Albendazole Tablets

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In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 3 Expert Committee has revised the Albendazole Tablets monograph. The purpose for the revision is to add Dissolution Test 2 to accommodate FDA-approved drug products with different dissolution conditions than the existing monograph. The addition of Dissolution Test 2 also necessitates a change to the Labeling section.

- 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.

The Albendazole Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Jane Li, Associate Scientific Liaison (301-230-6345 or jane.li@usp.org).
Albendazole Tablets

DEFINITION
Albendazole Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of albendazole (C₁₂H₁₅N₃O₂S).

IDENTIFICATION
• A. Spectroscopic Identification Tests (197), Ultraviolet-Visible Spectroscopy: 197U
  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 \( \text{C}_{12}\text{H}_{15}\text{N}_{3}\text{O}_{2}\text{S} \) 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 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 (RB 3-Mar-2021)

  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 \( \text{C}_{12}\text{H}_{15}\text{N}_{3}\text{O}_{2}\text{S} \) dissolved:

\[
\text{Result} = \left( \frac{A_U}{A_S} \right) \times \left( \frac{C_S}{L} \right) \times V \times D \times 100
\]
\[ A_U = \text{absorbance of } \text{Sample solution} \text{ at about 308 nm} - \text{absorbance of } \text{Sample solution} \text{ at about 350 nm} \]
\[ A_S = \text{absorbance of } \text{Standard solution} \text{ at about 308 nm} - \text{absorbance of } \text{Standard solution} \text{ at about 350 nm} \]
\[ C_S = \text{concentration of } \text{USP Albendazole RS} \text{ in the } \text{Standard solution} \text{ (mg/mL)} \]
\[ L = \text{label claim (mg/Tablet)} \]
\[ V = \text{volume of } \text{Medium}, 900 \text{ mL} \]
\[ D = \text{dilution factor of the } \text{Sample solution}, 25 \]

**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\textsubscript{12}H\textsubscript{15}N\textsubscript{3}O\textsubscript{2}S) dissolved:

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

- \( r_U \) = 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. ▲ (RB 3-Mar-2021)

- **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\textsubscript{12}H\textsubscript{15}N\textsubscript{3}O\textsubscript{2}S) in the Tablet taken:

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

- \( A_U \) = 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. ▲ (RB 3-Mar-2021) Tablets intended for veterinary use only are so labeled.

- **USP Reference Standards** (11):
  - USP Albendazole RS
  - USP Parbendazole RS