**Other requirements**—It meets the requirements under Injections (1).

**Assay**—

**Mobile phase**—Prepare a filtered and degassed mixture of acetonitrile, methanol, and water (106:55:39). Make adjustments if necessary (see System Suitability under Chromatography (621)).

**Standard preparation**—Dissolve an accurately weighed quantity of USP Ivermectin RS in methanol and dilute quantitatively, and stepwise if necessary, with methanol to obtain a 0.4 mg per mL solution.

**Assay preparation**—Dilute a volume of Injection in methanol and dilute quantitatively, and stepwise if necessary, with methanol to obtain a solution containing 0.4 mg of ivermectin per mL of solution, based on the label claim.

**Chromatographic system** (see Chromatography (621))—The liquid chromatograph is equipped with a 245-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the resolution, *R*, between the first peak (component H2B1a) and the second peak (component H2B1b) is not less than 3.0; and the relative standard deviation for replicate injections is not more than 2.0%, determined from the component H2B1b peak.

**Procedure**—Separately inject equal volumes (about 20 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the component H2B1a, plus component H2B1b. Calculate the percentage of ivermectin (H2B1a + H2B1b) in the portion of Injection taken by the formula:

\[
100(C_S / C_0)(r_T / r_S)
\]

in which *C* is the concentration, in mg per mL, of USP Ivermectin RS in the Standard preparation; *C* is the concentration, in mg per mL, of ivermectin in the Assay preparation; *r* is the total peak response of H2B1a plus H2B1b peaks obtained from the Assay preparation; and *r* is the total peak response of H2B1a plus H2B1b peaks obtained from the Standard preparation. Calculate the ratio of the contents, in percent, of H2B1a / (H2B1a + H2B1b) in the portion of Injection taken by the formula:

\[
100(r_U / r_S)
\]

in which *r* is the peak response of H2B1a, obtained from the Assay preparation; and *r* is as defined above.

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**Ivermectin Paste**

**DEFINITION**

Ivermectin Paste contains NLT 90.0% and NMT 110.0% of the labeled amount of ivermectin, calculated as the sum of component H2B1a (C48H74O14) and component H2B1b (C47H72O14), the ratio of the contents, H2B1a/(H2B1a + H2B1b), is NLT 90.0%.

**IDENTIFICATION**

- **A. Thin-Layer Chromatographic Identification Test** (201)

  **Sample solution**: 0.5 mg/mL of ivermectin dispersed in methanol from a quantity of Paste. Sonicate if necessary until completely dispersed.

  **Application volume**: 2 µL

  **Developing solvent system**: Methylene chloride, methanol, and ammonium hydroxide (90:9:1)

  **Analysis**: Develop the chromatogram in an unsaturated chamber. Remove the plate, allow to air dry, and examine under short- and long-wavelength UV light.

**Acceptance criteria**: Meets the requirements

- **B.** The retention times of the two principal component peaks of ivermectin from the Sample solution correspond to those of the two principal component peaks of ivermectin from the Standard solution, as obtained in the Assay.

**ASSAY**

**PROCEDURE**

**Mobile phase**: Acetonitrile, methanol, and water (106:55:39)

**Standard solution**: 0.4 mg/mL of USP Ivermectin RS in methanol

**Sample solution**: Disperse a quantity of Paste in methanol, using sonication if necessary, to obtain a solution containing 0.4 mg/mL of ivermectin.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode**: LC

**Detector**: UV 245 nm

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

**Flow rate**: 1.5 mL/min

**Injection size**: 20 µL

**System suitability**

**Sample: Standard solution**

**Suitability requirements**

**Resolution**: NLT 3.0 between the first peak (component H2B1a) and the second peak (component H2B1b)

**Relative standard deviation**: NMT 1.0%, determined from the component H2B1a peak

**Analysis**

**Samples**: Standard solution and Sample solution

Calculate the percentage of the labeled amount of ivermectin, component H2B1a (C48H74O14) and component H2B1b (C47H72O14), in the portion of Paste taken:

\[
\text{Result} = \frac{(r_U / r_S) \times (C_S / C_0)}{100}
\]

in which:

- *r* = sum of the peak responses for component H2B1a plus H2B1b peaks obtained from the Sample solution
- *r* = sum of the peak responses for component H2B1a plus H2B1b peaks obtained from the Standard solution
- *C* = concentration of USP Ivermectin RS in the Standard solution
- *C* = nominal concentration of ivermectin in the Sample solution

Calculate the ratio of the contents, in percent, of the components, H2B1a/(H2B1a + H2B1b), in the portion of Paste taken:

\[
\text{Result} = \left(\frac{r_T}{r_S}\right) \times 100
\]

in which:

- *r* = peak response of H2B1a from the Sample solution
- *r* = peak response of H2B1a from the Sample solution

**Acceptance criteria**: 90.0%–110.0% of the labeled amount of ivermectin, calculated as the sum of component H2B1a (C48H74O14) and component H2B1b (C47H72O14). The ratio of the contents, H2B1a/(H2B1a + H2B1b), is NLT 90.0%.

