Dicyclomine Hydrochloride Tablets

**Type of Posting**  Notice of Intent to Revise

**Posting Date**  24-Feb-2023

**Targeted Official Date**  To Be Determined, Revision Bulletin

**Expert Committee**  Small Molecules 3

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 3 Expert Committee intends to revise the Dicyclomine Hydrochloride Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the Dicyclomine Hydrochloride Tablets monograph to add *Dissolution Test 2*. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.¹

Should you have any questions, please contact V. Durga Prasad, Associate Scientific Liaison (+91-40-4448-8723 or durgaprasad.v@usp.org).

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¹ This text is not the official version of a USP–NF monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the USP–NF for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product’s final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF.
Dicyclomine Hydrochloride Tablets

DEFINITION
Dicyclomine Hydrochloride Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of dicyclomine hydrochloride (C$_{19}$H$_{35}$NO$_2$·HCl).

IDENTIFICATION
• A.
  Sample: Transfer a portion of finely powdered Tablets, equivalent to 100 mg of dicyclomine hydrochloride, to a separator containing 10 mL of water and 1 mL of hydrochloric acid. Extract the aqueous acid solution with two 30-mL portions of chloroform, transfer the chloroform extracts to a second separator containing 20 mL of water and 1 mL of sodium hydroxide solution (1 in 10), and shake. Filter the chloroform layer through anhydrous sodium sulfate into a suitable container. Add 3 mL of a freshly prepared 1-in-20 solution of acetyl chloride in anhydrous methanol, prepared by cautiously adding acetyl chloride dropwise to anhydrous methanol with stirring. Evaporate under reduced pressure at room temperature until the residue has been thoroughly dried. Use the residue so obtained to prepare a potassium bromide dispersion.
  Standard: Use a similarly prepared potassium bromide dispersion of USP Dicyclomine Hydrochloride RS.
  Acceptance criteria: The IR absorption spectrum of the Sample exhibits maxima and minima at the same wavelengths as those of the Standard.
• B. The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

ASSAY
• Procedure
  Buffer: Dissolve 2.72 g of monobasic potassium phosphate in 900 mL of water, adjust with 10% sodium hydroxide to a pH of 7.5 ± 0.1, and dilute with water to 1000 mL.
  Mobile phase: Acetonitrile and Buffer (70:30)
  Diluent: Acetonitrile and water (70:30)
  Standard solution: 0.4 mg/mL of USP Dicyclomine Hydrochloride RS in Diluent. [Note—This solution is stable for at least 2 days.]
  Sample solution: Transfer NLT 20 Tablets to a tared container, and determine the average Tablet weight. Grind the Tablets to a fine powder using a glass mortar and pestle. Transfer a portion of the powder, equivalent to 20 mg of dicyclomine hydrochloride, to a 50-mL volumetric flask, add 2.0 mL of water, and sonicate for at least 2 min to disperse the sample. Add 35 mL of acetonitrile, sonicate for at least 5 min, and shake by mechanical means for at least 30 min. Add 10 mL of water, allow the solution to equilibrate to room temperature, then dilute with water to volume. Centrifuge a portion of this solution in a 15-mL glass centrifuge tube for at least 5 min. Use the clear supernatant.

Chromatographic system
(See Chromatography (621), System Suitability.)
  Mode: LC
Detector: UV 215 nm
Column: 4.6-mm × 15-cm; 3.5-µm packing L7
Flow rate: 1 mL/min
Injection volume: 50 µL

System suitability
Sample: Standard solution
Suitability requirements
Tailing factor: NMT 1.5
Relative standard deviation: NMT 1.5%

Analysis
Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of dicyclomine hydrochloride (C₁₉H₂₅NO₃·HCl) in the portion of Tablets taken:

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

\(r_U\) = peak area of dicyclomine from the Sample solution
\(r_S\) = peak area of dicyclomine from the Standard solution
\(C_S\) = concentration of USP Dicyclomine Hydrochloride RS in the Standard solution (mg/mL)
\(C_U\) = nominal concentration of dicyclomine hydrochloride in the Sample solution (mg/mL)

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

Change to read:

• Dissolution (711)

Test 1 (TBD)

Medium: 0.01 N hydrochloric acid; 500 mL
Apparatus 2: 50 rpm
Time: 45 min

Determine the amount of dicyclomine hydrochloride (C₁₉H₂₅NO₃·HCl) dissolved by employing the following method.

