Amoxicillin powder for oral suspension (Amoxicillini pulvis pro suspensione perorali)

Category. Antibacterial.

Storage. The oral suspension should be stored in a tightly closed container at the temperature stated on the label and used within the period stated on the label.

The powder should be kept in a tightly closed container.

Labelling. The designation on the container of Amoxicillin oral suspension states that amoxicillin is in the trihydrate form and the quantity should be indicated in terms of equivalent amount of amoxicillin.

Additional information. Strengths in the current WHO Model list of essential medicines: 125 mg per 5 mL (25 mg per mL), 250 mg per 5 mL (50 mg per mL).

Requirements

Complies with the monograph for "Liquid preparations for oral use"; the powder complies with the section of the monograph entitled *"Powders for oral solutions, oral suspensions and oral drops"*.

Definition. Amoxicillin powder for oral suspension is a suspension of Amoxicillin trihydrate in a suitable vehicle which may be flavoured. It is prepared from the powder as stated on the label just before issue for use. When freshly constituted the oral suspension contains not less than 90.0% and not more than 120.0% of the amount of amoxicillin ($C_{16}H_{19}N_3O_5S$) stated on the label.

Manufacture. The product is formulated in such a way that when the suspension is constituted following manufacturer's instructions, stored at the temperature for the in-use period stated on the label and assayed using the method described below under Assay, it contains not less than 80.0% of the amount of amoxicillin ($C_{16}H_{19}N_3O_5S$) stated on the label.

The manufacturing process and the product packaging are designed and controlled so as to minimize the moisture content of the powder. They ensure that, if tested, the powder would comply with a water limit of not more than 30 mg/g when determined as described under 2.8 Determination of water by the Karl Fischer method, Method A, using 0.5 g of the powder.

Identity tests

A. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using a silica gel as the coating substance and a mixture of 10 volumes of acetone R and 90 volumes of a solution of ammonium acetate (~154 g/l) TS adjusted to pH 5.0 with glacial acetic acid R as the mobile phase. Apply separately to the plate 1 µl of each of the following solutions. For solution (A) dilute a quantity of the oral suspension in sufficient sodium hydrogen carbonate solution (40 g/l) TS to produce a solution containing the equivalent of 2.5 mg of amoxicillin per mL. For solution (B) use 2.9 mg of amoxicillin trihydrate RS per mL of sodium hydrogen carbonate solution (42 g/l) TS. For solution (C) use 2.9 mg of amoxicillin trihydrate RS and 2.9 mg of ampicillin trihydrate R per mL of sodium hydrogen carbonate solution (42 g/l) TS. After removing the plate from the chromatographic chamber, allow it to dry in a current of air. Expose the plate to iodine vapour until spots appear and examine the chromatogram in daylight.

The principal spot obtained with solution A corresponds in position, appearance and intensity with that obtained with solution B. The test is not valid unless the chromatogram obtained with solution C shows two clearly separated spots.

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

pH value (*1.13*). pH of the oral suspension, 4.0–7.5.

Assay

Use the oral suspension immediately after preparation. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, using a stainless steel column (25 cm × 4.6 mm) packed with base-deactivated 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 8 volumes of mobile phase B and 92 volumes of mobile phase A as described below.

Mobile phase A. Mix 1 volume of acetonitrile R and 99 volumes of a 250 g/l solution of potassium dihydrogen phosphate (27.2 g/l) TS adjusted to pH 5.0 with sodium hydroxide (~80 g/l) TS.

Mobile phase B. Mix 20 volumes of acetonitrile R and 80 volumes of a 250 g/l solution of potassium dihydrogen phosphate (27.2 g/l) adjusted to pH 5.0 with sodium hydroxide (~80 g/l) TS.

Prepare the following solutions. For solution (1) dilute an accurately weighed quantity of the oral suspension, containing the

equivalent of 60 mg of amoxicillin, with sufficient mobile phase A to produce 100 mL, mix and filter. For solution (2) use 0.70 mg of amoxicillin trihydrate RS per mL of mobile phase A. For solution (3) use 0.004 mg of cefadroxil R and 0.03 mg of amoxicillin trihydrate RS per mL of mobile phase A.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 254 nm.

Inject separately 50 µl each of solution (1), (2) and (3).

In the chromatogram obtained with solution (3) the following peak is eluted at the following relative retention, with reference to cefadroxil (retention time about 10 minutes): amoxicillin about 0.85. The test is not valid unless, in the chromatogram obtained with solution (3), the resolution factor between the peaks due to amoxicillin and cefadroxil is at least 2.0. If necessary, adjust the composition of the mobile phase to achieve the required resolution.

Measure the areas of the peak responses obtained in the chromatograms from solution (1) and (2).

Determine the weight per mL (1.3.1) of the oral suspension and calculate the content of amoxicillin ($C_{16}H_{19}N_3O_5S$), weight in volume in the oral suspension using the declared content of amoxicillin trihydrate ($C_{16}H_{19}N_3O_5S,3H_2O$) in amoxicillin trihydrate RS.

Each mg of $C_{16}H_{19}N_3O_5S,3H_2O$ is equivalent to 0.8711 mg of $C_{16}H_{19}N_3O_5S$.