Mefloquine tablets (Mefloquini compressi)

2015-01

Category. Antimalarial.

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

Labelling. The designation of the container of Mefloquine tablets should state that the active ingredient is in the hydrochloride form and the quantity should be indicated in terms of the equivalent amount of mefloquine.

Additional information. Strength in the current WHO Model List of Essential Medicines (EML): 250 mg (as hydrochloride). Strength in the current WHO EML for children: 250 mg (as hydrochloride).

Requirements

Comply with the monograph for *Tablets*;

Definition. Mefloquine tablets contain Mefloquine hydrochloride. They contain not less than 90.0% and not more than 110.0% of the amount of mefloquine ($C_{17}H_{16}F_6N_2O$) stated on the label.

Identity tests

· Any two of tests A, B or C may be applied together with test D.

A. Carry out test A.1 or, where UV detection is not available, test A.2.

A.1 Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R6 as the coating substance and a mixture of 70 volumes of toluene R, 30 volumes of ethanol R and 2 volumes of ammonia (~260 g/L) TS as the mobile phase. Apply separately to the plate 10 µL of each of the following two solutions in methanol R. For solution (A) sonicate, with intermittent shaking, a quantity of the powdered tablets containing the equivalent of about 250 mg of mefloquine for 5 minutes with 25 mL, filter and use the filtrate. For solution (B) use 10 mg of mefloquine hydrochloride RS per mL. After removing the plate from the chromatographic chamber allow it to dry in a current of air and examine the chromatogram in ultraviolet light (254 nm).

The principal spot obtained with solution (A) corresponds in position, appearance and intensity to that obtained with solution (B).

A.2 Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography using the conditions described above under test A.1 but using silica gel R5 as the coating substance. Stain the plate with iodine vapours. Examine the chromatogram in daylight.

The principal spot obtained with solution (A) corresponds in position, appearance and intensity to that obtained with solution (B).

B. See the test described under “Assay”. The retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that in the chromatogram obtained with solution (2).

C. To a quantity of the powdered tablets containing the equivalent of 50 mg of mefloquine add 100 mL of methanol R, shake and filter. Dilute 5 mL of the filtrate to 50 mL with the same solvent. The absorption spectrum (*1.6*) of the resulting solution, when observed between 250 nm and 290 nm, exhibits one maximum at about 283 nm.

D. To a quantity of powdered tablets containing the equivalent of about 0.5 g of mefloquine add 10 mL of water R, sonicate for 10 minutes and filter. The filtrate yields reaction B described under *2.1 General identification tests* as characteristic of chlorides.

Dissolution. Carry out the test as described under *5.5 Dissolution test for solid oral dosage forms* using as the dissolution medium 900 mL of hydrochloric acid (~4 g/L) TS and rotating the paddle at 75 revolutions per minute. At 30 minutes withdraw a sample of 10 mL of the medium through an in-line filter. Measure the absorbance (*1.6*) of a 1 cm layer of the filtered sample, suitably diluted if necessary, at the maximum at about 283 nm. At the same time measure the absorbance at the maximum at about 283 nm of a suitable solution of mefloquine hydrochloride RS, initially dissolved in methanol R and then diluted in hydrochloric acid (0.1 mol/L) VS, using hydrochloric acid (~4 g/L) TS as the blank. Each mg of mefloquine hydrochloride ($C_{17}H_{16}F_6N_2O,HCl$) is equivalent to 0.912 mg of mefloquine ($C_{17}H_{16}F_6N_2O$).

For each of the tablets tested calculate the total amount of mefloquine ($C_{17}H_{16}F_6N_2O$) in the medium using the declared content of $C_{17}H_{16}F_6N_2O$ in mefloquine hydrochloride RS. Evaluate the results as described under *5.5 Dissolution test for solid dosage forms, Acceptance criteria*. The amount in solution for each tablet is not less than 75% (Q) of the amount stated on the label.

Related substances

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

Use solutions (1) and (4) as described under “Assay”. For solution (5) transfer 1 mL of solution (1) as prepared for the assay to a 50 mL volumetric flask and make up to volume with the mobile phase. Dilute 2 mL of this solution to 20 mL with the mobile phase.

Inject 20 µL of solution (4). The test is not valid unless the resolution between the two principal peaks is at least 5.

Inject alternately 20 µL each of solutions (1) and (5). Record the chromatograms for about 10 times the retention time of mefloquine.

In the chromatogram obtained with solution (1) the following impurities, if present, are eluted at the following relative retention with reference to mefloquine (retention time about 3.9 minutes): impurity A about 0.9; impurity C about 3.6; and impurity B about 7.4.

In the chromatogram obtained with solution (1):

- -the area of any peak, other than the peak due to mefloquine, is not greater than the area of the principal peak in the chromatogram obtained with solution (5) (0.2%);
- -the sum of the areas of all peaks, other than the peak due to mefloquine, is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (5) (0.5%). Disregard any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

Assay

Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using a stainless steel column (25 cm x 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 22 volumes of methanol R, 38 volumes of acetonitrile R and 40 volumes of buffer pH 3.5 prepared as follows: dissolve 13.6 g *potassium dihydrogen phosphate* in about 900 mL of water R, adjust the pH to 3.5 by addition of phosphoric acid (~105 g/L) TS and dilute to 1000 mL.

Prepare the following solutions in mobile phase. For solution (1) weigh and powder 20 tablets. Transfer a quantity of the powder containing the equivalent of about 200 mg of mefloquine, accurately weighed, into a 100 mL volumetric flask. Add 70 mL of mobile phase and sonicate for about 10 minutes. Allow to cool to room temperature and make up to volume with mobile phase. Filter a portion of this solution, discarding the first few mL of the filtrate. For solution (2) dilute 5 mL of solution (1) to 50 mL with mobile phase. For solution (3) use 0.22 mg of mefloquine hydrochloride RS per mL. For solution (4) use about 0.22 mg of mefloquine hydrochloride RS and about 0.04 mg of sulfadoxine R 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 283 nm.

Inject 20 µL of solution (4). The assay is not valid unless the resolution between the two principal peaks is at least 5.

Inject alternately 20 µL each of solutions (2) and (3).

Measure the areas of the peaks responses obtained in the chromatograms from solutions (2) and (3) and calculate the content of mefloquine ($C_{17}H_{16}F_6N_2O$) in the tablets, using the declared content of mefloquine hydrochloride ($C_{17}H_{16}F_6N_2O,HCl$) in mefloquine hydrochloride RS. Each mg of mefloquine hydrochloride ($C_{17}H_{16}F_6N_2O,HCl$) is equivalent to 0.912 mg of mefloquine ($C_{17}H_{16}F_6N_2O$).

Impurities

The impurities limited by the requirements of this monograph include those listed in the monograph for Mefloquine hydrochloride.