Buffer: Dissolve 2.72 g of monobasic potassium phosphate in 450 mL of water, adjust with 10% sodium hydroxide to a pH of 7.5 ± 0.1, and dilute with water to 500 mL.

Mobile phase: Prepare as directed in the Assay.

Diluent: Acetonitrile and Buffer (1:1)

Standard stock solution: 40 µg/mL of USP Dicyclomine Hydrochloride RS in Medium
Standard solution: Mix 25.0 mL of Standard stock solution and 25.0 mL of Diluent.

Sample solution: Pass a portion of the solution under test through a glass microfiber filter of 0.7-µm pore size. Transfer 5.0 mL of the filtrate to a suitable flask, and add 5.0 mL of Diluent.

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

Mode: LC
Detector: UV 215 nm
Column: 4.6-mm × 15-cm; 3.5-µm packing L7
Flow rate: 1 mL/min
Injection volume: 250 µL

System suitability

Sample: Standard solution

Suitability requirements
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 2.0%

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of dicyclomine hydrochloride (C₁₉H₃₅NO₂·HCl) dissolved:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{L} \right) \times V \times D \times 100
\]

\( r_U \) = peak response of dicyclomine from the Sample solution
\( r_S \) = peak response of dicyclomine from the Standard solution
\( C_S \) = concentration of USP Dicyclomine Hydrochloride RS in the Standard solution (mg/mL)
\( L \) = label claim (mg/Tablet)
\( V \) = volume of Medium, 500 mL
\( D \) = dilution factor for the Sample solution

Tolerances: NLT 75% (Q) of the labeled amount of dicyclomine hydrochloride (C₁₉H₃₅NO₂·HCl) is dissolved.

▲ Test 2: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.

Medium: 0.1 N hydrochloric acid; 500 mL
Apparatus 1: 100 rpm
Time: 30 min

Solution A: Dissolve 2.72 g of monobasic potassium phosphate in 900 mL of water, adjust with 10% (w/v) sodium hydroxide in water to a pH of 7.5, and dilute with water to 1000 mL.

Solution B: Dissolve 2.72 g of monobasic potassium phosphate in 450 mL of water, adjust with 10% (w/v) sodium hydroxide in water to a pH of 7.5, and dilute with water to 500 mL.

Mobile phase: Acetonitrile and Solution A (70:30)
Diluent: Acetonitrile and Solution B (50:50)

Standard stock solution: 0.04 mg/mL of USP Dicyclomine Hydrochloride RS in Medium. Sonicate to dissolve, if necessary.

Standard solution: 0.004 mg/mL of USP Dicyclomine Hydrochloride RS from Standard stock solution in Diluent

Sample stock solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of filtrate.

Sample solution: Transfer 1.0 mL of Sample stock solution to a 10-mL volumetric flask and dilute with Diluent to volume. [NOTE—The Sample solution may be stable for 15 h at room temperature.]

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 215 nm
Column: 4.6-mm × 15-cm; 3.5-µm packing L7
Flow rate: 1 mL/min
Injection volume: 100 µL
Run time: NLT 1.8 times the retention time of dicyclomine

System suitability
Sample: Standard solution
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of dicyclomine hydrochloride (C_{19}H_{39}NO_{2}·HCl) dissolved:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times C_S \times V \times D \times \left( \frac{1}{L} \right) \times 100
\]

\( r_U \) = peak response of dicyclomine from the Sample solution
\( r_S \) = peak response of dicyclomine from the Standard solution
\( C_S \) = concentration of USP Dicyclomine Hydrochloride RS in the Standard solution (mg/mL)
\( V \) = volume of Medium, 500 mL
\( D \) = dilution factor for the Sample solution
\( L \) = label claim (mg/Tablet)

