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).

[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*.

Notice of Intent to Revise
Official: To Be Determined

Dicyclomine Hydrochloride Tablets

DEFINITION

Dicyclomine Hydrochloride Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$).

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 ($C_{19}H_{35}NO_2 \cdot HCl$) in the portion of Tablets taken:

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

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 ($C_{19}H_{35}NO_2 \cdot HCl$) 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 ($C_{19}H_{35}NO_2 \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times D \times 100$$

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 ($C_{19}H_{35}NO_2 \cdot HCl$) 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 volumteric 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 ($C_{19}H_{35}NO_2 \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times D \times (1/L) \times 100$$

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 ($C_{19}H_{35}NO_2 \cdot HCl$) 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

Time (min)	Solution A (%)	Solution B (%)
0	100	0
20	100	0
20.1	0	100
40	0	100

Time (min)	Solution A (%)	Solution B (%)
40.1	100	0
50	100	0

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:

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

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

Current DocID: