

## Carbinoxamine Maleate Tablets

<b>Type of Posting</b>	Notice of Intent to Revise
<b>Posting Date</b>	27-Jan-2023
<b>Targeted Official Date</b>	To Be Determined, Revision Bulletin
<b>Expert Committee</b>	Small Molecules 5

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 5 Expert Committee intends to revise the Carbinoxamine Maleate Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the Carbinoxamine Maleate 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.<sup>1</sup>

Should you have any questions, please contact Yanyin Yang, Senior Scientist II (301-692-3623 or [yanyin.yang@usp.org](mailto:yanyin.yang@usp.org)).

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<sup>1</sup> 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](#).

## Carbinoxamine Maleate Tablets

### DEFINITION

Carbinoxamine Maleate Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of carbinoxamine maleate ( $C_{16}H_{19}ClN_2O \cdot C_4H_4O_4$ ).

### IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **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

**Solution A:** 2.72 g/L of [monobasic potassium phosphate](#). Adjust with [phosphoric acid](#) to a pH of 4.0.

**Solution B:** [Methanol](#) and [acetonitrile](#) (80:20)

**Mobile phase:** See [Table 1](#).

**Table 1**

Time (min)	Solution A (%)	Solution B (%)
0	75	25
2	75	25
10	25	75
15	25	75
16	75	25
20	75	25

**Diluent 1:** 0.1 N [hydrochloric acid](#)

**Diluent 2:** [Methanol](#), [acetonitrile](#), and [water](#) (200:50:750)

**System suitability solution:** 0.1 mg/mL of [USP Carbinoxamine Maleate RS](#) and 0.01 mg/mL each of [USP Carbinoxamine Related Compound A RS](#) and [USP Carbinoxamine Related Compound B RS](#) in *Diluent 2*

**Standard solution:** 0.1 mg/mL of [USP Carbinoxamine Maleate RS](#) in *Diluent 2*

**Sample solution:** Nominally 0.1 mg/mL of carbinoxamine maleate prepared as follows. Transfer a suitable amount of powder from finely powdered Tablets (NLT 20) to a suitable volumetric flask. Add 70% of the flask volume of *Diluent 1* and shake for 15 min, then dilute with *Diluent 2* to volume.

Centrifuge the solution and filter the supernatant by passing through a suitable filter of 0.45- $\mu\text{m}$  pore size, discarding the first 2–3 mL of filtrate. Inject the freshly prepared solution immediately.

### Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

**Mode:** LC

**Detector:** UV 225 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

**Column:** 4.6-mm  $\times$  15-cm; 5- $\mu\text{m}$  packing [L7](#)

**Column temperature:** 40°

**Flow rate:** 1 mL/min

**Injection volume:** 10  $\mu\text{L}$

### System suitability

**Samples:** *System suitability solution* and *Standard solution*

[NOTE—See [Table 2](#) for relative retention times.]

#### Suitability requirements

**Resolution:** NLT 4.0 between carbinoxamine related compound A and carbinoxamine related compound B, *System suitability solution*

**Tailing factor:** NMT 1.5, *Standard solution*

**Relative standard deviation:** NMT 1.0%, *Standard solution*

### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of carbinoxamine maleate ( $\text{C}_{16}\text{H}_{19}\text{ClN}_2\text{O} \cdot \text{C}_4\text{H}_4\text{O}_4$ ) in the portion of Tablets taken:

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

$r_U$  = peak response of carbinoxamine from the *Sample solution*

$r_S$  = peak response of carbinoxamine from the *Standard solution*

$C_S$  = concentration of [USP Carbinoxamine Maleate RS](#) in the *Standard solution* (mg/mL)

$C_U$  = nominal concentration of carbinoxamine maleate in the *Sample solution* (mg/mL)

**Acceptance criteria:** 93.0%–107.0%

## PERFORMANCE TESTS

### Change to read:

- **DISSOLUTION** (711)

- ▲ **Test 1** ▲ (TBD)

**Medium:** [Water](#); 900 mL

**Apparatus 2:** 50 rpm

**Time:** 45 min

**Standard solution:** [USP Carbinoxamine Maleate RS](#) in *Medium* with a concentration similar to that expected in the *Sample solution*

**Sample solution:** Filter a portion of the solution under test and dilute with *Medium* as needed.

#### Instrumental conditions

**Mode:** UV

**Analytical wavelength:** Maximum absorbance at about 260 nm

## Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of carbinoxamine maleate ( $C_{16}H_{19}ClN_2O \cdot C_4H_4O_4$ ) dissolved:

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

$A_U$  = absorbance from the *Sample solution*

$A_S$  = absorbance of carbinoxamine maleate from the *Standard solution*

$C_S$  = concentration of [USP Carbinoxamine Maleate RS](#) in the *Standard solution* (mg/mL)

$V$  = volume of *Medium*, 900 mL

$D$  = dilution factor for the *Sample solution*

$L$  = label claim (mg/Tablet)

**Tolerances:** NLT 75% (Q) of the labeled amount of carbinoxamine maleate ( $C_{16}H_{19}ClN_2O \cdot C_4H_4O_4$ ) 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, deaerated

**Apparatus 1:** 100 rpm

**Time:** 30 min

**Buffer:** Dissolve 2.72 g of [potassium phosphate, monobasic](#) in 1000 mL of [water](#). Adjust with [phosphoric acid](#) to a pH of 4.0.

**Mobile phase:** [Methanol](#) and *Buffer* (45:55)

**Standard solution:** ( $L/500$ ) mg/mL of [USP Carbinoxamine Maleate RS](#) in *Medium*, where  $L$  is the label claim in mg/Tablet. Sonicate to dissolve.

