

Chlorzoxazone Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	22–Nov–2019
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Chemical Medicines Monographs 4

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the [Pending Monograph Guideline](#), this is to provide notice that the Chemical Medicines Monographs 4 Expert Committee intends to revise the Chlorzoxazone Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add another test for *Dissolution* to accommodate their dissolution conditions and tolerances, which differ from those in the existing test for *Dissolution. 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

Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

Should you have any questions, please contact Heather R. Joyce, Senior Scientific Liaison (301-998-6792 or hrj@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](#).

Chlorzoxazone Tablets

DEFINITION

Chlorzoxazone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of chlorzoxazone ($C_7H_4ClNO_2$).

IDENTIFICATION

A. ULTRAVIOLET ABSORPTION

Standard solution: 0.02 mg/mL of USP Chlorzoxazone RS in methanol

Sample stock solution: Nominally 1.0 mg/mL of chlorzoxazone from Tablets prepared as follows. Disperse a portion of powdered Tablets, equivalent to 100 mg of chlorzoxazone, in 100 mL of methanol and shake for 15 min. Pass the resulting solution through a suitable filter.

Sample solution: Nominally 0.02 mg/mL of chlorzoxazone from *Sample stock solution* in methanol

Acceptance criteria: The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the *Standard solution*, concomitantly measured.

- 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: Dilute 10 mL of glacial acetic acid with water to make 1000 mL of solution.

Mobile phase: Acetonitrile, water, and glacial acetic acid (30:70:1)

Internal standard solution: 1.25 mg/mL of phenacetin in acetonitrile

Standard stock solution: 1.25 mg/mL of USP Chlorzoxazone RS in *Mobile phase*

Standard solution: 0.125 mg/mL of USP Chlorzoxazone RS from *Standard stock solution* and 0.25 mg/mL of phenacetin from *Internal standard solution* in *Solution A*

System suitability stock solution: 8.5 mg/mL of *p*-chlorophenol in acetonitrile

System suitability solution: 0.17 mg/mL of *p*-chlorophenol from *System suitability stock solution*, 0.1 mg/mL of USP Chlorzoxazone RS from *Standard stock solution*, and 0.25 mg/mL of phenacetin from *Internal standard solution* in *Solution A*

Sample stock solution: Nominally 1.25 mg/mL of chlorzoxazone prepared as follows. Finely powder Tablets (NLT 20) and transfer a portion of powder to an appropriate volumetric flask. Add 70% of the flask volume of acetonitrile, and shake by mechanical means for about 30 min. Dilute with acetonitrile to volume. Filter a portion of this solution, discarding the first 10 mL of the filtrate.

Sample solution: Nominally 0.125 mg/mL of chlorzoxazone from *Sample stock solution* and 0.25 mg/mL of phenacetin from *Internal standard solution* in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard solution* and *System suitability solution*
[NOTE—The relative retention times for phenacetin, chlorzoxazone, and *p*-chlorophenol are about 0.7, 1.0, and 1.2, respectively.]

Suitability requirements

Resolution: NLT 2.0 between chlorzoxazone and *p*-chlorophenol, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of chlorzoxazone ($C_7H_4ClNO_2$) in the portion of Tablets taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of chlorzoxazone to phenacetin from the *Sample solution*

R_S = peak response ratio of chlorzoxazone to phenacetin from the *Standard solution*

C_S = concentration of USP Chlorzoxazone RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of chlorzoxazone in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

DISSOLUTION (711)

Test 1 (TBD)

[NOTE—Use 2-L vessels for this test.]

Medium: pH 6.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Solutions, Buffer Solutions*); 1800 mL

Apparatus 2: 75 rpm

Time: 60 min

Standard solution: USP Chlorzoxazone RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: 284 nm

Analysis

Samples: *Standard solution* and *Sample solution*
Determine the percentage of the labeled amount of chlorzoxazone ($C_7H_4ClNO_2$) dissolved.

Tolerances: NLT 75% (Q) of the labeled amount of chlorzoxazone ($C_7H_4ClNO_2$) is dissolved.

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

Medium: pH 6.8 phosphate buffer; 1800 mL

Apparatus 2: 75 rpm

Time: 90 min

Standard stock solution: 0.84 mg/mL of USP Chlorzoxazone RS in methanol. Sonicate as necessary.

Standard solution: 0.021 mg/mL of USP Chlorzoxazone RS from the *Standard stock solution* in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* (857).)

Mode: UV

Analytical wavelength: 284 nm

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0% for 5 replicate measurements

Analysis

Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of chlorzoxazone ($C_7H_4ClNO_2$) dissolved:

2 Chlorzoxazone

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

A_U	= absorbance of chlorzoxazone from the <i>Sample solution</i>
A_S	= absorbance of chlorzoxazone from the <i>Standard solution</i>
C_S	= concentration of USP Chlorzoxazone RS in the <i>Standard solution</i> (mg/mL)
V	= volume of <i>Medium</i> , 1800 mL
D	= dilution factor of the <i>Sample solution</i>
L	= label claim (mg/Tablet)

Tolerances: NLT 70% (Q) of the labeled amount of chlorzoxazone ($C_7H_4ClNO_2$) is dissolved.▲ (TBD)

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

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.

Add the following:

- ▲ **LABELING:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (TBD)
- **USP REFERENCE STANDARDS** (11)
USP Chlorzoxazone RS