Artenimol tablets (Artenimoli compressi)

Category. Antimalarial drug.

Storage. Artenimol tablets should be kept in a tightly closed container and protected from light.

Additional information. Available strength: 20mg.

Requirements

Comply with the monograph for "Tablets".

Artenimol tablets contain not less than **90.0%** and not more than **110.0%** of the amount of $C_{15}H_{24}O_5$ stated on the label.

Identity tests

• Either test A alone or tests B, C, and D may be applied.

A. To a quantity of the powdered tablets equivalent to 0.040 g of Artenimol add 40 mL of acetone R, shake to dissolve, and filter. Evaporate the filtrate at low temperature and dry overnight over desiccant silica gel R. Carry out the examination with the residue as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from artenimol RS or with the *reference spectrum* of artenimol.

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 a quantity of the powdered tablets equivalent to 10 mg of Artenimol add 20ml of dehydrated ethanol R, shake to dissolve, filter, and evaporate to dryness. To half of the residue (keep the remaining residue for test D) add 0.5 mL of dehydrated ethanol R, 1.0 mL of potassium iodide (80 g/l) TS, 2.5 mL of sulfuric acid (~100 g/l) TS, and 4 drops of starch TS; a violet colour is produced.

D. Evaporate the remaining filtrate from test C to dryness on a water-bath. Dissolve the residue in 0.5 mL of dehydrated ethanol R, add about 0.5ml of hydroxylamine hydrochloride TS2 and 0.25ml of sodium hydroxide (~80 g/l) TS. Heat the mixture in a water-bath to boiling, cool, add 2 drops of hydrochloric acid (~70 g/l) TS and 2 drops of ferric chloride (50 g/l) TS; a deep reddish-brown colour is immediately produced.

Related substances

• Either test A or test B may be applied.

Prepare fresh solutions and perform the tests without delay.

A. Carry out the test as described under 1.14.4 High-performance liquid chromatography, using a stainless steel column (10cm × 4.6mm) packed with particles of silica gel, the surface of which has been modified with chemically bonded octadecylsilyl groups (3µm). As the mobile phase for gradient elution, use a mixture of 6 volumes of acetonitrile R and 4 volumes of water for the first 17 minutes; then run a gradient, which should reach 100% acetonitrile within 13 minutes.

Prepare the following solutions. For solution (A) weigh and powder 20 tablets, shake a quantity of the powder equivalent to about 10mg of Artenimol, accurately weighed, with 2ml of acetone R, and filter. Evaporate the filtrate to dryness and dissolve the residue in 1.0 mL of methanol R with sonication. For solution (B) dissolve 50µg of Artenimol per mL in methanol R with sonication.

For the system suitability test prepare solution (C) by dissolving 1.0mg of artemisinin RS per mL and 1.0 mg of artenimol RS per mL in methanol R with sonication.

Operate with a flow rate of 0.6 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 216nm.

Inject alternately 20µl each of solutions A, B, and C.

The test is not valid unless the relative retention of α-artenimol compared with artemisinin is about 0.6, and the resolution between the peaks is not less than 2.0.

Measure the areas of the peak (twin-peak) responses obtained in the chromatograms from solutions A and B, 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 twin peak, is not greater than that obtained with solution B (0.5%). Not more than one peak is greater than half the area of the twin peak obtained with solution B (0.25%). The sum of the areas of all the peaks, other than the twin peak, is not greater than twice the area of the twin peak obtained with solution B (1.0%). Disregard any peak with an area less than 0.1 times the area of the twin peak in the chromatogram obtained with solution B.

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. For solution (A) shake a quantity of the powdered tablets equivalent to about 20 mg of Artenimol, with 2ml of acetone R, and filter. Use the filtrate. Prepare similarly solution (B) with the equivalent of about 0.05mg of Artenimol per mL, solution (C) with the equivalent of about 0.025mg of Artenimol per mL, and solution (D) with the equivalent of about 0.10mg of Artenimol per mL. For solution (E) use 0.10 mg of artenimol 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

• Either method A or method B may be applied.

Prepare fresh solutions and perform the tests without delay.

A. Determine by 1.14.4 High-performance liquid chromatography, using a stainless steel column (10cm × 4.6mm) packed with particles of silica gel, the surface of which has been modified with chemically bonded octadecylsilyl groups (3µm). As the mobile phase, use a mixture of 6 volumes of acetonitrile R and 4 volumes of water.

Prepare the following solutions in the mobile phase. For solution (A) weigh and powder 20 tablets, shake a quantity of the powder equivalent to about 1.0 mg of Artenimol, accurately weighed, with 2ml of acetone R, and filter. Evaporate the filtrate to dryness, and dissolve the residue in 1.0 mL. For solution (B) use 1.0 mg of artenimol RS per mL.

For the system suitability test prepare solution (C) containing 1.0mg of artemisinin RS per mL and 1.0 mg of artenimol RS per mL in a mixture of 8 volumes of acetonitrile R and 2 volumes of water.

Operate with a flow rate of 0.6 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 216nm.

Inject alternately 20µl each of solutions A, B, and C.

The test is not valid unless the relative retention of α-artenimol compared with artemisinin is about 0.6, and the resolution between the peaks is not less than 2.0.

Measure the areas of the peak (twin-peak) responses obtained in the chromatograms from solutions A and B, and calculate the percentage content of $C_{15}H_{24}O_5$.

B. Weigh and powder 20 tablets. To a quantity of the powder equivalent to about 0.05 g of Artenimol, accurately weighed, add sufficient ethanol (~750 g/l) TS to produce 100 mL, shake, and filter. Discard the initial 20ml of the filtrate and dilute 10 mL to 100 mL with the same solvent. Accurately transfer 10 mL to a 50-mL volumetric flask, dilute to volume with sodium hydroxide (0.05 mol/l) VS, mix thoroughly, and warm to 50 °C in a waterbath for 30 minutes. Cool to room temperature.

Measure the absorbance of a 1-cm layer at the maximum at about 292nm against a solvent cell containing a blank prepared with 10 mL of ethanol (~750 g/l) TS diluted with sufficient sodium hydroxide (0.05 mol/l) VS to produce 50 mL. Calculate the percentage content of $C_{15}H_{24}O_5$ in the substance being tested by comparison with artenimol RS, similarly and concurrently examined.

Dissolution. Carry out the test as described under 5.5 Dissolution test for solid oral dosage forms.