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Ivermectin and Pyrantel Pamoate Tablets

» Ivermectin and Pyrantel Pamoate Tablets contain not less than 90.0 percent and not more than 115.0 percent of the labeled amount of ivermectin components H_2B_{1a} ($C_{48}H_{74}O_{14}$) plus H_2B_{1b} ($C_{47}H_{72}O_{14}$) and not less than 90.0 percent and not more than 110.0 percent of the labeled amount of pyrantel pamoate ($C_{34}H_{30}N_2O_6S$).

Packaging and storage—Preserve in tight containers, protected from light, at a temperature not exceeding 30°, and avoid freezing.

Labeling—Label Tablets to indicate that they are intended for veterinary use only. Tablets that can be chewed are so labeled.

USP Reference standards ⟨11⟩—

USP Ivermectin RS
USP Pyrantel Pamoate RS

Identification—The retention times of the two major ivermectin peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* obtained as directed in the *Assay for ivermectin.* The retention time of the pyrantel peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, obtained as directed in the *Assay for pyrantel pamoate*.

Microbial enumeration tests ⟨61⟩ and **Tests for specified microorganisms ⟨62⟩**—The total aerobic microbial count does not exceed 1000 cfu per g, and the total combined molds and yeasts count does not exceed 100 cfu per g. Tablets meet the requirements of the test for absence of *Escherichia coli*.

Uniformity of dosage units ⟨905⟩: The requirements for dosage uniformity are met if the amount of ivermectin and pyrantel pamoate in each of the 10 dosage units as determined from the Content Uniformity method lies within the range of 75.0% to 125.0% of the label claim, and the RSD is less than or equal to 7%.

If not more than 3 units are outside the range of 75.0% to 125.0% of label claim, and no unit is outside the range of 75.0% to 135.0% of label claim, or if the RSD is greater than 7%, or if both conditions prevail, test 20 additional units. The requirements are met if not more than 3 units of the 30 are outside the range of 75.0% to 125.0% of label claim, and no unit is outside the range of 75.0% to 135.0% of label claim and the RSD of the 30 dosage units does not exceed 9%.

pH ⟨791⟩: between 4 and 6, in a solution prepared as follows. Grind about 15 g of Tablets in a blender. Transfer 10 g of the coarse powder thus obtained to a blender jar, add 250 mL of water, previously adjusted to a pH of 7.0 with 0.01 N sodium hydroxide or 0.01 N hydrochloric acid, and blend for about 5 minutes. Allow to settle, and filter a portion of the supernatant. Determine the pH of the filtrate.

Assay for ivermectin—

Mobile phase—Prepare a mixture of acetonitrile, methanol, 0.05 M monobasic sodium phosphate, and water (1130:670:200:5), adjust with phosphoric acid to a pH of 3.0, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Diluent—Prepare a mixture of methanol and water (95:5).

Alumina column—Add about 30 mL of water to about 500 g of neutral alumina, and shake for about 2 hours on a reciprocating shaker. Add about 4 g of the resulting suspension to a 10-mm × 10-cm chromatographic tube fitted with a stopcock, tapping the sides of the column to facilitate settling of the alumina to a height of between 5 and 6 cm. Prepare a separate column for each solution to be tested.

Standard stock solution—Prepare a solution of USP Ivermectin RS in methanol having a known concentration of about 0.28 mg of USP Ivermectin RS per mL. Transfer 4.0 mL of this solution and 5.0 mL of water to a 100-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 5.0 mL of this solution to a second 100-mL volumetric flask, dilute with *Diluent* to volume, and mix. This solution contains about 0.56 µg of USP Ivermectin RS per mL.

Standard preparation—Transfer 15.0 mL of the *Standard stock solution* to a 50-mL centrifuge tube, add 4.0 mL of water, and mix on a vortex mixer. Extract this solution with 10 mL of hexanes by shaking for about 10 minutes. Centrifuge, and discard the hexanes layer. Repeat the extraction with 5 mL of hexanes by shaking for 5 minutes. Centrifuge, and discard the hexanes layer. Add the aqueous layer to the *Alumina column,* and allow to elute. Discard the first 2 mL of eluant, and collect the next 5 mL of eluant in a stoppered tube.

Assay stock solution—Grind an accurately weighed Tablet until it is completely broken up and free from lumps and transfer to a screw-capped, wide-mouth, amber bottle of appropriate volume. Add an accurately measured volume of *Diluent* to the bottle to obtain the estimated concentration of ivermectin of about 0.55 µg per mL. Cap the bottle, and mix on a vortex mixer for about 1 minute. Ultrasonicate for 15 minutes then mechanically shake for an additional 30 minutes. Centrifuge a portion of the suspension thus obtained for about 5 minutes.

