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Moxidectin Oral Solution

General Notices

Moxidectin Oral Drench

Action and use

Antihelminthic; ectoparasiticide

DEFINITION

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

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

Content of moxidectin, $C_{37}H_{53}NO_8$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in *methanol*.
(1) Dilute a quantity of the oral solution to produce a solution containing 0.04% w/v of Moxidectin.
(2) 0.04% w/v of *moxidectin BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* (Merck silica gel 60 plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with *anisaldehyde solution R1*, heat at 105° for 5 to 10 minutes and allow to cool.

MOBILE PHASE

8 volumes of a 15% w/v solution of *ammonium acetate* adjusted to pH 9.6 with *ammonia*, 19 volumes of *propan-2-ol* and 43 volumes of *ethyl acetate*.

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 retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Dilute the oral solution, if necessary, with *water* to produce a solution containing of 0.1% w/v moxidectin. Transfer 2 mL of this solution into a 50-mL conical flask. Add 20 mL of a 0.5% w/v solution of *sodium chloride* in *water* and 15 mL of *dichloromethane*. Mix thoroughly using a magnetic stirring bar for 45 minutes ensuring that the aqueous and organic layers are mixed. Immediately transfer the mixture into a 50-mL centrifuge tube and centrifuge for 15 minutes. Transfer the lower *dichloromethane* layer into a 50-mL conical flask and transfer the upper aqueous layer and the suspended solid layer into a separate 50-mL conical flask. Add 5 mL of *dichloromethane* into the flask containing the aqueous and suspended solid layer and stir for 10 minutes. Transfer this solution to a centrifuge tube and centrifuge for 10 minutes. Combine the *dichloromethane* layers and discard the aqueous layer and any suspended solids. Add approximately 1g *sodium sulfate* to the flask and allow to stand for 15 minutes. Filter the solution into a 25-mL volumetric flask and dilute to volume with *dichloromethane*. Pass 2 mL of this solution with the aid of vacuum through a solid-phase extraction cartridge of 6 mL capacity containing 1g *silica gel* sorbent previously washed with 50 mL *acetonitrile*, followed by 20 mL *dichloromethane* and allow to elute by gravity until the flow stops. Force through any residual *dichloromethane* with vacuum. Add 6 mL *acetonitrile* to the cartridge allowing it to elute by gravity into a 5-mL volumetric flask until the flow stops. Force through any residual *acetonitrile* with vacuum. Dilute to volume with *acetonitrile*.
(2) Dilute 1 volume of solution (1) to 100 volumes with *acetonitrile*.
(3) 0.025% w/v of *moxidectin for system suitability EPCRS* in *acetonitrile*.
(4) Dilute 1 volume of solution (2) to 10 volumes with *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (4 µm) (Novapak C18 is suitable) fitted with a guard column (1.5 cm × 3.2 mm RP-18 (7 µm) is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 2.5 mL per minute.
(d) Use a column temperature of 50°
(e) Use a detection wavelength of 242 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

Mobile phase A A 0.7%w/v solution of *ammonium acetate* adjusted to pH 6.0 with either *glacial acetic acid* or *ammonium hydroxide*.

Mobile phase B *acetonitrile*

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-50	60→20	40→80	linear gradient
50-55	20	80	isocratic
55-56	20→60	80→40	linear gradient
56-65	60	40	re-equilibration

When the chromatograms are recorded under the prescribed conditions the relative retention with respect to moxidectin (retention time about 29 minutes) of Impurity D is about 0.98.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 2.0 where H_p is the height above the baseline of the peak due to impurity D and H_v is the height above the baseline of the lowest point of

the curve separating this peak from the peak due to moxidectin.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of all the *secondary peaks* is not greater than seven times the area of the principal peak in the chromatogram obtained with solution (2) (7%);

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 the following solutions in *acetonitrile*.

(1) Dilute the oral solution to produce a solution containing 0.05% w/v of Moxidectin, shake and allow to settle.
(2) 0.05% w/v of *moxidectin BPCRS*.
(3) 0.1% w/v of *moxidectin for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (4 µm) (Novapak C18 is suitable) fitted with a guard column (1.5 cm × 3.2 mm RP-18 (7 µm) is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2.5 mL per minute.
(d) Use a column temperature of 50°.
(e) Use a detection wavelength of 242 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

40 volumes of a 1.925% w/v solution of *ammonium acetate* in *water*, adjusted to pH 4.8 with *glacial acetic acid*, and 60 volumes of *acetonitrile*.

When the chromatograms are recorded under the prescribed conditions the relative retention with reference to moxidectin (retention time about 12 minutes) of impurity D is about 0.94.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 3.0 where H_p is the height above the baseline of the peak due to impurity D and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to moxidectin.

DETERMINATION OF CONTENT

Calculate the content of $C_{37}H_{53}NO_8$, weight in volume, using the declared content of $C_{37}H_{53}NO_8$ in *moxidectin BPCRS*.

STORAGE

Moxidectin Oral Solution should be protected from light

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Moxidectin.