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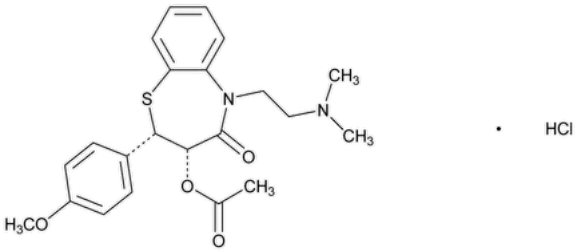
Diltiazem Hydrochloride

Change to read:



$C_{22}H_{26}N_2O_4S \cdot HCl$ 450.98

1,5-Benzothiazepin-4(5*H*)-one, 3-(acetyloxy)-5-[2-(dimethyl amino)ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride, (+)-*cis*-; ▲(2*S*,3*S*)-5-[2-(Dimethylamino)ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetrahydrobenzo[*b*][1,4]thiazepin-3-yl acetate monohydrochloride▲ (CN 1-Dec-2024) CAS RN®: 33286-22-5; UNII: OLH94387TE.

DEFINITION
Diltiazem Hydrochloride contains NLT 98.0% and NMT 102.0% of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$), 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 *Standard solution*, as obtained in the *Assay*.
- **C.** **Identification Tests—General *Chloride*⟨191⟩:** Meets the requirements

ASSAY
- **Procedure**

Buffer: 1.16 g/L of *d*-10-camphorsulfonic acid in 0.1 M sodium acetate. Adjust with 0.1 N sodium hydroxide to a pH of 6.2.

Mobile phase: Acetonitrile, methanol, and *Buffer* (25:25:50)

System suitability solution: 12 µg/mL each of USP Diltiazem Hydrochloride RS and USP Desacetyl Diltiazem Hydrochloride RS in methanol

Standard solution: 1.2 mg/mL of USP Diltiazem Hydrochloride RS in methanol

Sample solution: 1.2 mg/mL of Diltiazem Hydrochloride in methanol

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.6 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for desacetyl diltiazem and diltiazem are about 0.65 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3 between desacetyl diltiazem and diltiazem, *System suitability solution*

Column efficiency: NLT 1200 theoretical plates for the diltiazem peak, *System suitability solution*

Relative standard deviation: NMT 2.0% determined from replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) in the portion of sample 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 Diltiazem Hydrochloride RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Buffer, Mobile phase, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: Use the *System suitability solution* prepared as directed in the *Assay*.

System suitability: Proceed as directed in the *Assay*, except for the following:

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 10.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of desacetyl diltiazem hydrochloride in the portion of Diltiazem Hydrochloride taken:

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

r_U = peak response of desacetyl diltiazem from the *Sample solution*

r_S = peak response of desacetyl diltiazem from the *Standard solution*

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

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

Calculate the percentage of each impurity peak, other than the main peak and the desacetyl diltiazem peak:

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

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

r_S = peak response of desacetyl diltiazem from the *Standard solution*

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

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

Acceptance criteria: NMT 0.5% of desacetyl diltiazem hydrochloride; NMT 0.5% of each individual impurity; and NMT 1.0% total impurities, including desacetyl diltiazem hydrochloride

SPECIFIC TESTS

• **Optical Rotation** *Specific Rotation*⟨781⟩

Sample solution: 10 mg/mL in water

Acceptance criteria: Between +110° and +116°

• **Loss on Drying ⟨731⟩**

Sample: Dry a sample at 105° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Desacetyl Diltiazem Hydrochloride RS

d-cis-3-Hydroxy-2,3-dihydro-5-[2-dimethylamino)ethyl]-2-(*p*-methoxyphenyl)-1,5-benzothiazepin-4(5*H*)-one hydrochloride.

$C_{20}H_{24}N_2O_3S \cdot HCl$ ▲408.94▲ (CN 1-Dec-2024)

USP Diltiazem Hydrochloride RS

Topic/Question	Contact	Expert Committee
DILTIAZEM HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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