Edition: BP 2025 (Ph. Eur. 11.6 update)

Ivermectin Oral Solution

General Notices

Action and use

Antihelminthic.

DEFINITION

Ivermectin Oral Solution is a solution of Ivermectin in a suitable vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of ivermectin, calculated as the sum of component H_2B_{1a} ($C_{48}H_{74}O_{14}$) and component H_2B_{1b} ($C_{47}H_{72}O_{14}$)

95.0 to 105.0% of the stated amount.

The ratio of the contents H_2B_{1a} / (H_2B_{1a} + H_2B_{1b}) is at least 90.0%.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Dilute a quantity of the oral solution with sufficient *methanol* to produce a solution containing 0.05% w/v of Ivermectin.
(2) 0.05% w/v of *ivermectin BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 2 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

1 volume of *concentrated ammonia R1*, 9 volumes of *methanol* and 90 volumes of *dichloromethane*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position, colour and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (1) shows peaks with the same retention times as the peaks due to Ivermectin H_2B_{1a} and Ivermectin H_2B_{1b} in the chromatogram obtained with solution (2).

TESTS

Related substances

Prepare a 0.0002% w/v solution of *moxidectin BPCRS* (internal standard) in *acetonitrile* (solution A).

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared immediately before use.

(1) Dilute a weighed quantity of the oral solution containing 4 mg of Ivermectin with about 190 mL of *acetonitrile*, mix, allow to cool to room temperature and add sufficient *acetonitrile* to produce 200 mL. Dilute 5 volumes of this solution to 50 volumes with solution A. Dry a portion of the resulting solution over *anhydrous sodium sulfate* and filter through a 0.45-µm filter.
(2) Dilute 2 volumes of a 0.02% w/v solution of *ivermectin BPCRS* in *acetonitrile* to 200 volumes with solution A.
(3) Dilute 2 volumes of solution (1) to 200 volumes with *acetonitrile*.
(4) Dilute 5 volumes of solution (3) to 50 volumes with *acetonitrile*.

Derivatise the solutions prior to analysis using the following method.

Transfer 300 µL of the solution being examined to a 2-mL HPLC vial and add 130 µL of *1-methylimidazole* and mix for 5 seconds using a vortex mixer, allow to settle and mix again for 5 seconds. Add 200 µL of a 50% v/v solution of *trifluoroacetic anhydride* in *acetonitrile* and mix for 5 seconds using a vortex mixer, allow to settle and mix again for 5 seconds.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 3.0 mm) packed with *octadecylsilyl silica gel for chromatography* (2.5 µm) (Phenomenex Luna C18 HST is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a fluorescence detector with an excitation wavelength of 365 nm and an emission wavelength of 470 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

To 120 mL of *water* add 1.2 mL of *orthophosphoric acid* and 1.2 mL of *triethylamine*. Add 1880 mL of *acetonitrile*, mix and filter through a 0.45-µm filter.

When the chromatograms are recorded under the prescribed conditions the retention times relative to ivermectin H_2B_{1a} (retention time, about 7 minutes) are: avermectin B1, about 0.6; ivermectin H_2B_{1b}, about 0.8; ivermectin H_4B_{1a}, about 1.2).

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (2), the *resolution factor* between the peaks due to ivermectin H_2B_{1a} and ivermectin H_2B_{1b} is at least 3.0;

in the chromatogram obtained with solution (4), the *signal-to-noise ratio* of the principal peak is at least 10.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (3) (2.5%);

the area of not more than one *secondary peak* is greater than the area of the principal peak in the chromatogram obtained with solution (3) (1%);

the sum of the areas of all the *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (3) (5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using derivatised solutions (1) and (2) described under Related substances.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *resolution factor* between the peaks due to ivermectin H_2B_{1a} and ivermectin H_2B_{1b} is at least 3.0.

DETERMINATION OF CONTENT

Determine the *weight per ml* of the oral solution, Appendix V G, and calculate the content of ivermectin (H_2B_{1a} + H_2B_{1b}), weight in volume, and the ratio H_2B_{1a} / (H_2B_{1a} + H_2B_{1b}) using as the declared content the contents of $C_{48}H_{74}O_{14}$ (H_2B_{1a}) and $C_{47}H_{72}O_{14}$ (H_2B_{1b}) in *ivermectin BPCRS*.