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

Co-amilozide Tablets

General Notices

Amiloride and Hydrochlorothiazide Tablets

Action and use

Potassium-sparing diuretic + thiazide diuretic.

DEFINITION

Co-amilozide Tablets contain Amiloride Hydrochloride Dihydrate and Hydrochlorothiazide in the proportions one part of anhydrous amiloride hydrochloride to ten parts of Hydrochlorothiazide.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of anhydrous amiloride hydrochloride, $C_6H_8ClN_7O,HCl$

95.0 to 105.0% of the stated amount.

Content of hydrochlorothiazide, $C_7H_8ClN_3O_4S_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Shake a quantity of the powdered tablets containing 0.1 g of Hydrochlorothiazide with 50 mL of *acetone*, filter, evaporate the filtrate to dryness and dry the residue at 105° for 1 hour. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of hydrochlorothiazide *(RS 178)*.
B. In the test for Methyl 3,5-diamino-6-chloropyrazine-2-carboxylate, the principal spot in the chromatogram obtained with solution (3) corresponds to that in the chromatogram obtained with solution (4).
C. In the Assay, the retention times of the two principal peaks in the chromatogram obtained with solution (4) correspond to those in the chromatograms obtained with solutions (2) and (3).

TESTS

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using *silica gel G* as the coating substance and a mixture of 85 volumes of *ethyl acetate* and 15 volumes of *propan-2-ol* as the mobile phase. Apply separately to the plate 5 µL of each of the following solutions. For solution (1) shake vigorously a quantity of the powdered tablets containing 50 mg of Hydrochlorothiazide with 10 mL of acetone and filter. For solution (2) dilute 1 volume of solution (1) to 100 volumes with *acetone*. After removal of the plate, dry it in a current of air and reveal the spots by *Method I*. Any *secondary spot* in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2). Disregard any spot remaining on the line of application.

Methyl 3,5-diamino-6-chloropyrazine-2-carboxylate

Carry out the method for *thin-layer chromatography*, Appendix III A, protected from light, using a silica gel precoated plate (Merck silica gel 60 plates are suitable) and a freshly prepared mixture of 90 volumes of *1,4-dioxan* and 12 volumes of 3M *ammonia* as the mobile phase. Apply separately to the plate 10 µL of each of the following solutions. For solution (1) shake a quantity of the powdered tablets containing the equivalent of 17.5 mg of anhydrous amiloride hydrochloride with 10 mL of *methanol* and centrifuge. Solution (2) contains 0.0010% w/v of *methyl 3,5-diamino-6-chloropyrazine-2-carboxylate BPCRS* in *methanol*. For solution (3) dilute 1 volume of solution (1) to 20 volumes with *methanol*. Solution (4) contains 0.010% w/v of *amiloride hydrochloride BPCRS* in *methanol*. After removal of the plate, allow it to dry in air and examine under *ultraviolet light (365 nm)*. Any spot corresponding to methyl 3,5-diamino-6-chloropyrazine-2-carboxylate in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Solution (1) contains 0.0010% w/v of *4-amino-6-chlorobenzene-1,3-disulfonamide BPCRS* in solution (3). For solution (2) dissolve 50 mg of *amiloride hydrochloride BPCRS* in sufficient *methanol* to produce 200 mL, to 20 mL of the resulting solution add 4 mL of *0.1M hydrochloric acid* and dilute to 100 mL with *water*. For solution (3) dissolve 50 mg of *hydrochlorothiazide BPCRS* in a mixture of 20 mL of *methanol* and 4 mL of *0.1M hydrochloric acid* and dilute to 100 mL with *water*. For solution (4) add a mixture of 20 mL of *methanol* and 4 mL of *0.1M hydrochloric acid* to a quantity of the powdered tablets containing 50 mg of Hydrochlorothiazide, mix with the aid of ultrasound for 15 minutes, dilute to 100 mL with *water*, mix and filter.

The chromatographic procedure may be carried out using (a) a stainless steel column (20 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (Nucleosil C18 is suitable), (b) a mixture of 76 volumes of *water*, 20 volumes of *methanol* and 4 volumes of *phosphate buffer pH 3.0* as the mobile phase with a flow rate of 2 mL per minute and (c) a detection wavelength of 286 nm.

The assay is not valid unless a peak due to 4-amino-6-chlorobenzene-1,3-disulfonamide appears immediately before the principal peak in the chromatogram obtained with solution (1). Increase the sensitivity, if necessary, to obtain at least 10% of full-scale deflection on the chart paper for this peak. The assay is also not valid unless the height of the trough separating the two peaks is less than 10% of the height of the peak due to 4-amino-6-chlorobenzene-1,3-disulfonamide. The resolution between the two peaks may be improved by decreasing the methanol content of the mobile phase.

Calculate the content of $C_6H_8ClN_7O,HCl$ and $C_7H_8ClN_3O_4S_2$ using the declared content of $C_6H_8ClN_7O,HCl$ and $C_7H_8ClN_3O_4S_2$ in *amiloride hydrochloride BPCRS* and *hydrochlorothiazide BPCRS* respectively.

STORAGE

Co-amilozide Tablets should be protected from light.

LABELLING

The quantity of Amiloride Hydrochloride Dihydrate is stated in terms of the equivalent amount of anhydrous amiloride hydrochloride.