurities	—	—	2.5

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature, protected from light.

• **USP Reference Standards** ⟨11⟩

USP Alosetron Hydrochloride RS

USP Alosetron Related Compound A RS

Dealkyl alosetron;
5-Methyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indol-1-one.

$C_{12}H_{12}N_2O$ 200.24▲ (USP 1-Dec-2019)

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

Topic/Question	Contact	Expert Committee
ALOSETRON TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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