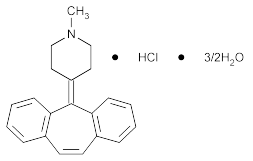
Cyproheptadine Hydrochloride



$C_{21}H_{21}N \cdot HCl \cdot 1^1/_2H_2O$ 350.88
Piperidine, 4-(5*H*-dibenzo[*a*,*d*]cycloheptен-5-ylidene)-1-methyl-, hydrochloride, sesquihydrate.
4-(5*H*-Dibenzo[*a*,*d*]cycloheptен-5-ylidene)-1-methylpiperidine hydrochloride sesquihydrate [41354-29-4].
Anhydrous 323.87 [969-33-5].

» Cyproheptadine Hydrochloride contains not less than 98.5 per cent and not more than 100.5 percent of $C_{21}H_{21}N \cdot HCl$, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Cyproheptadine Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 16 µg per mL.

Medium: alcohol.

Absorptivities at 286 nm do not differ by more than 3.0%.

C: Dissolve 100 mg of Cyproheptadine Hydrochloride in 10 mL of methanol. Place 1 drop of the solution on a filter paper, dry, and view under short-wavelength UV light: a bright blue fluorescence is observed.

Acidity—Dissolve 1.0 g of Cyproheptadine Hydrochloride in 25 mL of methanol, add methyl red TS, and titrate with 0.10 N sodium hydroxide: not more than 0.15 mL is required (0.05% as HCl).

Water, *Method I* ⟨921⟩**:** between 7.0% and 9.0%.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Heavy metals, *Method II* ⟨231⟩**:** 0.003%.

Assay—Dissolve about 650 mg of Cyproheptadine Hydrochloride, accurately weighed, in 50 mL of glacial acetic acid, heating to dissolve. Cool, add 10 mL of mercuric acetate TS, 0.5 mL of acetic anhydride, and 1 drop of crystal violet TS, and titrate with 0.1 N perchloric acid VS to a green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 32.39 mg of $C_{21}H_{21}N \cdot HCl$.

Cyproheptadine Hydrochloride Oral Solution

» Cyproheptadine Hydrochloride Oral Solution contains not less than 90.0 per cent and not more than 110.0 per cent of the labeled amount of cyproheptadine hydrochloride ($C_{21}H_{21}N \cdot HCl$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩**—**
USP Cyproheptadine Hydrochloride RS

Identification—Place about 50 mL of Oral Solution in a separator, add 25 mL of sodium bicarbonate solution (2 in 100), and extract with three 15-mL portions of isooctane. Wash the combined isooctane extracts with 15 mL of sodium bicarbonate solution (2 in 100), and discard the washing. Evaporate the isooctane solution on a steam bath to dryness, and dissolve the residue in 1 mL of carbon disulfide, filtering if necessary. Determine the IR absorption spectrum as directed under *Identification—Organic Nitrogenous Bases* ⟨181⟩, obtaining the spectrum of USP Cyproheptadine Hydrochloride RS as directed: the Oral Solution meets the requirements of the test.

pH ⟨791⟩: between 3.5 and 4.5.

Assay—

Methanesulfonic acid solution, *Mobile phase*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Cyproheptadine Hydrochloride Tablets*.

Standard preparation—Dissolve an accurately weighed quantity of USP Cyproheptadine Hydrochloride RS in *Mobile phase* to obtain a solution having a known concentration of about 0.02 mg per mL.

Assay preparation—Transfer an accurately measured volume of Oral Solution, equivalent to about 2 mg of cyproheptadine hydrochloride, to a 100-mL volumetric flask. Dilute with *Mobile phase* to volume, and mix. Pass the solution through a filter having a 0.45-µm or finer porosity.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of cyproheptadine hydrochloride ($C_{21}H_{21}N \cdot HCl$) in the portion of Oral Solution taken by the formula:

$$100C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Cyproheptadine Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the cyproheptadine peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Cyproheptadine Hydrochloride Tablets

» Cyproheptadine Hydrochloride Tablets contain not less than 90.0 per cent and not more than 110.0 percent of the labeled amount of $C_{21}H_{21}N \cdot HCl$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Cyproheptadine Hydrochloride RS

Identification—Tablets meet the requirements under *Identification—Organic Nitrogenous Bases* ⟨181⟩.

Dissolution ⟨711⟩**—**

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{21}H_{21}N \cdot HCl$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 285 nm on filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Cyproheptadine Hydrochloride RS in the same *Medium*.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{21}H_{21}N \cdot HCl$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Methanesulfonic acid solution—Prepare a solution of methanesulfonic acid in water (3:1000).