

## Artemether capsules (Artemetheri capsulae)

2015-01

**Category.** Antimalarial drug.

**Storage.** Artemether should be kept in a hermetically closed container.

**Additional information.** Available strengths: 40 mg, 50 mg.

Requirements

Comply with the monograph for [Capsules](#).

Artemether capsules contain not less than 90.0% and not more than 110.0% of the amount of  $C_{16}H_{26}O_5$  stated on the label.

### Identity tests

-Either tests A and B or tests B, C and D may be applied.

A. To a quantity of the contents of the capsules equivalent to 0.040 g of Artemether 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 artemether RS or with the *reference spectrum* of artemether.

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 contents of the capsules equivalent to 0.08 g of Artemether add 40 mL of dehydrated ethanol R, shake to dissolve and filter. Evaporate half of the filtrate to about 1 mL (keep the remaining filtrate for test D), add 0.10 g of potassium iodide R and heat; a yellow colour is produced.

D. Evaporate the remaining filtrate from test C on a water-bath to a volume of about 5 mL. 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.

### 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", method A.

Inject alternately 20 µL 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 7 volumes of light petroleum R1 and 3 volumes of ethyl acetate R as the mobile phase. Apply separately to the plate 10 µL of each of the following 5 solutions in acetone R. For solution (A) shake a quantity of the contents of the capsules equivalent to about 20 mg of Artemether with 2 mL of acetone R, filter and use the filtrate. Prepare similarly solution (B) with the equivalent of about 0.05 mg of Artemether per mL, solution (C) with the equivalent of about 0.025 mg of Artemether per mL and solution (D) with the equivalent of about 0.10 mg of Artemether per mL. For solution (E) use 0.10 mg of artemether 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.

A. Determine by [1.14.4 High-performance liquid chromatography](#) using a stainless steel column (25 cm × 4 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 62 volumes of acetonitrile R and 38 volumes of water.

Prepare the following solutions in the mobile phase. For solution (A) mix the contents of 20 capsules, shake a quantity equivalent to about 0.05 g of Artemether, accurately weighed, with 2 ml of acetone R and filter. Evaporate the filtrate to dryness and dissolve the residue in 5 mL of the mobile phase. For solution (B) use 10 mg of artemether RS per mL and for solution (C) dilute a suitable volume of solution A to obtain a concentration equivalent to 0.05 mg of Artemether 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 216 nm.

Inject alternately 20 µL 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  $C_{16}H_{26}O_5$ .

B. Mix the contents of 20 capsules and transfer a quantity equivalent to about 13 mg of Artemether, accurately weighed, to a 100 mL volumetric flask and dilute to volume with dehydrated ethanol R. Shake the flask for 15 minutes and filter, discarding the first 10 mL of the filtrate. Accurately measure 5 mL of the clear filtrate into a 50 mL volumetric flask and dilute to volume with hydrochloric acid/ethanol (1 mol/L) VS. Stopper the flask and place it in a water-bath at 55 °C for 5 hours. Allow to cool to room temperature. For the blank use 5 mL of dehydrated ethanol R diluted with sufficient hydrochloric acid/ethanol (1 mol/L) VS to produce 50 mL.

Measure the absorbance of a 1 cm layer at the maximum at about 254 nm against a solvent cell containing the blank. Calculate the percentage content of  $C_{16}H_{26}O_5$  in the capsules being examined using the absorptivity value of 38.5 ( $A_{1\text{cm}}^{1\%} = 385$ ).

**Dissolution.** Carry out the test as described under [5.5 Dissolution test for solid oral dosage forms](#).