Tolerances: NLT 80% \((Q)\) of the labeled amount of dicyclomine hydrochloride \((C_{19}H_{39}NO_{2}·HCl)\) is dissolved. \(▲\) (TBD)

• **Uniformity of Dosage Units** \((905)\): Meet the requirements

**IMPURITIES**

• **Limit of Dicyclomine Related Compound A**
  Buffer: Dissolve 2.72 g of monobasic potassium phosphate in 900 mL of water, adjust with phosphoric acid to a pH of 3.5, and dilute with water to 1000 mL.
  Solution A: Acetonitrile and Buffer (55:45)
  Solution B: Acetonitrile and Buffer (80:20)
  Mobile phase: See Table 1.

Table 1

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<th>Time (min)</th>
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<th>Solution B (%)</th>
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<td>Solution B (%)</td>
</tr>
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<td>-----------</td>
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<tr>
<td>50</td>
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</tbody>
</table>

Diluent: Acetonitrile and water (70:30)

**Standard stock solution:** 0.1 mg/mL of USP Dicyclomine Related Compound A RS in Diluent. Sonication may be used.

**Standard solution:** 4.0 µg/mL of USP Dicyclomine Related Compound A RS in Diluent from Standard stock solution

**Sensitivity solution:** 2.0 µg/mL of USP Dicyclomine Related Compound A RS in Diluent from Standard solution

**Sample solution:** Nominally 2.0 mg/mL of dicyclomine hydrochloride in Diluent prepared as follows.

Transfer NLT 20 Tablets to a tared container, and determine the average Tablet weight. Grind the Tablets to a fine powder using a glass mortar and pestle. Transfer a portion of the powder, equivalent to 200 mg of dicyclomine hydrochloride, to a 100-mL volumetric flask, add about 10 mL of water, and sonicate for at least 2 min to disperse the sample. Add 70 mL of acetonitrile, sonicate for at least 5 min, and shake by mechanical means for at least 30 min. Add 10 mL of water, allow the solution to equilibrate to room temperature, then dilute with water to volume. Centrifuge a portion of this solution, and use the supernatant.

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

- Mode: LC
- Detector: UV 215 nm
- Column: 4.6-mm × 15-cm; 3.5-µm packing L7
- Flow rate: 1 mL/min
- Injection volume: 100 µL

**System suitability**
- **Samples:** Standard solution and Sensitivity solution
- **Suitability requirements**
  - Relative standard deviation: NMT 5.0%, Standard solution
  - Signal-to-noise ratio: NLT 10, Sensitivity solution

**Analysis**
- **Samples:** Standard solution and Sample solution
  - Calculate the percentage of dicyclomine related compound A in the portion of Tablets taken:
    \[
    \text{Result} = \left(\frac{r_U}{r_S}\right) \times \left(\frac{C_S}{C_U}\right) \times 100
    \]
    
    \(r_U\) = peak response of dicyclomine related compound A from the Sample solution
    
    \(r_S\) = peak response of dicyclomine related compound A from the Standard solution
    
    \(C_S\) = concentration of USP Dicyclomine Related Compound A RS in the Standard solution (mg/mL)
    
    \(C_U\) = nominal concentration of dicyclomine hydrochloride in the Sample solution (mg/mL)

**Acceptance criteria:** NMT 0.2%
ADDITIONAL REQUIREMENTS

• Packaging and Storage: Preserve in well-closed containers. Store at controlled room temperature.

Add the following:

▲ Labeling: When more than one Dissolution test is given, the labeling states the test used only if Test 1 is not used.▲ (TBD)

• USP Reference Standards (11).
  USP Dicyclomine Hydrochloride RS
  USP Dicyclomine Related Compound A RS

[1,1’-Bi(cyclohexane)]-1-carboxylic acid.

\[ C_{13}H_{22}O_2 \] 210.32

Page Information:

Not Applicable

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