Amodiaquine tablets (Amodiaquini compressi)

Category. Antimalarial.

Storage. Amodiaquine tablets should be kept in a well-closed container.

Labelling. The designation of the container of Amodiaquine 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 amodiaquine.

Additional information. Strengths in the current WHO Model list of essential medicines: 153 mg and 200 mg of amodiaquine. Strengths in the current WHO Model list of essential medicines for children: 153 mg and 200 mg of amodiaquine.

153 mg of amodiaquine is approximately equivalent to 200 mg of amodiaquine hydrochloride; 200 mg of amodiaquine is approximately equivalent to 260 mg of amodiaquine hydrochloride.

Requirements

Comply with the monograph for "Tablets".

Definition. Amodiaquine tablets contain Amodiaquine hydrochloride. They contain not less than 90.0% and not more than 110.0% of the amount of amodiaquine ($C_{20}H_{22}ClN_3O$) stated on the label.

Identity tests

• Either test A and E or any two of tests B, C and D together with test E may be applied.

A. Shake a quantity of powdered tablets containing the equivalent of about 50 mg of amodiaquine with 20 mL of water R and transfer to a separating funnel. Add 1 mL of ammonia (~260 g/l) TS and 25 mL of dichloromethane R and shake well. Let the layers separate and filter the dichloromethane extract through glass-fibre paper or a cotton plug previously washed and moistened with dichloromethane R. Evaporate the dichloromethane and dry the residue at 105°C for one hour. 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 amodiaquine hydrochloride RS, treated in the same way as the test substance, or with the *reference spectrum* of amodiaquine.

B. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography. Prepare a solution of chloroform saturated with ammonia by shaking chloroform R with ammonia (~260 g/l) TS and separate the chloroform layer (solution Chl). Use silica gel R5 as the coating substance and a mixture of 9 volumes of solution Chl, and 1 volume of dehydrated ethanol R as the mobile phase. Apply separately to the plate 10 µl of each of the following two solutions in solution Chl. For solution (A) shake vigorously a quantity of the powdered tablets containing the equivalent of about 0.15 g of amodiaquine with 10 mL of solution Chl for 2 minutes in a glass-stoppered test-tube, filter through a 0.45-µm filter and use the filtrate. For solution (B) shake vigorously 20 mg of amodiaquine hydrochloride RS per mL of solution Chl for 2 minutes in a glass stoppered test-tube, allow the precipitate formed to settle and use the clear supernatant. After removing the plate from the chromatographic chamber, allow it to dry in air or in a current of cool air and examine the chromatogram in daylight.

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

C. To a quantity of the powdered tablets containing the equivalent of about 30 mg of amodiaquine, add 100 mL of hydrochloric acid (~4 g/l) TS, shake, and filter. Dilute 5 mL of the filtrate to 100 mL with the same solvent. The absorption spectrum (1.6) of the resulting solution,, when observed between 300 nm and 400 nm, exhibits one maximum at about 342 nm.

D. 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 obtainedwith solution (2).

E. To a quantity of powdered tablets containing the equivalent of about 0.15 g of amodiaquine add 10 mL of water R, shake well, 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, 500 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 342 nm. At the same time measure the absorbance at the maximum at about 342 nm of a suitable solution of amodiaquine hydrochloride RS in hydrochloric acid (~4 g/l) TS using hydrochloric acid (~4 g/l) TS as the blank. Each mg of amodiaquine hydrochloride ($C_{20}H_{22}ClN_3O,2HCl,2H_2O$) is equivalent to 0.7656 mg of amodiaquine ($C_{20}H_{22}ClN_3O$).

For each of the six tablets tested, calculate the total amount of amodiaquine ($C_{20}H_{22}ClN_3O$) in the medium. The amount in solution for each tablet is not less than 80% of the amount declared on the label. If the amount obtained for one of the six tablets is less than 80%, repeat the test using a further six tablets; the average amount for all 12 tablets tested is not less than 75% and the amount obtained for no tablet is less than 60%.

Related substances

Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography. Prepare a solution of chloroform saturated with ammonia by shaking chloroform R with ammonia (~260 g/l) TS and separate the chloroform layer (solution Chl). Use silica gel R6 as the coating substance and a mixture of 9 volumes of solution Chl and 1 volume of dehydrated ethanol R as the mobile phase. Apply separately to the plate 10 µl of each of the following two solutions in solution Chl. For solution (A) shake a quantity of the powdered tablets containing the equivalent of 0.15 g of amodiaquine with 10 mL of solution Chl vigorously for 2 minutes in a glass-stoppered test-tube, filter through a 0.45-µm filter and use the filtrate. For solution (B) dilute 1.0 mL of solution A to 200 mL with solution Chl. After removing the plate from the chromatographic chamber, allow it to dry in air or in a current of cool air and examine the chromatogram in ultraviolet light (254 nm).

Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B (0.5%).

Assay

Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, using a stainless steel column (15 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 62 volumes of methanol R and 38 volumes of buffer pH 9.0 prepared as follows: dilute a mixture of 100 mL of potassium dihydrogen phosphate (13.6 g/l) TS and 1.4 mL of triethylamine R to 900 mL, adjust the pH to 9.0 by addition of potassium hydroxide (~55 g/l) TS and dilute to 1000 mL.

Prepare the following solutions in water R. For solution (1), weigh and powder 20 tablets. To a quantity of the powder containing the equivalent of about 115 mg of amodiaquine, accurately weighed, add 70 mL of water R and sonicate for about 15 minutes. Dilute to 100 mL. Filter a portion of this solution through a 0.45-µm filter, discarding the first few mL of the filtrate. Dilute 5 mL of the filtrate to 50 mL. For solution (2), use 0.15 mg of amodiaquine hydrochloride RS per mL. For solution (3) use 0.15 mg of amodiaquine hydrochloride RS and 0.15 mg of chloroquine sulfate 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 254 nm.

Inject 20 µl of solution (3). The assay is not valid unless the resolution between the two principal peaks is at least 3.5.

Inject alternately 20 µl each of solutions (1) and (2).

Measure the areas of the peak responses in the chromatograms obtained with solutions (1) and (2) and calculate the content of amodiaquine ($C_{20}H_{22}ClN_3O$) in the tablets, using the declared content of amodiaquine hydrochloride ($C_{20}H_{22}ClN_3O,2HCl,2H_2O$) in amodiaquine hydrochloride RS. Each mg of $C_{20}H_{22}ClN_3O,2HCL,2H_2O$ is equivalent to 0.7656 mg of $C_{20}H_{22}ClN_3O$.