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45- $\mu$ m pore size, discarding the first 4 mL of the filtrate.

### Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

**Mode:** LC

**Detector:** UV 262 nm

**Column:** 4.6-mm  $\times$  15-cm; 5- $\mu$ m packing [L1](#)

**Column temperature:** 40°

**Flow rate:** 1 mL/min

**Injection volume:** 20  $\mu$ L

**Run time:** NLT 2 times the retention time of carbinoxamine

### 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 carbinoxamine maleate ( $C_{16}H_{19}ClN_2O \cdot C_4H_4O_4$ ) dissolved:

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

$r_U$  = peak response of carbinoxamine from the *Sample solution*

$r_S$  = peak response of carbinoxamine from the *Standard solution*

$C_S$  = concentration of [USP Carbinoxamine Maleate RS](#) in the *Standard solution* (mg/mL)

$V$  = volume of *Medium*, 500 mL

$L$  = label claim (mg/Tablet)

**Tolerances:** NLT 80% (Q) of the labeled amount of carbinoxamine maleate ( $C_{16}H_{19}ClN_2O \cdot C_4H_4O_4$ ) is dissolved. ▲ (TBD)

- **UNIFORMITY OF DOSAGE UNITS** (905): Meet the requirements

## IMPURITIES

### • ORGANIC IMPURITIES

**Solution A, Solution B, Mobile phase, Diluent 1, Diluent 2, and System suitability**

**solution:** Prepare as directed in the *Assay*.

**Standard stock solution:** 0.028 mg/mL of [USP Carbinoxamine Maleate RS](#) (equivalent to 0.02 mg/mL of carbinoxamine) and 0.02 mg/mL each of [USP Carbinoxamine Related Compound A RS](#) and [USP Carbinoxamine Related Compound B RS](#) in *Diluent 2*

**Standard solution:** 0.0014 mg/mL of [USP Carbinoxamine Maleate RS](#) (equivalent to 0.001 mg/mL of carbinoxamine) and 0.001 mg/mL each of [USP Carbinoxamine Related Compound A RS](#) and [USP Carbinoxamine Related Compound B RS](#) in *Diluent 2*, from *Standard stock solution*

**Sample solution:** Nominally 1.0 mg/mL of carbinoxamine maleate prepared as follows. Transfer a suitable quantity of powder from finely powdered Tablets (NLT 20) to a suitable volumetric flask. Add 75% of the flask volume of *Diluent 1*, shake for 15 min, and dilute with *Diluent 2* to volume. Centrifuge the solution and filter the supernatant by passing through a suitable filter of 0.45- $\mu$ m pore size, discarding the first 2–3 mL of filtrate. Inject the freshly prepared solution immediately.

### Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

**Mode:** LC

**Detector:** UV 225 nm

**Column:** 4.6-mm  $\times$  15-cm; 5- $\mu$ m packing [L7](#)

**Column temperature:** 40°

**Flow rate:** 1 mL/min

**Injection volume:** 10  $\mu$ L

### System suitability

**Samples:** *System suitability solution* and *Standard solution*

[NOTE—See [Table 2](#) for relative retention times.]

### Suitability requirements

**Resolution:** NLT 4.0 between carbinoxamine related compound A and carbinoxamine related compound B, *System suitability solution*

**Relative standard deviation:** NMT 5.0% for each corresponding compound present in the *Standard solution*

## Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of carbinoxamine related compound A and carbinoxamine related compound B in the portion of Tablets taken:

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

$r_U$  = peak response of carbinoxamine related compound A or carbinoxamine related compound B from the *Sample solution*

$r_S$  = peak response of the corresponding Reference Standard from the *Standard solution*

$C_S$  = concentration of the corresponding Reference Standard in the *Standard solution* (mg/mL)

$C_U$  = nominal concentration of carbinoxamine maleate in the *Sample solution* (mg/mL)

Calculate the percentage of each unspecified degradation product in the portion of Tablets taken:

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

$r_U$  = peak response of each unspecified degradation product from the *Sample solution*

$r_S$  = peak response of carbinoxamine from the *Standard solution*

$C_S$  = concentration of [USP Carbinoxamine Maleate RS](#) (as the free base) in the *Standard solution* (mg/mL)

$C_U$  = nominal concentration of carbinoxamine maleate in the *Sample solution* (mg/mL)

**Acceptance criteria:** See [Table 2](#). The reporting threshold is 0.05%.

**Table 2**

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Carbinoxamine related compound C <sup>a,b</sup>	0.68	—
Carbinoxamine	1.0	—
Carbinoxamine related compound B	1.25	0.2
Carbinoxamine related compound A	1.36	0.2
Each unspecified degradation product	—	0.2
Total degradation products	—	2.0

<sup>a</sup> Process impurity included for identification only and not included in the calculation of total degradation products.

<sup>b</sup> *N,N*-Dimethyl-2-[phenyl(pyridin-2-yl)methoxy]ethan-1-amine.

## ADDITIONAL REQUIREMENTS

● **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store at controlled room temperature.

### **Add the following:**

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

● **USP REFERENCE STANDARDS** (11).

[USP Carbinoxamine Maleate RS](#)

[USP Carbinoxamine Related Compound A RS](#)

(4-Chlorophenyl)(pyridin-2-yl)methanone.

$C_{12}H_8ClNO$                       217.65

[USP Carbinoxamine Related Compound B RS](#)

(4-Chlorophenyl)(pyridin-2-yl)methanol.

$C_{12}H_{10}ClNO$                       219.67

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### Page Information:

Not Applicable

### Current DocID:

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