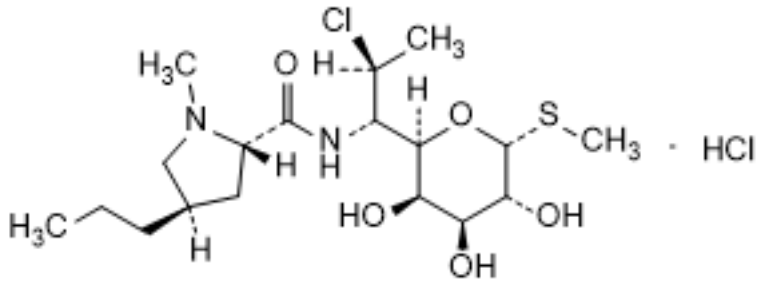
Clindamycin hydrochloride (Clindamycini hydrochloridum)

2016-01

Molecular formula. $C_{18}H_{33}ClN_2O_5S.HCl$

Relative molecular mass. 461.4

Graphic formula



Chemical name

methyl
7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidin-2-carboxamido]-1-thio-l-*threo*-α-d-*galacto*-octopyranoside hydrochloride; (7*S*)-7-chloro-7-deoxylincomycin hydrochloride; (2*S*,4*R*)-*N*-{(1*S*,2*S*)-2-chloro-1-[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-trihydroxy-6-(methylsulfanyl)oxan-2-yl]propyl}-1-methyl-4-propylpyrrolidine-2-carboxamide hydrochlorid; CAS Reg.No.21462-39-5.

Description. A white or almost white, crystalline powder.

Solubility. Very soluble in water, freely soluble in methanol R, and slightly soluble in ethanol (~750 g/L) TS.

Category. Antibacterial.

Storage. Clindamycin hydrochloride should be kept in a tightly closed container.

Requirements

Definition. Clindamycin hydrochloride contains not less than 91.0% and not more than 102.0% of $C_{18}H_{33}ClN_2O_5S$, HCl, calculated with reference to the anhydrous substance.

Identity test

-Either tests A and E or B, D and E or C, D and E 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 clindamycin hydrochloride RS or with the *reference spectrum* of clindamycin hydrochloride.

B. Carry out the test as described under *1.14.1. Thin layer chromatography* using silica gel R1 as the coating substance and the upper layer of a mixture of 19 volumes of 2-propanol R, 38 volumes of a solution of ammonium acetate (~150 g/L) TS adjusted to pH 9.6 with ammonia (~260 g/L) TS and 43 volumes of ethyl acetate R as the mobile phase. Apply separately to the plate 5 µL of each of the following three solutions in methanol R. For solution (A) use 1 mg test substance per mL. For solution (B) use 1 mg of clindamycin hydrochloride RS per mL. For solution (C) use 1 mg of clindamycin hydrochloride RS and 1 mg of lincomycin hydrochloride RS per mL. After removing the plate from the chromatographic chamber dry the plate in air and spray with potassium permanganate (~1 g/L) TS. Examine the chromatogram in daylight.

The principal spot obtained with solution (A) corresponds in position, appearance and intensity with that obtained with solution (B). The test is not valid unless the chromatogram obtained with solution (C) shows 2 clearly separated spots.

C. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using the conditions given under “Assay”. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to the retention time of the peak due to Clindamycin in the chromatogram obtained with solution (2).

D. Dissolve about 10 mg in 2 mL of hydrochloric acid (~200 g/L) TS and heat on a water-bath for 3 minutes. Add 3 mL of sodium carbonate (106 g/L) TS and 1 mL of sodium nitroprusside (20 g/L) TS. A violet-red colour develops.

E. A 0.01 g/mL solution yields reaction A described under *2.1 General identification tests* as characteristic of chlorides.

Specific optical rotation *(1.4)*. Use a 40.0 mg/mL solution and calculate with reference to the anhydrous substance: $[\alpha]_D^{20\,°C}$ = +135° to +150°.

Sulfated ash (*2.3*). Not more than 5.0 mg/g.

