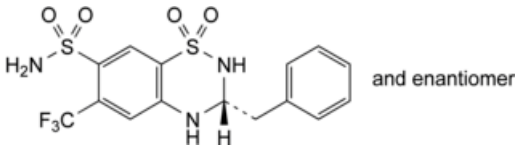
Edition: BP 2025 (Ph. Eur. 11.6 update)

Bendroflumethiazide

General Notices

(Ph. Eur. monograph 0370)



$C_{15}H_{14}F_3N_3O_4S_2$ 421.4 *73-48-3*

Action and use

Thiazide diuretic.

Preparations

Bendroflumethiazide Tablets

Bendroflumethiazide Oral Suspension

Ph Eur

DEFINITION

(3*RS*)-3-Benzyl-6-(trifluoromethyl)-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide.

Content

98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in acetone, soluble in ethanol (96 per cent).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison bendroflumethiazide CRS.

TESTS

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use.*

Solvent mixture Mix 40 volumes of methanol R and 60 volumes of a 2.0 g/L solution of citric acid monohydrate R.

Test solution Dissolve 10.0 mg of the substance to be examined in the solvent mixture and dilute to 50.0 mL with the solvent mixture.

Reference solution (a) Dissolve 2 mg of bendroflumethiazide impurity A CRS and 2.5 mg of altizide CRS in the solvent mixture and dilute to 10 mL with the solvent mixture. Mix 1 mL of this solution with 1 mL of the test solution and dilute to 100 mL with the solvent mixture.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 3.0 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 40 °C.

Mobile phase Mix 15 volumes of tetrahydrofuran R, 25 volumes of methanol R and 60 volumes of a 2.0 g/L solution of citric acid monohydrate R.

Flow rate 0.8 mL/min.

Detection Spectrophotometer at 273 nm.

Injection 20 µL.

Run time Twice the retention time of bendroflumethiazide.

Relative retention With reference to bendroflumethiazide (retention time = about 8 min): impurity A = about 0.2; altizide = about 0.5.

System suitability Reference solution (a):

— resolution: minimum 10 between the peaks due to altizide and bendroflumethiazide.

Limits:

— *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Loss on drying (2.2.32)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

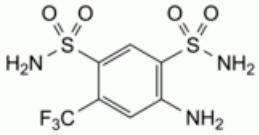
ASSAY

Dissolve 0.150 g in 50 mL of *dimethyl sulfoxide R*. Titrate to the 2nd point of inflexion with *0.1 M tetrabutylammonium hydroxide in 2-propanol*, determining the end-point potentiometrically (*2.2.20*). Carry out a blank titration.

1 mL of *0.1 M tetrabutylammonium hydroxide in 2-propanol* is equivalent to 21.07 mg of $C_{15}H_{14}F_3N_3O_4S_2$.

IMPURITIES

Specified impurities *A.*



A. 4-amino-6-(trifluoromethyl)benzene-1,3-disulfonamide.

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