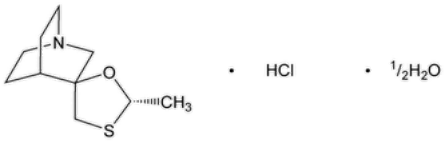
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Aug-2023
Document Type: USP Monographs
DocId: GUID-804E3035-0E85-4D77-9700-6F19D81C51CA_2_en-US
DOI: https://doi.org/10.31003/USPNF_M14810_02_01
DOI Ref: iq6fm

Add the following:

▲Cevimeline Hydrochloride



and enantiomer

$C_{10}H_{17}NOS \cdot HCl \cdot ½\ H_2O$ 244.78
$C_{10}H_{17}NOS$ 199.31

Spiro[1-azabicyclo[2.2.2]octane-3,5'-[1,3]oxathiolane], 2'-methyl-,hydrochloride, hydrate (2:1), *cis*-.
(±)-*cis*-2-Methylspiro[1,3-oxathiolane-5,3'-quinuclidine] hydrochloride, hemihydrate.

(2*RS*,2'*RS*)-2'-Methyl-4-azaspiro{bicyclo[2.2.2]octane-2,5'-[1,3]oxathiolane} hydrochloride hemihydrate CAS RN®: 153504-70-2; UNII: P81Q6V85NP.

Free base CAS RN®: 107233-08-9; UNII: K9V0CDQ56E.

DEFINITION

Cevimeline Hydrochloride contains NLT 98.0% and NMT 102.0% of cevimeline hydrochloride ($C_{10}H_{17}NOS \cdot HCl$) calculated on the anhydrous basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

ASSAY

- **Procedure**

Solution A: To each liter of water, add 1.0 mL of phosphoric acid and 1.0 g of sodium 1-hexanesulfonate monohydrate.
Solution B: To each liter of acetonitrile, add 1.0 mL of phosphoric acid.
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
3.4	89	11
10.7	10	90
12.7	10	90
13.0	95	5
14.0	95	5

Diluent: Acetonitrile and water (50:50)
System suitability solution: 0.022 mg/mL of USP Cevimeline *trans*-Isomer RS and 7.4 mg/mL of USP Cevimeline Hydrochloride RS in *Diluent*
Standard solution: 0.2 mg/mL of USP Cevimeline Hydrochloride RS in *Diluent*. Sonication may be used to promote dissolution.
Sample solution: 0.2 mg/mL of Cevimeline Hydrochloride in *Diluent*. Sonication may be used to promote dissolution.
Chromatographic system

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

Mode: LC

Detector: UV 200 nm

Column: 2.1-mm × 5-cm; 1.7-µm packing L1

Column temperature: 60°

Flow rate: 0.7 mL/min

Injection volume: 1 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 cevimeline and cevimeline *trans*-isomer, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cevimeline hydrochloride ($C_{10}H_{17}NOS \cdot HCl$) in the portion of Cevimeline Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard stock solution: 0.44 mg/mL of USP Cevimeline Hydrochloride RS in *Diluent*. Sonication may be used to promote dissolution.

Standard solution: 0.022 mg/mL of USP Cevimeline Hydrochloride RS from *Standard stock solution* in *Diluent*. Sonication may be used to promote dissolution.

Sensitivity solution: 0.011 mg/mL of USP Cevimeline Hydrochloride RS from *Standard solution* in *Diluent*

Sample solution A: 7.4 mg/mL of Cevimeline Hydrochloride in *Diluent*. Sonication may be used to promote dissolution.

Sample solution B: 22.1 mg/mL of Cevimeline Hydrochloride in *Diluent*. Sonication may be used to promote dissolution.

System suitability

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

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

Suitability requirements

Resolution: NLT 1.5 between cevimeline and cevimeline *trans*-isomer, *System suitability solution*

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

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

Analysis

Samples: *Standard solution*, *Sample solution A*, and *Sample solution B*

Calculate the percentage of cevimeline *trans*-isomer in the portion of Cevimeline Hydrochloride taken:

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

r_U = peak response of cevimeline *trans*-isomer from *Sample solution A*

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

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

C_U = concentration of Cevimeline Hydrochloride in *Sample solution A* (mg/mL)

Calculate the percentage of any unspecified impurity in the portion of Cevimeline Hydrochloride taken:

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

r_U = peak response of each unspecified impurity from *Sample solution B*

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

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

C_U = concentration of Cevimeline Hydrochloride in *Sample solution B* (mg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Chloride[a]	0.05	—
Cevimeline	1.0	—
Cevimeline *trans*-isomer[b]	1.14	0.50
Any unspecified impurity	—	0.10
Total impurities	—	1.0

[a] This peak is due to the chloride counterion; hence it is not an impurity. It is not to be reported or included in the Total impurities.

[b] (2*RS*,2'*SR*)-2'-Methyl-4-azaspiro{bicyclo[2.2.2]octane-2,5'-[1,3]oxathiolane}.

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I, Method Ic*:** 3.2%–4.50%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Cevimeline Hydrochloride RS

USP Cevimeline *trans*-Isomer RS

(2*RS*,2'*SR*)-2'-Methyl-4-azaspiro{bicyclo[2.2.2]octane-2,5'-[1,3]oxathiolane}hydrochloride hemihydrate.

$C_{10}H_{17}NOS \cdot HCl \cdot \frac{1}{2}H_2O$ 244.78▲ (USP 1-Aug-2023)

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

Topic/Question	Contact	Expert Committee
CEVIMELINE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(4)

Current DocID: GUID-804E3035-0E85-4D77-9700-6F19D81C51CA_2_en-US

DOI: https://doi.org/10.31003/USPNF_M14810_02_01

DOI ref: iq6fm