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Add the following:

▲Azelastine Hydrochloride Ophthalmic Solution

DEFINITION

Azelastine Hydrochloride Ophthalmic Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of azelastine hydrochloride ($C_{22}H_{24}ClN_3O \cdot HCl$).

IDENTIFICATION

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

ASSAY

- **Procedure**

Buffer 1: 2.88 g/L of octanesulfonic acid sodium salt and 0.91 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Buffer 2: 0.87 g/L of dibasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 6.5.

Solution A: Acetonitrile and *Buffer 1* (25:75)

Solution B: Acetonitrile

Mobile phase: See *Table 1*. Return to the original conditions, and re-equilibrate the system for NLT 5 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
20	85	15
35	65	35
45	45	55
60	45	55

Diluent: Acetonitrile and *Buffer 2* (25:75)

System suitability solution: 2.5 µg/mL each of USP Azelastine Hydrochloride RS and USP Azelastine Related Compound F RS in *Diluent*

Standard solution: 0.08 mg/mL of USP Azelastine Hydrochloride RS in *Diluent*

Sample stock solution: Combine the contents of NLT 5 containers of Ophthalmic Solution.

Sample solution: Nominally 0.08 mg/mL of azelastine hydrochloride from the *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Column temperature: 30°

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between azelastine and azelastine related compound F, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of azelastine hydrochloride ($C_{22}H_{24}ClN_3O \cdot HCl$) in the portion of Ophthalmic Solution taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

Mobile phase, Diluent, System suitability solution, Standard solution, Sample stock solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.0005 mg/mL of USP Azelastine Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of azelastine hydrochloride (use the *Sample stock solution*)

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between azelastine and azelastine related compound F, *System suitability solution*. [Note—If azelastine related compound F splits into two peaks, use the first peak for the determination of *Resolution*.]

Relative standard deviation: NMT 2.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Ophthalmic Solution taken:

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

r_U = peak response of each degradation product from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Benzohydrazide[a]	0.12	—	—
Azelastine related compound B[a,b]	0.17	—	—
Chlorophenylacetylbenzoic acid[a,c]	0.65	—	—
Azelastine related compound D[d]	0.7	1.20	0.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Azelastine	1.0	—	—
Azelastine related compound F[e]	1.08	0.71	1.5
Azelastine related compound E[a,f]	1.68	—	—
Any individual degradation product	—	1.0	0.5
Total degradation products	—	—	1.5

[a] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance and are not to be reported or included in the total degradation products.

[b] *N*'-(1-Methylazepan-4-yl)benzohydrazide hydrochloride; also known as 1-Benzoyl-2-[(4*RS*)-1-methylhexahydro-1*H*-azepin-4-yl]diazane.

[c] 2-[2-(4-Chlorophenyl)acetyl]benzoic acid.

[d] 4-(4-Chlorobenzyl)phthalazin-1(2*H*)-one.

[e] If the peak splits into two, identify both the peaks and quantify together.

[f] 3-(4-Chlorobenzylidene)isobenzofuran-1(3*H*)-one.

SPECIFIC TESTS

- **pH ⟨791⟩:** 5.0–6.5
- **Osmolality and Osmolarity ⟨785⟩:** 265–375 mOsmol/kg
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **Other Requirements:** It meets the requirements in *Ophthalmic Products—Quality Tests ⟨771⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers at controlled room temperature.
- **USP Reference Standards ⟨11⟩**
  USP Azelastine Hydrochloride RS
  USP Azelastine Related Compound F RS

4-[4-(4-Chlorobenzyl)-1-oxophthalazin-2(1*H*)-yl]-1-methylazepane 1-oxide.

$C_{22}H_{24}ClN_3O_2$ 397.90▲ (USP 1-Aug-2019)

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

Topic/Question	Contact	Expert Committee
AZELASTINE HYDROCHLORIDE OPHTHALMIC SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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