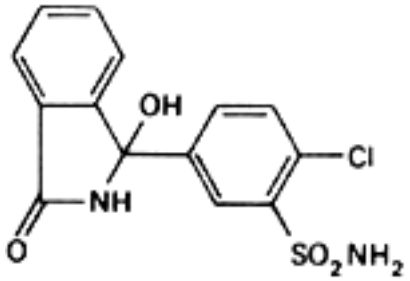
Chlortalidone (Chlortalidonum)

Molecular formula. $C_{14}H_{11}ClN_2O_4S$

Relative molecular mass. 338.8

Graphic formula.



Chemical name. 2-Chloro-5-(1-hydroxy-3-oxo-1-isoindolinyl)benzenesulfonamide; 2-chloro-5-(2,3-dihydro-1-hydroxy-3-oxo-1*H*-isoindol-1-yl)benzenesulfonamide; CAS Reg. No. 77-36-1.

Description. A white to yellowish white, crystalline powder; odourless or almost odourless.

Solubility. Practically insoluble in water and ether R; soluble in methanol R; slightly soluble in ethanol (~750 g/l) TS.

Category. Diuretic.

Storage. Chlortalidone should be kept in a well-closed container.

Requirements

Definition. Chlortalidone contains not less than 98.0% and not more than 102.0% of $C_{14}H_{11}ClN_2O_4S$, calculated with reference to the dried substance.

Identity tests

• Either tests A and B or tests B and C may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from chlortalidone RS or with the *reference spectrum* of chlortalidone.

B. See the test described below under "Related substances". The principal spot obtained with solution A corresponds in position, appearance, and intensity with that obtained with solution B.

C. Dissolve 20 mg in 1 mL of sulfuric acid (~1760 g/l) TS; an intense yellow colour is produced. Warm the mixture in a water-bath and add 10 mg of 1-naphthol R; a red-violet colour is produced.

Solution in alkali. A solution of 1.0 g in 10 mL of sodium hydroxide (~200 g/l) TS is clear and not more intensely coloured than standard colour solution Yw2 when compared as described under 1.11 Colour of liquids.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105°C; it loses not more than 5.0 mg/g.

Related substances. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R2 as the coating substance and a mixture of 15 volumes of 1-butanol R and 3 volumes of ammonia (~17 g/l) TS as the mobile phase. Apply separately to the plate 10 µl of each of 3 solutions in methanol R containing (A) 10 mg of the test substance per mL, (B) 10 mg of chlortalidone RS per mL, and (C) 0.10 mg of 2-(4-chloro-3-sulfamoylbenzoyl)benzoic acid RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254 nm). Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution C.

Assay. Dissolve about 0.3 g, accurately weighed, in 50 mL of pyridine R and titrate with tetrabutylammonium hydroxide (0.1 mol/l) VS, determining the end-point potentiometrically as described under 2.6 Non-aqueous titration, Method B. Each mL of tetrabutylammonium hydroxide (0.1 mol/l) VS is equivalent to 33.88 mg of $C_{14}H_{11}ClN_2O_4S$.