Assay preparation—Transfer 15.0 mL of the *Assay stock solution* to a 50-mL centrifuge tube, add 4.0 mL of water, and mix on a vortex mixer. Proceed as directed under *Standard preparation,* beginning with "Extract this solution." The solution thus obtained is the *Assay preparation.*

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 1.2 mL per minute. The column temperature is maintained at about 30°. Chromatograph the *Standard preparation,* and record the peak areas as directed for *Procedure:* the relative retention times are about 0.8 for component H_2B_{1b} and 1.0 for component H_2B_{1a}; the resolution, *R*, between the component H_2B_{1b} peak and the component H_2B_{1a} peak is not less than 2.5; the column efficiency determined from the component H_2B_{1a} peak is not less than 2000 theoretical plates; the tailing factor at 5.0% of peak height for the H_2B_{1a} peak is not more than 2.2; and the relative standard deviation for replicate injections determined from the sum of the component H_2B_{1b} peak and the component H_2B_{1a} peak is not more than 2.0%. [Note—After the column has been used, if the system suitability requirements are not met, regenerate the column as follows. Wash the column with 50 mL of water, slowly increasing the flow rate to 1 mL per minute. Make at least seven 100-µL injections of a dimethyl sulfoxide and water solution (1:1) at 5-minute intervals using water as a mobile phase. Purge the column with 100 mL of methanol, 200 mL of methylene chloride, and again with 100 mL of methanol, slowly increasing the flow rate to 1 mL per minute after each solvent changeover. Finally, purge the column with *Mobile phase,* increasing the flow rate to that used for the analysis.]

Procedure—Separately inject equal volumes (about 100 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of label claim of ivermectin [component H_2B_{1a} ($C_{48}H_{74}O_{14}$) plus component H_2B_{1b} ($C_{47}H_{72}O_{14}$)] in the Tablet taken by the formula:

$$100(P(C_S/C_U))(r_U/r_S)$$

in which C_S is the concentration, in µg per mL, of USP Ivermectin RS in the *Standard stock solution;* C_U is the nominal concentration, in µg per mL, of ivermectin in the *Assay stock solution*; *P* is the purity of the USP Ivermectin RS [percent (w/w) H_2B_{1a} plus percent (w/w) H_2B_{1b}], expressed as a decimal; and r_U and r_S are the sums of the peak areas for component H_2B_{1a} and component H_2B_{1b} obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Assay for pyrantel pamoate—[Note—Use amber glassware in preparing solutions of pyrantel pamoate, and otherwise protect the solutions from unnecessary exposure to bright light. Complete the *Assay for pyrantel pamoate* without prolonged interruption.]

Extraction solvent—Prepare a mixture of tetrahydrofuran and trifluoroacetic acid (94:6).

Mobile phase—Prepare a degassed mixture of acetonitrile, water, acetic acid, and triethylamine (940:25: 25:10). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*). [Note—Increasing the amount of acetonitrile in the *Mobile phase* increases retention times.]

Standard preparation—Prepare a solution of USP Pyrantel Pamoate RS in *Extraction solvent* having a known concentration of about 1.7 mg per mL. Transfer 4.0 mL of this solution to a 25-mL volumetric flask, dilute with tetrahydrofuran to volume, and mix. This solution contains about 0.27 mg of USP Pyrantel Pamoate RS per mL. [Note—Stable for 72 hours if stored at room temperature in a dark area.]

Assay preparation—Grind an accurately weighed Tablet until it is completely broken up and free from lumps and transfer to a 300-mL stock bottle, add 50.0 mL of *Extraction solvent*, mix, sonicate for about 15 minutes, and shake by mechanical means for about 1 hour. Allow to settle, and decant the supernatant into a second 300-mL bottle. Add a second 50-mL portion of *Extraction solvent* to the stock bottle, and shake by mechanical means for about 1 hour. Allow to settle, and decant the supernatant to the second 300-mL bottle. Add a third 50-mL portion of *Extraction solvent* to the stock bottle, and shake by mechanical means for about 1 hour. Transfer the contents of the second 300-mL bottle to the stock bottle. Rinse the second bottle with 50.0 mL of *Extraction solvent*, and transfer this rinsing to the stock bottle. Sonicate the stock bottle for about 10 minutes, and centrifuge a portion of the liquid. Transfer an accurately measured volume of the clear supernatant, equivalent to about 6.5 mg of pyrantel pamoate, to a 25-mL volumetric flask, dilute with tetrahydrofuran to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 313-nm detector and a 4.6-mm × 25-cm column that contains packing L3. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation,* and record the peak areas as directed for *Procedure:* the column efficiency determined from the pyrantel peak is not less than 8000 theoretical plates; the tailing factor is not more than 1.3; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of label claim of pyrantel pamoate ($C_{34}H_{30}N_2O_6S$) in the Tablet taken by the formula:

$$100\ (C_S/C_U)(r_U/r_S)$$

in which C_S is the concentration, in mg per mL, of USP Pyrantel Pamoate RS in the *Standard preparation;* C_U is the nominal concentration of pyrantel pamoate in the *Assay preparation*; and r_U and r_S are the pyrantel peak areas obtained from the *Assay preparation* and the *Standard*

preparation, respectively. [NOTE—Where the test for *Uniformity of dosage units* has been performed using the *Assay for pyrantel pamoate* procedure as a test for *Content uniformity,* use the average of these determinations as the *Assay for pyrantel pamoate* value.]

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
IVERMECTIN AND PYRANTEL PAMOATE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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