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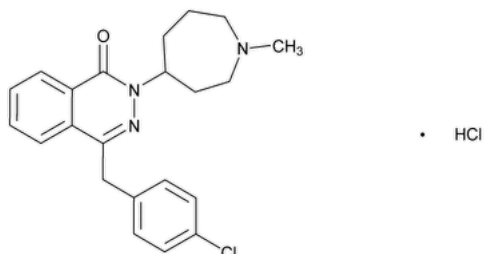
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Azelastine Hydrochloride


 $C_{22}H_{24}ClN_3O \cdot HCl$ 418.36

1(2H)-Phthalazinone, 4-[(4-chlorophenyl)methyl]-2-(hexahydro-1-methyl-1H-azepin-4-yl), monohydrochloride;

4-(p-Chlorobenzyl)-2-(hexahydro-1-methyl-1H-azepin-4-yl)-1(2H)-phthalazinone monohydrochloride CAS RN®: 79307-93-0.

UNII: 0L591QR10I

DEFINITION

Azelastine Hydrochloride contains NLT 99.0% and NMT 101.0% of azelastine hydrochloride ($C_{22}H_{24}ClN_3O \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Identification solution*, as obtained in the test for *Organic Impurities*.
- **C. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride:** Meets the requirements

ASSAY

Change to read:

PROCEDURE

Sample: 300 mg**Blank:** 5 mL of [anhydrous formic acid](#) and 30 mL of [acetic anhydride](#)

Titrimetric system

(See [Titrimetry \(541\)](#).)**Mode:** Direct titration**Titrant:** ▲0.1 N perchloric acid in glacial acetic acid VS▲ (USP 1-Dec-2021)**Endpoint detection:** Potentiometric**Analysis:** In order to avoid overheating in the reaction medium, mix thoroughly throughout and stop the titration immediately after the endpoint has been reached.Dissolve the *Sample* in 5 mL of [anhydrous formic acid](#), and add 30 mL of [acetic anhydride](#). Titrate with *Titrant*.Calculate the percentage of azelastine hydrochloride ($C_{22}H_{24}ClN_3O \cdot HCl$) in the portion of Azelastine Hydrochloride taken:

$$\text{Result} = \{[(V_s - V_b) \times N \times F] / W\} \times 100$$

 V_s = *Titrant* volume consumed by the *Sample* (mL) V_b = *Titrant* volume consumed by the *Blank* (mL) N = actual normality of the *Titrant* (mEq/mL) F = equivalency factor, ▲418.4▲ (USP 1-Dec-2021) mg/mEq W = weight of the *Sample* (mg)**Acceptance criteria:** 99.0%–101.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION (281):** NMT 0.2%

Change to read:**• ORGANIC IMPURITIES**

▲**Solution A:** 127 mL/L of [phosphoric acid](#) in [water](#)▲ (USP 1-Dec-2021)

Buffer: ▲2.9 g/L of [octanesulfonic acid sodium salt](#) and 0.9 g/L of monobasic potassium phosphate in [water](#). Adjust with *Solution A* to a pH of 3.0.▲ (USP 1-Dec-2021)

Mobile phase: [Acetonitrile](#) and *Buffer*▲(23:77)▲ (USP 1-Dec-2021)

Diluent: [Acetonitrile](#) and [water](#) (45:55)

Identification solution: 2.5 mg/mL of [USP Azelastine Hydrochloride RS](#) in *Diluent*. [NOTE—This solution is used for *Identification B*.]

System suitability stock solution: 0.5 mg/mL each of ▲[benzoyl hydrazide](#)▲ (USP 1-Dec-2021) [USP Azelastine Related Compound B RS](#), ▲[chlorophenylacetylbenzoic acid](#)▲ (USP 1-Dec-2021) [USP Azelastine Related Compound D RS](#), and [USP Azelastine Related Compound E RS](#) in [acetonitrile](#). ▲[NOTE—The concentration of each related compound is in terms of the free form.]▲ (USP 1-Dec-2021)

System suitability solution: ▲0.05 mg/mL▲ (USP 1-Dec-2021) each of ▲[benzoyl hydrazide](#)▲ (USP 1-Dec-2021) [USP Azelastine Related Compound B RS](#), ▲[chlorophenylacetylbenzoic acid](#)▲ (USP 1-Dec-2021) [USP Azelastine Related Compound D RS](#), and [USP Azelastine Related Compound E RS](#) from the *System suitability stock solution* and 2.5 mg/mL of [USP Azelastine Hydrochloride RS](#) in *Diluent*. ▲[NOTE—The concentration of each related compound is in terms of the free form.]▲ (USP 1-Dec-2021)

Standard stock solution: ▲0.05 mg/mL▲ (USP 1-Dec-2021) of [USP Azelastine Hydrochloride RS](#) in [acetonitrile](#)

Standard solution: ▲0.0025 mg/mL▲ (USP 1-Dec-2021) of [USP Azelastine Hydrochloride RS](#) in *Diluent*

▲**Sensitivity solution:** 0.0013 mg/mL of [USP Azelastine Hydrochloride RS](#) in *Diluent* from the *Standard solution*▲ (USP 1-Dec-2021)

Sample solution: 2.5 mg/mL of Azelastine Hydrochloride in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; ▲5-μm packing▲ (USP 1-Dec-2021) [L10](#)

Column temperature: 30°

Flow rate: 2 mL/min

Injection volume: 10 μL

Run time: ▲NLT▲ (USP 1-Dec-2021) 2.4 times the retention time of azelastine

System suitability

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

▲[NOTE—See [Table 1](#) for the relative retention times.]▲ (USP 1-Dec-2021)

Suitability requirements

Resolution: ▲NLT 1.5 between benzoyl hydrazide and azelastine related compound B; NLT 1.5 between chlorophenylacetylbenzoic acid and azelastine related compound D;▲ (USP 1-Dec-2021) NLT 1.5 between azelastine related compound D and azelastine; NLT 1.5 between azelastine and azelastine related compound E, *System suitability solution*

▲**Tailing factor:** 0.9–2.0, *Standard solution*▲ (USP 1-Dec-2021)

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

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2021)

Analysis

Samples: ▲▲ (USP 1-Dec-2021) *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Azelastine Hydrochloride taken:

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

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

r_S = peak area of azelastine from the *Standard solution*

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

C_U = concentration of Azelastine Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see [Table 1](#))