Albendazole Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	28–Feb–2020
Official Date	To Be Determined, Revision Bulletin
Expert Committee	Chemical Medicines Monographs 3

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 3 Expert Committee intends to revise the Albendazole Tablets monograph.

Based on the supporting data received from manufacturers awaiting FDA approval, the Expert Committee proposes to add *Dissolution Test 2* to the monograph.

- The chromatographic procedure in *Dissolution Test 2* was validated using an Inertsil ODS-3V brand of L1 column. The typical retention time for albendazole is about 3 min.

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

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 Jane Li, Associate Scientific Liaison to the Chemical Medicines Monographs 3 Expert Committee (301-230-6345 or jane.li@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*.

Albendazole Tablets

DEFINITION

Albendazole Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of albendazole ($C_{12}H_{15}N_3O_2S$).

IDENTIFICATION

Change to read:

- **A. ▲SPECTROSCOPIC IDENTIFICATION TESTS ⟨197⟩,** *Ultraviolet-Visible Spectroscopy*: 197U▲ (CN 1-May-2020)

Acidified methanol: Prepare as directed in *Dissolution Test 1*.

Standard stock solution and **Sample stock solution:** Prepare as directed in the *Assay*.

Standard solution: About 10 µg/mL of albendazole in *Acidified methanol*, from *Standard stock solution*

Sample solution: About 10 µg/mL of albendazole in *Acidified methanol*, from *Sample stock solution*

Acceptance criteria: Meet the requirements

- **B.** The retention time of the major peak for albendazole of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

Mobile phase: Dissolve 0.50 g of monobasic ammonium phosphate in 400 mL of water. Add 600 mL of methanol, mix, and filter, discarding the first 15 mL of the filtrate. Degas the clear filtrate before use.

Solution A: Methanol and sulfuric acid (99:1)

Internal standard solution: 3 mg/mL of USP Parbendazole RS prepared as follows. Transfer 150 mg of USP Parbendazole RS to a 50-mL volumetric flask, add 5 mL of *Solution A* and 25 mL of methanol, and shake to dissolve. Dilute with methanol to volume and mix.

Standard stock solution: 2 mg/mL of USP Albendazole RS prepared as follows. Transfer 100 mg of USP Albendazole RS to a 50-mL volumetric flask, add 5 mL of *Solution A* and 25 mL of methanol, and shake to dissolve. Dilute with methanol to volume and mix.

Standard solution: 0.2 mg/mL of USP Albendazole RS and 0.3 mg/mL of USP Parbendazole RS in methanol, from *Standard stock solution* and *Internal standard solution*

Sample stock solution: Nominally 2 mg/mL of albendazole prepared as follows. Weigh and finely powder NLT 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of albendazole, to a 50-mL volumetric flask. Add 5 mL of *Solution A* and 20 mL of methanol, and shake by mechanical means for about 15 min. Dilute with methanol to volume, mix, and filter, discarding the first 15 mL of the filtrate.

Sample solution: Nominally 0.2 mg/mL of albendazole and 0.3 mg/mL of USP Parbendazole RS in methanol, from *Sample stock solution* and *Internal standard solution*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between albendazole and parbendazole

Column efficiency: NLT 1000 theoretical plates

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 albendazole ($C_{12}H_{15}N_3O_2S$) in the portion of Tablets taken:

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

R_U = peak height ratio of albendazole to parbendazole from the *Sample solution*

R_S = peak height ratio of albendazole to parbendazole from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION ⟨711⟩**

▲Test 1▲ (TBD)

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Acidified methanol: Methanol and hydrochloric acid (98:2)

Standard stock solution: 0.36 mg/mL of USP Albendazole RS prepared as follows. Dissolve about 90 mg of USP Albendazole RS, accurately weighed, in 10 mL of *Acidified methanol* in a 250-mL volumetric flask with shaking. Dilute with 0.1 N hydrochloric acid to volume.

Standard solution: 0.009 mg/mL of USP Albendazole RS in 0.1 N sodium hydroxide, from *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter. Prepare a 1-in-25 dilution of the filtrate with 0.1 N sodium hydroxide.

Blank: 0.1 N sodium hydroxide

Instrumental conditions

Mode: UV

Analytical wavelengths: Maximum absorbance at about 308 nm and minimum absorbance at about 350 nm

Analysis:

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of albendazole ($C_{12}H_{15}N_3O_2S$) dissolved:

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

A_U = absorbance of *Sample solution* at about 308 nm – absorbance of *Sample solution* at about 350 nm

A_S = absorbance of *Standard solution* at about 308 nm – absorbance of *Standard solution* at about 350 nm

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*, 25

Tolerances: NLT 80% (Q) of the labeled amount 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; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Determine the percentage of the labeled amount of albendazole ($C_{12}H_{15}N_3O_2S$) dissolved by using one of the following procedures.

Spectrophotometric procedure

Acidified methanol, Standard stock solution, Standard solution, Sample solution, Blank, Instrumental conditions, and **Analysis:** Proceed as directed in *Dissolution Test 1*.

[NOTE—If the absorbance at about 350 nm in the *Sample solution* is below zero, then consider the absorbance as zero.]

Chromatographic procedure

Buffer: 1.05 g/L of potassium phosphate dibasic and 1.0 g/L of potassium phosphate monobasic in water

Mobile phase: Acetonitrile, *Buffer*, and water (54: 40.5: 5.5)

Diluent: Methanol, water, and sulfuric acid (75:24:1)

Standard solution: 0.22 mg/mL of USP Albendazole RS prepared as follows. Transfer about 55.0 mg of USP Albendazole RS to a 250-mL volumetric flask. Add 10 mL of *Diluent* and sonicate to dissolve. Dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 5 µL

Run time: NLT 6 min

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of albendazole ($C_{12}H_{15}N_3O_2S$) dissolved:

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

r_U = peak response of albendazole from the *Sample solution*

r_S = peak response of albendazole from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount is dissolved.▲ (TBD)

• **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩**:** Meet the requirements

Procedure for content uniformity (if applicable)

Acidified methanol and **Standard solution:** Prepare as directed in *Dissolution Test 1*.

Sample stock solution: Place 1 Tablet in a 500-mL volumetric flask, add about 300 mL of *Acidified methanol*, shake by mechanical means for about 30 min, and dilute with *Acidified methanol* to volume. Filter a portion of this solution, discarding the first 20 mL of the filtrate.

Sample solution: Transfer 4.0 mL of the *Sample stock solution* to a 200-mL volumetric flask, and dilute with 0.1 N sodium hydroxide to volume and mix.

Blank: 0.1 N sodium hydroxide

Instrumental conditions

Mode: UV

Analytical wavelengths: Maximum absorbance at about 308 nm and minimum absorbance at about 350 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of albendazole ($C_{12}H_{15}N_3O_2S$) in the Tablet taken:

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

A_U = absorbance of *Sample solution* at about 308 nm – absorbance of *Sample solution* at about 350 nm

A_S = absorbance of *Standard solution* at about 308 nm – absorbance of *Standard solution* at about 350 nm

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

L = label claim (mg/Tablet)

V = volume of the *Sample solution*, 500 mL

D = dilution factor of the *Sample solution*, 50

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers, and store at controlled room temperature.

Change to read:

• **LABELING:** ▲When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (TBD) Tablets intended for veterinary use only are so labeled.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Albendazole RS

USP Parbendazole RS