**IMPURITIES**

- **Organic Impurities**

**Mobile phase**, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

**Standard solution**: 0.004 mg/mL of USP Ivermectin RS in methanol
Ivermectin Tablets

Ivermectin Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of Ivermectin components H₂B₁₆ (C₄₈H₇₄O₁₄) plus H₂B₁₇ (C₄₇H₇₂O₁₄). They may contain a suitable antioxidant.

Packaging and storage—Preserve in well-closed containers, and store at a temperature not higher than 30°.

USP Reference standards (11)—
USP Ivermectin RS
USP 3-tert-Butyl-4-hydroxyanisole RS

Identification—The retention times of the H₂B₁₆ and H₂B₁₇ peaks in the chromatogram of the Assay preparation correspond to those in the chromatogram of the Standard preparation, as obtained in the Assay.

Dissolution (711)—
Medium: 0.01 M phosphate buffer, pH 7, with 0.5% of sodium dodecyl sulfate (prepared by dissolving 50 g of sodium dodecyl sulfate in approximately 9 L of water, adding 100 mL of 1 M monobasic sodium phosphate monohydrate, adjusting with sodium hydroxide to a pH of 7, and diluting with water to 10 L); 900 mL.
Apparatus 2: 50 rpm.
Time: 45 minutes.
Determine the amount of C₄₈H₇₄O₁₄ (component H₂B₁₆) plus C₄₇H₇₂O₁₄ (component H₂B₁₇) dissolved by employing the following method.
Mobile phase—Prepare a degassed solution of acetonitrile, methanol, and water (53:35:12).
Standard stock solution—Prepare a 0.13 mg per mL solution of USP Ivermectin RS in Medium.
Standard solution—Using the accompanying table, dilute the Standard stock solution with Medium to volume, and mix.

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of each impurity in the portion of Paste taken, disregarding any peak below 0.05%:

Result = (rᵣ/rₛ) × (Cₛ/Cᵣ) × 100

rᵣ = peak response for each impurity from the Sample solution
rₛ = peak response of the principal peak from the Standard solution
Cₛ = concentration of the Standard solution (mg/mL)
Cᵣ = nominal concentration of ivermectin in the Sample solution (mg/mL)

Acceptance criteria: NMT 3.0% of any peak with a relative retention time of 1.3–1.5, relative to that of the principal peak.
Any other impurity: NMT 1.0%
Total impurities: NMT 6.0%

ADDITIONAL REQUIREMENTS

PACKAGING AND STORAGE: Preserve in well-closed containers. Store at a temperature not higher than 30°.

LABELING: Label it to indicate that it is for oral veterinary use only.

USP REFERENCE STANDARDS (11)
USP Ivermectin RS

Procedure—Separately inject equal volumes (about 100 µL) of the Test solution and the Standard solution into the liquid chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the combined quantities, in percentage, of H₂B₁₆ plus H₂B₁₇ dissolved based on the peak responses obtained from the Test solution and the Standard solution by the formula:

\[ \frac{100(A_U)(W_S)(P(D_U))/[(A_U)D_S]}{L} \]

in which Aᵣ is the total peak area of H₂B₁₆ plus H₂B₁₇ obtained from the Test solution; Wᵣ is the weight, in mg, of the USP Ivermectin RS taken to prepare the Standard stock solution; P is the purity of the USP Ivermectin RS (percent [w/w] H₂B₁₆ plus percent [w/w] H₂B₁₇), expressed as a decimal; Dᵣ is the Test solution dilution factor; Aᵣ is the total peak area of H₂B₁₆ plus H₂B₁₇ obtained from the Standard solution; Dₛ is the Standard solution dilution factor; and L is the label claim of ivermectin, in mg per Tablet.

TOLERANCES—Not less than 80% (Q) of the labeled amount of C₄₈H₇₄O₁₄ (H₂B₁₆) plus C₄₇H₇₂O₁₄ (H₂B₁₇) is dissolved in 45 minutes.

Uniformity of dosage units (905): meet the requirements for Content uniformity.

PROCEDURE FOR CONTENT UNIFORMITY—
Mobile phase—Prepare as directed in the Assay.
Standard solution A—Use the Standard preparation from the Assay.
Standard solution B—Dissolve an accurately weighed quantity of USP Ivermectin RS in methanol to obtain a solution containing 0.125 mg per mL.
Stock sensitivity solution (1%)—Use the Stock sensitivity solution (1%) from the Assay.
Sensitivity solution (0.2%)—Use the Sensitivity solution (0.2%) from the Assay.
Test solution—Transfer 1 Tablet into each of ten 25-mL volumetric flasks. Add 5.0 mL of water, and sonicate for 10 minutes. Add approximately 15 mL of methanol, sonicate for 5 minutes, and mix. Allow the solution to cool to room temperature. Dilute with methanol to volume, and mix. Pass a portion of each solution through a 1.0- to 1.2-µm chemically resistant filter prior to analysis.
Chromatographic system (see Chromatography (621))—Proceed as directed in the Assay.
Procedure—Separately inject equal volumes (about 10 µL) of Standard solution A (for the 6 mg per Tablet dose) or Standard solution B (for the 3 mg per Tablet dose), the Sensi-