Chlorphenamine hydrogen maleate (Chlorphenamini hydrogenomaleas)

Molecular formula. $C_{16}H_{19}ClN_2C_4H_4O_4$ or $C_{20}H_{23}ClN_2O_4$

Relative molecular mass. 390.9

Graphic formula.

Chemical name. 2-[p-Chloro-α-[2-(dimethylamino)ethyl]benzyl]pyridine maleate (1:1); γ-(4-chlorophenyl)-N,N-dimethyl-2-pyridinepropanamine (Z)-2-butenedioate (1:1); CAS Reg. No. 113-92-8.

Other name. Chlorpheniramine hydrogen maleate.

Description. A white, crystalline powder; odourless.

Solubility. Soluble in 4 parts of water; soluble in ethanol (~750 g/l) TS; slightly soluble in ether R.

Category. Antihistaminic.

Storage. Chlorphenamine hydrogen maleate should be kept in a tightly closed container, protected from light.

Additional information. Even in the absence of light, Chlorphenamine hydrogen maleate is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperatures.

Requirements

Definition. Chlorphenamine hydrogen maleate contains not less than 98.0% and not more than 101.0% of $C_{16}H_{19}ClN_2C_4H_4O_4$, calculated with reference to the dried substance.

Identity tests

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

  A. 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 chlorphenamine hydrogen maleate RS or with the reference spectrum of chlorphenamine hydrogen maleate.

  B. Dissolve 1 mg in 5 mL of water. To 1 mL of this solution add 1 mL of buffer phthalate, pH 3.5, TS and 1 mL of cyanogen bromide TS. Allow to stand for 10 minutes with intermittent, gentle shaking. Add 2 mL of a solution composed of 1 mL of aniline R diluted to 25 mL with dichloroethane R, and shake; an orange-yellow colour is produced in the lower layer.

  C. Dissolve 0.5 g in 5 mL of water, add 0.2 mL of sulfuric acid (~100 g/l) TS and extract 4 times with ether R, using 25 mL each time. Combine the ethereal extracts, dry them over anhydrous sodium sulfate R, filter, and evaporate the filtrate in a current of warm air; melting temperature of the residue, about 132°C (maleic acid).

Sulfated ash. Not more than 1.5 mg/g.

Loss on drying. Dry to constant weight at 105°C; it loses not more than 5.0 mg/g.

pH value. pH of a 20 mg/mL solution, 4.0-5.2.

Related substances. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R2 as the coating substance and a mixture of 5 volumes of ethyl acetate R, 3 volumes of methanol R, and 2 volumes of acetic acid (~60 g/l) TS as the mobile phase. Apply separately to the plate 2 μl of each of 2 solutions in chloroform R containing (A) 50 mg of the test substance per mL and (B) 0.10 mg of the test substance per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254 nm). Any spot obtained with solution A, other than the two principal spots due to chlorphenamine and maleic acid, is not more intense than that obtained with solution B.

Assay. Dissolve about 0.4 g, accurately weighed, in 30 mL of glacial acetic acid R1, and titrate with perchloric acid (0.1 mol/l) VS as described under 2.6 Non-aqueous titration. Method A. Each mL of perchloric acid (0.1 mol/l) VS is equivalent to 19.54 mg of $C_{16}H_{19}ClN_2C_4H_4O_4$. 

Additional requirements for Chlorphenamine hydrogen maleate for parenteral use
Complies with the monograph for "Parenteral preparations".

**Bacterial endotoxins.** Carry out the test as described under [3.4 Test for bacterial endotoxins](#); contains not more than 8.8 IU of endotoxin RS per mg.