Water. Determine as described under *2.8 Determination of water by Karl Fischer Method*, method A, using about 0.5 g of the substance. The water content is not less than 30 mg/g and not more than 60 mg/g.

pH value (*1.13*). pH of a 100 mg/mL solution in carbon-dioxide-free water R, 3.0–5.0.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using the conditions given below under “Assay”.

Prepare the following solutions in the mobile phase. For solution (1) dissolve about 100 mg of the test substance and dilute to 25.0 mL. For solution (2) dilute 2.0 mL of solution (1) to 100.0 mL.

Inject alternately 20 µL each of solution (1) and (2). Record the chromatograms for about 2 times the retention time of clindamycin (retention time about 10 minutes).

In the chromatogram obtained with solution (1) the following impurities, if present, are eluted at the following relative retention with reference to clindamycin (retention time about 10 minutes): impurity A (lincomycin) about 0.4; impurity B (clindamycin B) about 0.65; impurity C (7-epiclindamycin) about 0.8.

In the chromatogram obtained with solution (1):

- -the area of any peak corresponding to either impurity B or impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);
- -the area of any other peak, other than the principal peak, is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);
- -the sum of the areas of all peaks, other than the principal peak, is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (6.0%). Disregard any peak with an area less than 0.025 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

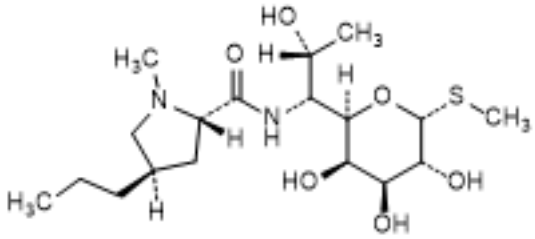
Assay. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using a stainless steel column (25 cm × 4.6 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (5 µm). As the mobile phase use a mixture of 45 volumes of acetonitrile R and 55 volumes of potassium dihydrogen phosphate (6.8 g/L) TS adjusted to pH 7.5 with potassium hydroxide (~400 g/L) TS.

Prepare the following solutions in mobile phase. For solution (1) use a solution containing 1.0 mg of the test substance per mL. For solution (2) use a solution containing 1.0 mg of clindamycin hydrochloride RS per mL.

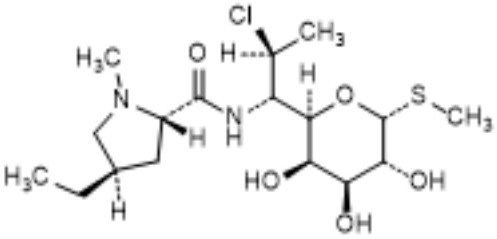
Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 210 nm. Inject alternately 20 µL each of solutions (1) and (2).

Measure the areas of the peaks corresponding to clindamycin obtained in the chromatograms from solution (1) and (2) and calculate the percentage content of clindamycin hydrochloride ($C_{18}H_{33}ClN_2O_5S,HCl$) using the declared content of $C_{18}H_{33}ClN_2O_5S,HCl$ in clindamycin hydrochloride RS.

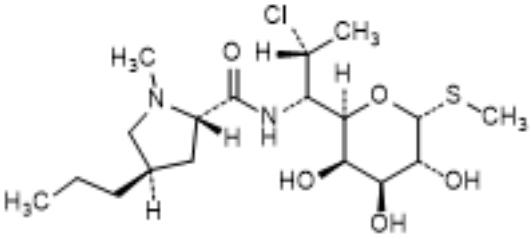
Impurities



A. Methyl
6,8-dideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidin-2-carboxamido]-1-thio-d-*erythro*-α-d-*galacto*-octopyranoside (lincomycin)



B. Methyl
7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-4-ethyl-1-methylpyrrolidin-2-carboxamido]-1-thio-l-*threo*-α-d-*galacto*-octopyranoside (clindamycin B)



C. Methyl
7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidin-2-carboxamido]-1-thio-d-*erythro*-α-d-*galacto*-octopyranoside (7-*epi*-clindamycin)