Dextromethorphan Hydrobromide

Type of Posting	Revision Bulletin
Posting Date	27–May–2016, updated 30–Dec–2016[1]
Target Official Date	01–Mar–2017
Expert Committee	Chemical Medicines Monographs 6
Reason for Revision	Safety

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 6 Expert Committee has revised the Dextromethorphan Hydrobromide monograph.

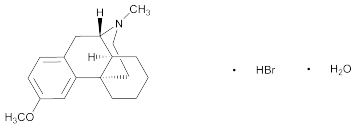
The purpose of this revision is to introduce a procedure to quantitatively monitor the presence of levomethorphan in Dextromethorphan Hydrobromide.

The Dextromethorphan Hydrobromide Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated into *USP 40–NF 35*.

Should you have questions, please contact Clydewyn M. Anthony, Ph. D, Senior Scientific Liaison (301-816-8139 or cma@usp.org).

[1] The official date for the Dextromethorphan Hydrobromide Revision Bulletin was changed from January 1, 2017 to March 1, 2017 on December 30, 2016.

Dextromethorphan Hydrobromide



$C_{18}H_{25}NO \cdot HBr \cdot H_2O$ 370.32
Morphinan, 3-methoxy-17-methyl-, (9α,13α,14α)-, hydrobromide, monohydrate;
3-Methoxy-17-methyl-9α,13α,14α-morphinan hydrobromide monohydrate [6700-34-1].
Anhydrous [125-69-9].
352.32

DEFINITION

Dextromethorphan Hydrobromide contains NLT 98.0% and NMT 102.0% of dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A. INFRARED ABSORPTION ⟨197K⟩**
Sample: Dry under vacuum over •silica• (RB 1-Mar-2017) for 4 h.
Acceptance criteria: Meets the requirements

Delete the following:

•• **B. ULTRAVIOLET ABSORPTION ⟨197U⟩**
Analytical wavelength: 278 nm
Sample solution: 100 µg/mL in 0.1 N hydrochloric acid
Acceptance criteria: Absorptivities, calculated on the anhydrous basis, do not differ by more than 3.0%.• (RB 1-Mar-2017)

Add the following:

•• **B.**
Buffer: 1.54 g of ammonium acetate in 1 L of water, adjusted with phosphoric acid to a pH of 4.1
Mobile phase: Methanol and *Buffer* (90:10)
Diluent: Methanol and water (90:10)
System suitability solution: 10 µg/mL of levomethorphan from USP Levomethorphan Solution RS and 10 mg/mL of USP Dextromethorphan Hydrobromide RS in *Diluent*
Standard solution: 10 µg/mL of USP Dextromethorphan Hydrobromide RS in *Diluent*
Sample solution: 10.0 mg/mL of Dextromethorphan Hydrobromide in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: 225 nm
Column: 4.6-mm × 25-cm; 5-µm packing L88
Flow rate: 1 mL/min
Injection volume: 4 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for dextromethorphan and levomethorphan are 1.0 and 1.28, respectively.]
Suitability requirements
Resolution: NLT 2.0 between dextromethorphan and levomethorphan, *System suitability solution*
Relative standard deviation: NMT 5.0% for dextromethorphan, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of levomethorphan in the portion of Dextromethorphan Hydrobromide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of levomethorphan from the *Sample solution*
r_S = peak response of dextromethorphan from the *Standard solution*
C_S = concentration of USP Dextromethorphan Hydrobromide RS in the *Standard solution* (mg/mL)
C_U = concentration of Dextromethorphan Hydrobromide in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of dextromethorphan, 271.40
M_{r2} = molecular weight of dextromethorphan hydrobromide, 352.32
Acceptance criteria: NMT 0.10%• (RB 1-Mar-2017)

Delete the following:

•• **C.**
Sample solution: 5 mg/mL
Analysis: To 5 mL of the *Sample solution* add 5 drops of 2 N nitric acid and 2 mL of silver nitrate TS.
Acceptance criteria: A yellowish white precipitate is formed.• (RB 1-Mar-2017)

ASSAY

• **PROCEDURE**
Mobile phase: 0.007 M docusate sodium and 0.007 M ammonium nitrate in acetonitrile and water (70:30), filtered and degassed. Dissolve the docusate sodium in the acetonitrile and water mixture before adding the ammonium nitrate. Adjust the solution with glacial acetic acid to a pH of 3.4.
Standard stock solution: 1 mg/mL of USP Dextromethorphan Hydrobromide RS in water
Standard solution: 0.1 mg/mL of USP Dextromethorphan Hydrobromide RS from *Standard stock solution* in *Mobile phase*
Sample stock solution: 1 mg/mL of Dextromethorphan Hydrobromide in water
Sample solution: 0.1 mg/mL of Dextromethorphan Hydrobromide from *Sample stock solution* in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC
Detector: UV 280 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.5
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr$) in the portion of Dextromethorphan Hydrobromide 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 Dextromethorphan Hydrobromide RS in the *Standard solution* (mg/mL)
C_U = concentration of Dextromethorphan Hydrobromide in the *Sample solution* (mg/mL)

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Limit of Phenolic Compounds**
Sample: 5 mg of Dextromethorphan Hydrobromide
Analysis: To the *Sample* add 1 drop of 3 N hydrochloric acid, 1 mL of water, and 2 drops of ferric chloride TS. Add 2 drops of potassium ferricyanide TS, and observe after 2 min.
Acceptance criteria: No blue-green color develops.
- **Limit of *N,N*-Dimethylaniline**
Standard solution: Transfer 50 mg of *N,N*-dimethylaniline to a 100-mL volumetric flask. Add 70.0 mL of water, insert the stopper tightly, shake for 20 min using a mechanical wrist-action shaker or equivalent, and dilute with water to volume. Transfer 1.0 mL to a 100-mL volumetric flask, and dilute with water to volume. Transfer 1.0 mL of the resulting solution to a 25-mL volumetric flask, and add 19 mL of water.
Sample solution: Transfer 500 mg of Dextromethorphan Hydrobromide to a 25-mL volumetric flask. Add 19 mL of water and 1 mL of 3 N hydrochloric acid. Dissolve by warming on a steam bath, and cool.
Analysis: Add 2 mL of 1 N acetic acid and 1 mL of sodium nitrite solution (1 in 100) to the *Sample solution*, and dilute with water to volume. This solution shows no more color than the straw yellow to greenish yellow color of the *Standard solution* similarly treated.
Acceptance criteria: NMT 0.001% of *N,N*-dimethylaniline

SPECIFIC TESTS

Delete the following:

- **Optical Rotation ⟨781S⟩,** *Procedures, Specific Rotation*
Analytical wavelength: 325 nm
Standard solution: 18 mg/mL of USP Dextromethorphan Hydrobromide RS (warm, if necessary, to dissolve)
Sample solution: 18 mg/mL of Dextromethorphan Hydrobromide (warm, if necessary, to dissolve)
Analysis: Determine photoelectrically.
Acceptance criteria: The *Sample solution* does not differ from that of the *Standard solution* by more than 1.0%. (RB 1-Mar-2017)
- **pH ⟨791⟩**
Sample solution: 10 mg/mL
Acceptance criteria: 5.2–6.5
- **Water Determination ⟨921⟩,** *Method I, Method Ia*: 3.5%–5.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.

Change to read:

- **USP Reference Standards ⟨11⟩**
USP Dextromethorphan Hydrobromide RS
USP Levomethorphan Solution RS
3-Methoxy-17-methylmorphinan.
$C_{18}H_{25}NO$ 271.40
This solution contains 0.1 mg/mL of levomethorphan in methanol. (RB 1-Mar-2017)