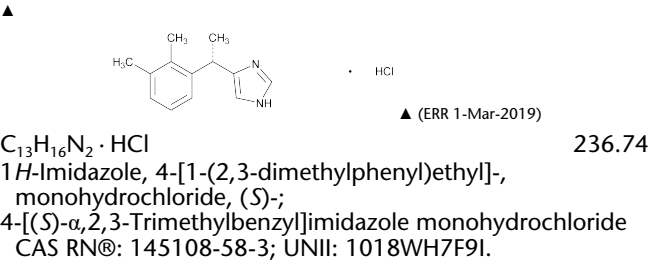


Change to read:

Dexmedetomidine Hydrochloride



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:

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-(1H-imidazol-5-yl)ethanol.
^b 1-(1-Benzyl-1H-imidazol-5-yl)-1-(2,3-dimethylphenyl)ethanol.
^c 5-[1-(2,3-Dimethylphenyl)ethyl]-1-ethyl-1H-imidazole.
^d 1-Benzyl-5-[1-(2,3-dimethylphenyl)ethyl]-1H-imidazole.
^e 1-Benzyl-5-[1-(2,3-dimethylphenyl)vinyl]-1H-imidazole.

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

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:

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]-1H-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]-1H-imidazole hydrochloride.
C₁₃H₁₆N₂ · HCl 236.74