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# Clenbuterol Oral Solution

General Notices

Clenbuterol Syrup

**Action and use**

Beta$_2$-adrenoceptor agonist; bronchodilator.

## DEFINITION

Clenbuterol Oral Solution contains Clenbuterol Hydrochloride in a suitable vehicle.

*The Oral Solution complies with the requirements stated under Oral Liquids and with the following requirements.*

**Content of clenbuterol hydrochloride, $C_{12}H_{18}Cl_2N_2O,HCl$**

95.0 to 105.0% of the stated amount.

## IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 200 to 400 nm:

the UV spectrum of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2);

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

*Solution A* 2 volumes of *acetonitrile*, 2 volumes of *methanol* and 6 volumes of *water*.

(1) To a volume of the oral solution containing 0.375 mg of Clenbuterol Hydrochloride, add 2 g of *sodium chloride* and shake for 15 minutes. Dilute to 25 mL with solution A, mix and filter (a 0.45-µm PTFE filter is suitable), discarding the first 3 mL of filtrate.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A.
(3) 0.0015% w/v of *clenbuterol hydrochloride BPCRS* and 0.000015% w/v each of *clenbuterol impurity B EPCRS* and *clenbuterol impurity D BPCRS* in solution A.
(4) Dilute 1 volume of solution (2) to 10 volumes with solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl amorphous organosilica polymer* (5 µm) (XTerra MS C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient temperature.
(e) Use a detection wavelength of 300 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

*Mobile phase A* 0.05M *sodium hexanesulfonate* in *water*.

*Mobile phase B* *methanol*.

*Mobile phase C* *acetonitrile*.

| Time (Minutes) | Mobile phase A (% v/v) | Mobile phase B (% v/v) | Mobile phase C (% v/v) | Comment |
|---|---|---|---|---|
| 0-10 | 80 | 15 | 5 | isocratic |
| 10-15 | 80 | 15→0 | 5→20 | linear gradient |
| 15-33 | 80→50 | 0 | 20→50 | linear gradient |
| 33-34 | 50→5 | 0 | 50→95 | linear gradient |
| 34-44 | 5 | 0 | 95 | isocratic |
| 44-45 | 5→80 | 0→15 | 95→5 | linear gradient |
| 45-50 | 80 | 15 | 5 | re-equilibration |

When chromatograms are recorded under the prescribed conditions, the relative retentions with reference to clenbuterol (retention time about 8 minutes) are: impurity D, about 0.3; impurity A; about 0.5 and impurity B, about 1.3.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and clenbuterol is at least 1.5.

LIMITS

Identify any peaks corresponding to impurities A, B and D in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3) and the relative retentions, and multiply the peak areas by the following correction factors: impurity D, 0.1; impurity A, 0.1 and impurity B, 0.2.

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 any *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (2.5%).

Disregard any peak with an area less than 3 times the area of the principal peak in the chromatogram obtained with solution (4) (0.3%).

## ASSAY

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

*Solution A* 2 volumes of *acetonitrile*, 2 volumes of *methanol* and 6 volumes of *water*.

(1) To a weighed quantity of the oral solution containing 0.375 mg of Clenbuterol Hydrochloride, add 2 g of *sodium chloride* and shake for 15 minutes. Dilute to 25 mL with solution A, mix and filter (a 0.45-µm PTFE filter is suitable), discarding the first 3 mL of filtrate.
(2) 0.0015% w/v of *clenbuterol hydrochloride BPCRS* in solution A.

(3) 0.0015% w/v of *clenbuterol hydrochloride BPCRS* and 0.000015% w/v of *clenbuterol impurity B EPCRS* in solution A.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related Substances may be used with a detection wavelength of 211 nm.

SYSTEM SUITABILITY

The Assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and clenbuterol is at least 1.5.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_{12}H_{18}Cl_2N_2O$,HCl, weight in volume, using the declared content of $C_{12}H_{18}Cl_2N_2O$,HCl in *clenbuterol hydrochloride BPCRS*.

## STORAGE

Clenbuterol Oral Solution should be protected from light.

## IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B and D listed under Clenbuterol Hydrochloride.