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Ivermectin and Clorsulon Injection

» Ivermectin and Clorsulon Injection is a sterile solution of Ivermectin and Clorsulon in a suitable vehicle. It contains not less than 95.0 percent and not more than 110.0 percent of the labeled amount of ivermectin [component B_{1a} ($C_{48}H_{74}O_{14}$) plus component B_{1b} ($C_{47}H_{72}O_{14}$)] and not less than 95.0 percent and not more than 105.0 percent of the labeled amount of clorsulon ($C_8H_8Cl_3N_3O_4S_2$).

Packaging and storage—Preserve in single-dose or multi-dose containers, preferably of Type I glass or plastic. Store at a temperature not higher than 30°.

Labeling—Label it to indicate that it is for veterinary use only.

USP Reference standards ⟨11⟩—

USP Clorsulon RS
USP Ivermectin RS

Identification—

A: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—

Test solution: about 0.5 mg of ivermectin and 5 mg of clorsulon per mL in methanol.

Application volume: 2 µL.

Developing solvent system: a mixture of methylene chloride, methanol, and ammonium hydroxide (90:9:1).

B: The retention times of the two major peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay for ivermectin.* The retention time of the major clorsulon peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay for clorsulon.*

[Note—The two major ivermectin components are not separated by this method.]

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 2.3 USP Endotoxin Units per mg of combined ivermectin and clorsulon.

Sterility Tests ⟨71⟩ **:** meets the requirements.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

Assay for ivermectin—

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, methanol, and water (530:350:70). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩). Increasing the proportion of water increases the resolution.

Standard preparation—Prepare a solution of USP Ivermectin RS in methanol having a known concentration of about 0.3 mg per mL.

Assay preparation—Transfer an accurately measured portion of Injection, equivalent to about 30 mg of ivermectin, to a 100-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-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. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure* [Note—The relative retention times are about 0.8 for component B_{1b} and 1.0 for component B_{1a}.]: the resolution, *R,* between component B_{1b} and component B_{1a} is not less than 2.0; the column efficiency determined from the component B_{1a} peak is not less than 2000 theoretical plates; and the relative standard deviation for replicate injections determined for the component B_{1a} peak is not more than 1.0%.

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 area responses for the major peaks. Calculate the quantity, in mg, of ivermectin component B_{1a} ($C_{48}H_{74}O_{14}$) plus ivermectin component B_{1b} ($C_{47}H_{72}O_{14}$) in the portion of Injection taken by the formula:

$$CP(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Ivermectin RS in the *Standard preparation; P* is the designated percentage of the sum of component B_{1a} plus component B_{1b} in USP Ivermectin RS; and r_U and r_S are the sums of the peak area responses for ivermectin component B_{1a} plus ivermectin component B_{1b} obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Assay for clorsulon—

Mobile phase—Prepare a filtered and degassed mixture of chloroform, methanol, and water (900:100:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Prepare a solution of USP Clorsulon RS in methanol having a known concentration of about 2.4 mg per mL. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with chloroform to volume, and mix.

Assay preparation—Transfer an accurately measured portion of Injection, equivalent to about 240 mg of clorsulon, to a 100-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with chloroform to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L3. The flow rate is about 0.8 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure* [Note—The relative retention times are about 0.6 for ivermectin (the major components of ivermectin co-elute) and 1.0 for clorsulon.]: the column efficiency determined from the clorsulon peak is not less than 4000 theoretical plates; the tailing factor for the clorsulon peak is not more than 2.0; and the relative standard deviation for replicate injections determined for the clorsulon peak is not more than 1.0%.

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 area responses for the major peaks. Calculate the quantity, in mg, of clorsulon ($C_8H_8Cl_3N_3O_4S_2$) in the portion of Injection taken by the formula:

$$1000C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Clorsulon RS in the *Standard preparation;* and r_U and r_S are the clorsulon peak area responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
IVERMECTIN AND CLORSULON INJECTION	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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