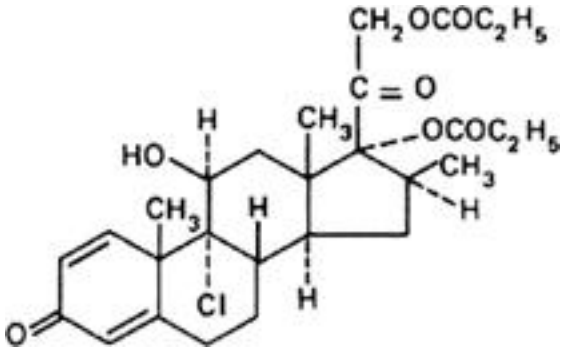
Beclometasone dipropionate (Beclometasoni dipropionas)

Molecular formula. $C_{28}H_{37}ClO_7$

Relative molecular mass. 521.0

Graphic formula.



Chemical name.

9-Chloro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17,21-dipropionate; 9-chloro-11β-hydroxy-16β-methyl-17,21-bis(1-oxopropoxy)pregna-1,4-diene-3,20-dione; CAS Reg. No. 5534-09-8.

Description. A white to creamy white powder; odourless.

Solubility. Practically insoluble in water; soluble in 60 parts of ethanol (~750 g/l) TS.

Category. Antiasthmatic drug.

Storage. Beclometasone dipropionate should be kept in a well-closed container, protected from light.

Requirements

Definition. Beclometasone dipropionate contains not less than 96.0% and not more than 104.0% of $C_{28}H_{37}ClO_7$, calculated with reference to the dried substance.

Identity tests

• Either test A or test B 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 beclometasone dipropionate RS or with the *reference spectrum* of beclometasone dipropionate.

B. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using kieselguhr R1 as the coating substance and a mixture of 1 volume of propylene glycol R and 9 volumes of acetone R to impregnate the plate, dipping it about 5 mm into the liquid. After the solvent has reached a height of at least 16 cm, remove the plate from the chromatographic chamber and allow it to stand at room temperature until the solvent has completely evaporated. Use the impregnated plate within 2 hours, carrying out the chromatography in the same direction as the impregnation. Use a mixture of 4 volumes of cyclohexane R and 1 volume of toluene R as the mobile phase. Apply separately to the plate 2 µl of each of 2 solutions in a mixture of 9 volumes of chloroform R and 1 volume of methanol R containing (A) 2.5 mg of the test substance per mL and (B) 2.5 mg of beclometasone dipropionate RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in air until the solvents have evaporated, heat it at 120 °C for 15 minutes, spray the hot plate with sulfuric acid/ethanol TS, and then heat at 120 °C for 10 minutes. Allow to cool, and examine the chromatogram in daylight and in ultraviolet light (365 nm). The principal spot obtained with solution A corresponds in position, appearance, and intensity with that obtained with solution B.

Specific optical rotation. Use a 10 mg/mL solution in dioxan R; $[\alpha]_D^{20\,°C}$ = +88° to +94°.

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 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of 95 volumes of dichloroethane R, 5 volumes of methanol R, and 0.2 volumes of water as the mobile phase. Apply separately to the plate 10 µl of each of 2 solutions in a mixture of 9 volumes of chloroform R

and 1 volume of methanol R containing (A) 15 mg of the test substance per mL and (B) 0.30 mg of the test substance per mL. After removing the plate from the chromatographic chamber, allow it to dry in air until the solvents have evaporated and heat at 105 °C for 10 minutes; allow it to cool, spray it with blue tetrazolium/sodium hydroxide TS, and examine the chromatogram in daylight. Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Assay

• The solutions must be protected from light throughout the assay.

Dissolve about 20 mg, accurately weighed, in sufficient aldehyde-free ethanol (~750 g/l) TS to produce 100 mL. Dilute 20 mL of this solution with sufficient aldehyde-free ethanol (~750 g/l) TS to produce 100 mL. Transfer 10.0 mL of the diluted solution to a 25-mL volumetric flask, add 2.0 mL of blue tetrazolium/ethanol TS, and displace the air in the flask with oxygen-free nitrogen R. Immediately add 2.0 mL of tetramethylammonium hydroxide/ethanol TS and again displace the air with oxygen-free nitrogen R. Stopper the flask, mix the contents by gentle swirling, and allow to stand for 1 hour in a water-bath at 30 °C. Cool rapidly, add sufficient aldehyde-free ethanol (~750 g/l) TS to produce 25 mL, and mix. Measure the absorbance of a 1-cm layer at the maximum at about 525 nm against a solvent cell containing a solution prepared by treating 10 mL of aldehyde-free ethanol (~750 g/l) TS in a similar manner. Calculate the amount of $C_{28}H_{37}ClO_7$ in the substance being tested by comparison with beclometasone dipropionate RS, similarly and concurrently examined.