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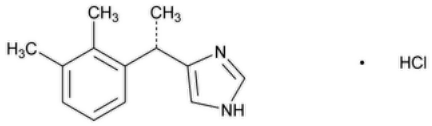
Change to read:

Dexmedetomidine Hydrochloride

▲



▲ (ERR 1-Mar-2019)

$C_{13}H_{16}N_2 \cdot HCl$ 236.74

1*H*-Imidazole, 4-[1-(2,3-dimethylphenyl)ethyl]-, monohydrochloride, (*S*)-;

4-[(*S*)-α,2,3-Trimethylbenzyl]imidazole monohydrochloride CAS RN®: 145108-58-3; UNII: 1018WH7F9I.

DEFINITION

Dexmedetomidine Hydrochloride contains NLT 98.0% and NMT 102.0% of dexmedetomidine hydrochloride ($C_{13}H_{16}N_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the test for *Enantiomeric Purity*.

• **C.** **Identification Tests—General, *Chloride* ⟨191⟩:** Meets the requirements

ASSAY

• **Procedure**

Buffer: 0.89 g/L dibasic sodium phosphate dihydrate solution prepared as follows. Dissolve a suitable amount of dibasic sodium phosphate dihydrate with 90% of total volume of water, adjust with 16 g/L of monobasic sodium phosphate dihydrate solution in water to a pH of 7.0, and dilute with water to volume.

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: 0.2 mg/mL of USP Dexmedetomidine Hydrochloride RS in *Mobile phase*

Sample solution: 0.2 mg/mL of Dexmedetomidine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4-mm × 12.5-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dexmedetomidine hydrochloride ($C_{13}H_{16}N_2 \cdot HCl$) in the portion of the sample taken:

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

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

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

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

C_U = concentration of Dexmedetomidine 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 and **Mobile phase:** Proceed as directed in the *Assay*.

Standard solution: 2 µg/mL of USP Dexmedetomidine Hydrochloride RS in *Mobile phase*

Sensitivity solution: 0.8 µg/mL of USP Dexmedetomidine Hydrochloride RS in *Mobile phase*

Sample solution: 2 mg/mL of sample in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay* except for the following.

Run time: NLT 9 times the retention time of the dexmedetomidine peak

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

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

Relative standard deviation: NMT 5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—The relative retention times of known impurities are given in *Table 1*.]

Table 1

Name	Relative Retention Time
Hydroxymedetomidine[a]	0.36
Dexmedetomidine	1.00
N-Benzyl hydroxymedetomidine[b]	2.22
Ethylmedetomidine[c]	2.47
N-Benzyl medetomidine[d]	6.25
N-Benzyl vinyl analog[e]	6.31

[a] 1-(2,3-Dimethylphenyl)-1-(1*H*-imidazol-5-yl)ethanol.

[b] 1-(1-Benzyl-1*H*-imidazol-5-yl)-1-(2,3-dimethylphenyl)ethanol.

[c] 5-[1-(2,3-Dimethylphenyl)ethyl]-1-ethyl-1*H*-imidazole.

[d] 1-Benzyl-5-[1-(2,3-dimethylphenyl)ethyl]-1*H*-imidazole.

[e] 1-Benzyl-5-[1-(2,3-dimethylphenyl)vinyl]-1*H*-imidazole.

Calculate the percentage of each impurity in the portion of the sample taken:

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

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

r_S = peak response of dexmedetomidine in the *Standard solution*

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

C_U = concentration of Dexmedetomidine Hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: Disregard peaks below 0.04%.

Individual impurities: NMT 0.10%

Total impurities: NMT 0.3%

• **Enantiomeric Purity**

Buffer: To 1 L of 5.34 g/L dibasic sodium phosphate dihydrate solution, adjust with a suitable amount (about 700–800 mL) of 4.08 g/L monobasic potassium phosphate solution to a pH of 7.0.

Mobile phase: Acetonitrile and *Buffer* (35:165)

System suitability solution: 1 µg/mL of USP Levomedetomidine RS and 50 µg/mL of USP Dexmedetomidine Hydrochloride RS in *Mobile phase*

Standard solution: 0.5 µg/mL of USP Levomedetomidine RS in *Mobile phase*

Sensitivity solution: 0.05 µg/mL of USP Levomedetomidine RS in *Mobile phase*

Sample solution: 50 µg/mL of sample in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4-mm × 10-cm; 5-µm packing L41

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between levomedetomidine and dexmedetomidine, *System suitability solution*

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

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levomedetomidine hydrochloride in the portion of sample taken:

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

r_U = peak height of levomedetomidine in the *Sample solution*

r_S = peak height of levomedetomidine in the *Standard solution*

C_S = concentration of USP Levomedetomidine RS in the *Standard solution* (µg/mL)

C_U = concentration of Dexmedetomidine Hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Levomedetomidine[a]	0.69	1.0
Dexmedetomidine	1.00	—

[a] (*R*)-4-[1-(2,3-Dimethylphenyl)ethyl]-1*H*-imidazole hydrochloride.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Sample: 1.0 g

Analysis: Dry the *Sample* at 105° for 3 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store at controlled room temperature in tight containers in a dry place.

• **USP Reference Standards ⟨11⟩**

USP Dexmedetomidine Hydrochloride RS

USP Levomedetomidine RS

(*R*)-4-[1-(2,3-Dimethylphenyl)ethyl]-1*H*-imidazole hydrochloride.

$C_{13}H_{16}N_2 \cdot HCl$ 236.74

Topic/Question	Contact	Expert Committee
DEXMEDETOMIDINE HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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