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

Clenbuterol Granules

General Notices

Action and use

Beta$_2$-adrenoceptor agonist; bronchodilator.

DEFINITION

Clenbuterol Granules contain Clenbuterol Hydrochloride.

The granules comply with the requirements stated under Granules and with the following requirements.

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

90.0 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 25 volumes of *methanol R1* and 75 volumes of a solution containing 0.435% w/v *dipotassium hydrogen orthophosphate*, adjusted to pH 3.0 with *orthophosphoric acid*.

(1) Mix with the aid of ultrasound a quantity of the granules containing 0.064 mg of Clenbuterol Hydrochloride in 10 mL of solution A. Centrifuge and filter through a 0.45-µm membrane filter (Whatman RC is suitable), discarding the first 1 mL of the filtrate.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A.
(3) 63 ng per mL 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 (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Reprosil Pur ODS-3 is suitable) fitted with a pre-column (0.5 cm × 4 mm) packed with the same material.
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 30°.
(e) Use detection wavelengths of 211 nm and 320 nm.
(f) Inject 100 µL of each solution.
(g) Allow the chromatography to proceed for twice the retention time of clenbuterol.

MOBILE PHASE

20 volumes of *methanol R1* and 80 volumes of a solution containing 0.435% w/v *dipotassium hydrogen orthophosphate* adjusted to pH 3.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to clenbuterol (retention time about 26 minutes) are: impurity D, about 0.4 and impurity B, about 0.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3) at 211 nm, the *resolution* between the peaks due to impurity D and impurity B is at least 8.0.

LIMITS

At 320 nm

Identify any peak corresponding to impurity D in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of this peak by a correction factor of 0.5.

In the chromatogram obtained with solution (1), the area of any peak corresponding to impurity B or impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1% of each).

At 211 nm

In the chromatogram obtained with solution (1):

the area of any *secondary peak*, excluding any peaks due to impurity B or impurity D, is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%).

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%).

The total impurity content is not greater than 3.0%.

ASSAY

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

Solution A 25 volumes of *methanol R1* and 75 volumes of a solution of 0.435% w/v *dipotassium hydrogen orthophosphate*, adjusted to pH 3.0 with *orthophosphoric acid*.

(1) Mix with the aid of ultrasound a quantity of the granules containing 0.064 mg of Clenbuterol Hydrochloride in 10 mL of solution A. Centrifuge and filter through a 0.45-µm membrane filter (Whatman RC is suitable), discarding the first 1 mL of the filtrate.
(2) 0.00064% w/v of *clenbuterol hydrochloride BPCRS* in solution A.

CHROMATOGRAPHIC CONDITIONS

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

DETERMINATION OF CONTENT

Calculate the content of clenbuterol hydrochloride, $C_{12}H_{18}Cl_2N_2O,HCl$, in the granules from the chromatograms obtained and using the declared content of $C_{12}H_{18}Cl_2N_2O,HCl$ in *clenbuterol hydrochloride BPCRS*.

STORAGE

Clenbuterol Granules should be protected from light.

IMPURITIES

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