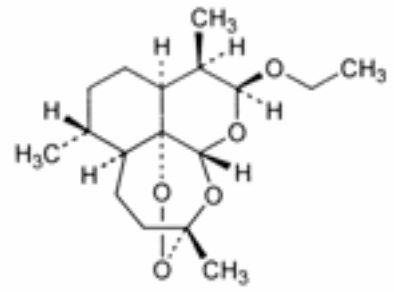
Artemotil (Artemotilum)

$C_{17}H_{28}O_5$



Relative molecular mass. 312.4

Chemical name. (3*R*,5a*S*,6*R*,8a*S*,9*R*,10*S*,12*R*,12a*R*)-Decahydro-10-ethoxy-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin; CAS Reg. No. 75887-54-6.

Other names. Arteether, β-arteether.

Description. A white or almost white, crystalline powder.

Solubility. Practically insoluble in water; sparingly soluble in dichloromethane R, ethanol (~750 g/l) TS and methanol R; soluble in arachis oil R and sesame oil R.

Category. Antimalarial drug.

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

Labelling. The designation Artemotil for parenteral use indicates that the substance complies with the additional requirements and may be used for parenteral administration.

Additional information. The parenteral form is normally intended for intramuscular administration.

Requirements

Artemotil contains not less than **97.0%** and not more than the equivalent of **102.0%** of $C_{17}H_{28}O_5$ calculated with reference to the dried substance.

Identity tests

• Either tests A and B or tests B, C, and D 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 artemotil RS or with the *reference spectrum* of artemotil.

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

C. To 30mg add about 1ml of dehydrated ethanol R and about 0.1 g of potassium iodide R. Heat the mixture on a water-bath; a yellow colour is produced.

D. Dissolve 30 mg in 6.0 mL of dehydrated ethanol R. Place a few drops of the mixture on a white porcelain dish and add 1 drop of vanillin/sulfuric acid TS1; a pink colour is produced.

Melting range. 81.0 - 84.0 °C.

Specific optical rotation. Use a 20 mg/mL solution in dehydrated ethanol R and calculate with reference to the dried substance; $[\alpha]_D^{20\,°C}$ = +155° to +157°.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry over phosphorus pentoxide R under reduced pressure (not exceeding 2.67 kPa or 20 mm of mercury); it loses not more than 5.0 mg/g.

Related substances

• Either test A or test B may be applied.

A. Carry out the test as described under 1.14.4 High-performance liquid chromatography, using the conditions given below under Assay.

Inject alternately 20µl each of solutions A and C.

Measure the areas of the peak responses obtained in the chromatograms from solutions A and C, and calculate the content of the related substances as a percentage. In the chromatogram obtained with solution A, the area of any peak, other than the principal peak, is not greater than that obtained with solution C (0.5%). Not more than one peak is greater than half the area of the principal peak obtained with solution C (0.25%). The sum of the areas of all the peaks, other than the principal peak, is not greater than twice the area of the principal peak obtained with solution C (1.0%). Disregard any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution C.

B. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of equal volumes of light petroleum R1 and ether R as the mobile phase. Apply separately to the plate 10µl of each of the following 5 solutions in toluene R containing (A) 10 mg of Artemotil per mL, (B) 0.05 mg of Artemotil per mL, (C) 0.025 mg of Artemotil per mL, (D) 0.10 mg of Artemotil per mL, and (E) 0.10 mg of artemotil RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, and spray with vanillin/ sulfuric acid TS1. 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 (0.5%). Furthermore, not more than one such spot is more intense than that obtained with solution C (0.25%).

Assay

Determine by 1.14.4 High-performance liquid chromatography, using a stainless steel column (25cm × 4mm) packed with particles of silica gel, the surface of which has been modified with chemically bonded octadecylsilyl groups (5µm). As the mobile phase, use a mixture of 62 volumes of acetonitrile R and 38 volumes of water.

Prepare the following solutions in acetonitrile R: solution (A) 10 mg of Artemotil per mL; solution (B) 10 mg of artemotil RS per mL; and for solution (C) dilute solution A to obtain a concentration equivalent to 0.05 mg of Artemotil per mL.

Operate with a flow rate of 1.5 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 216nm.

Inject alternately 20µl each of solutions A and B.

Measure the areas of the peak responses obtained in the chromatograms from solutions A and B, and calculate the percentage content of $C_{17}H_{28}O_5$ with reference to the dried substance.

Additional requirement for Artemotil for parenteral use

Complies with the monograph for "Parenteral preparations" and with 5.6 Extractable volume for parenteral preparations, and 5.7.2 Tests for particulate contamination, Visible particles.