Phenytoin sodium tablets (Phenytoini natrici compressi)

Category. Antiepileptic drug.

Additional information. Strength in the current WHO Model list of essential medicines: 25mg, 50mg, 100mg.

Requirements

Comply with the monograph for "Tablets".

Phenytoin sodium tablets contain not less than **90.0%** and not more than **110.0%** of the amount of $C_{15}H_{11}N_2NaO_2$ stated on the label.

Identity tests

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

To a quantity of the powdered tablets equivalent to about 0.1g of Phenytoin sodium add 20ml of water, shake, and filter. Acidify the filtrate with hydrochloric acid (~70g/l) TS and extract with chloroform R. Wash the chloroform extract with water, dry with anhydrous sodium sulfate R, and evaporate to dryness. Use the residue for tests A and B.

A. 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 phenytoin RS or with the *reference spectrum* of phenytoin.

B. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R4 as the coating substance and a mixture of 9 volumes of chloroform R and 1 volume of acetone R as the mobile phase. Apply separately to the plate 10 µl of each of the following 2 solutions in chloroform R. For solution (A) use 1mg of the residue per mL. For solution (B) use 1mg of phenytoin RS per mL. After removing the plate from the chromatographic chamber, allow it to dry, and examine the chromatogram in ultraviolet light (254nm).

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

C. To a quantity of the powdered tablets equivalent to about 40mg of Phenytoin sodium add 2.0ml of ammonia (~100g/l) TS and heat until boiling begins. Add 1 drop of copper(II) sulfate (160g/l) TS and shake; a blue-violet solution with a blue-green precipitate is produced. Allow to stand for 3 minutes, filter, and wash with water; pink needles remain on the filter.

D. To a quantity of the powdered tablets equivalent to about 40mg of Phenytoin sodium add 5ml of water, shake, and filter. The filtrate yields reaction B described under 2.1 General identification tests as characteristic of sodium.

Benzophenone. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R4 as the coating substance and a mixture of 75 volumes of hexane R and 30 volumes of dioxan R as the mobile phase. Apply separately to the plate 5 µl of each of the following 2 solutions. For solution (A) shake a quantity of the powdered tablets equivalent to about 0.1g of Phenytoin sodium with 5ml of methanol R, warm on a water-bath while shaking, filter, and use the filtrate. For solution (B) use 0.10mg of benzophenone R per mL of methanol R. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254nm).

Any spot corresponding to benzophenone obtained with solution A is not more intense than that obtained with solution B.

Assay. Weigh and powder 20 tablets. Transfer to a separatory funnel a quantity of the powdered tablets equivalent to about 0.3g of Phenytoin sodium, add 25ml of water, and shake. Add 50ml of ether R, shake, and add 10 drops of bromophenol blue/ethanol TS. Titrate with hydrochloric acid (0.1mol/l) VS, shaking vigorously, until the colour of the aqueous layer turns to bluish-grey. Transfer the aqueous layer to a stoppered conical flask. Wash the ether layer with 5ml of water and combine the washing with the aqueous layer in the conical flask. Add 20ml of ether R and continue the titration with hydrochloric acid (0.1mol/l) VS, shaking vigorously, until the colour of the aqueous layer turns to pale green.

Each mL of hydrochloric acid (0.1mol/l) VS is equivalent to 27.43mg of $C_{15}H_{11}N_2NaO_2$.

Dissolution. Carry out the test as described under 5.5 Dissolution test for solid oral dosage forms.