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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	—



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