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

\[
\text{C}_{18}\text{H}_{25}\text{NO} \cdot \text{HBr} \cdot \text{H}_2\text{O} \quad 370.32
\]

Morphinan, 3-methoxy-17-methyl-\(\cdot\)-(9\(\alpha\),13\(\alpha\),14\(\alpha\))-hydrobromide, monohydrate;
3-Methoxy-17-methyl-9\(\alpha\),13\(\alpha\),14\(\alpha\)-morphinan hydrobromide monohydrate [6700-34-1].

Anhydrous [125-69-9].

DEFINITION
Dextromethorphan Hydrobromide contains NLT 98.0% and NMT 102.0% of dextromethorphan hydrobromide (\(\text{C}_{18}\text{H}_{25}\text{NO} \cdot \text{HBr}\)), 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 \(\mu\)g/mL in 0.1 N hydrochloric acid
  - Acceptance criteria: Absorptivities, calculated on the anhydrous basis, do not differ by more than 3.0%.

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 \(\mu\)g/mL of levomethorphan from USP Levomethorphan Solution RS and 10 mg/mL of USP Dextromethorphan Hydrobromide RS in Diluent
  - Standard solution: 10 \(\mu\)g/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 \(\times\) 25-cm; 5-\(\mu\)m packing L88
Flow rate: 1 mL/min
Injection volume: 4 \(\mu\)L

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:

\[
\text{Result} = \left(\frac{r_U}{r_S}\right) \times \left(\frac{C_S}{C_U}\right) \times \frac{M_{r1}}{M_{r2}} \times 100
\]

**r_U** = peak response of levomethorphan from the Standard solution
**r_S** = peak response of dextromethorphan from the Standard solution
**C_S** = concentration of USP Dextromethorphan RS in the Standard solution (mg/mL)
**C_U** = concentration of Dextromethorphan Hydrobromide in the Sample solution (mg/mL)
**M_{r1}** = molecular weight of levomethorphan, 271.40
**M_{r2}** = molecular weight of dextromethorphan hydrobromide, 352.32

Acceptance criteria: NMT 0.10%

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 from **Sample stock solution** in **Mobile phase**

Chromatographic system
(See Chromatography (621), System Suitability.)

©2016 The United States Pharmacopeial Convention All Rights Reserved.

C174611 C184476-M24120-CHM62015, Rev. 1 20161230
**Dextromethorphan**

**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%
  - **System suitability shows no more color than the straw yellow to greenish yellow color of the Standard solution similarly treated.**

**Analysis**

- **Samples:** Standard solution and Sample solution
- Calculate the percentage of dextromethorphan hydrobromide (C₁₈H₂₅NO·HBr) in the portion of Dextromethorphan Hydrobromide taken:

  \[ \text{Result} = \frac{r_0}{r_s} \times \left( \frac{C_s}{C_U} \right) \times 100 \]

  - \( r_0 \): 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**

  **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 (781), 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%.

- **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, C₁₇H₂₃NO
  - 271.40

  This solution contains 0.1 mg/mL of levomethorphan in methanol. © (08.1-Mar-2017)