

## Artemotil injection (Artemotili injectio)

2015-01

**Description.** A clear, colourless to slightly yellowish, oily solution.

**Category.** Antimalarial drug.

**Storage.** Artemotil injection should be kept protected from light.

**Labelling.** The oil used in the formulation should be indicated.

**Additional information.** Available strengths: 50 mg/mL (paediatric formulation), 75 mg/mL, 150 mg/mL (adult formulation).

Artemotil injection is normally intended for intramuscular administration.

### Requirements

Complies with the monograph for [Parenteral preparations](#) and with [5.6 Extractable volume for parenteral preparations](#), [3.4 Test for bacterial endotoxins](#) and [5.7.2 Tests for particulate contamination, Visible particles](#).

**Definition.** Artemotil injection is a sterile solution of artemotil in an oil suitable for injection. The solution is sterilized by a suitable method (see [5.8 Methods of sterilization](#)).

Artemotil injection contains not less than 95.0% and not more than 105.0% of the amount of  $C_{17}H_{28}O_5$  stated on the label.

### Identity tests

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

A. To a volume of the injection equivalent to 0.050 g of Artemotil add 25 mL of acetone R, mix and filter. Evaporate the filtrate at low temperature and dry overnight over desiccant silica gel R. 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 a volume of the injection equivalent to about 30 mg of Artemotil, add 6 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.

### 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 20  $\mu$ L 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 10  $\mu$ L of each of the following 5 solutions in toluene R. For solution (A) dilute a volume of the injection with toluene R to obtain a concentration equivalent to 10 mg of Artemotil per mL. Prepare similarly solution (B) with the equivalent of about 0.05 mg of Artemotil per mL, solution (C) with the equivalent of about 0.025 mg of Artemotil per mL and solution (D) with the equivalent of 0.10 mg of Artemotil per mL. For solution (E) use 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 (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 acetonitrile R. For solution (A) dilute a volume of the injection to obtain a concentration equivalent to 10 mg of Artemotil per mL, for solution (B) use 10 mg of artemotil RS per mL and for solution (C) dilute a suitable volume of 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 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  $C_{17}H_{28}O_5$ .

**Bacterial endotoxins.** Carry out the test as described under [3.4 Test for bacterial endotoxins](#); contains less than 1.04 IU of endotoxin per mg Artemotil.