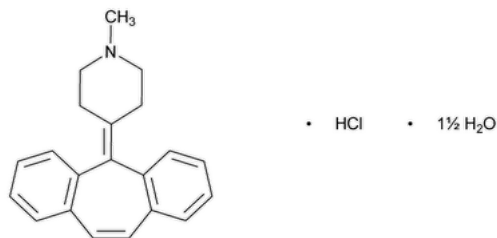


Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-0C234B5A-5341-4053-A621-C0CE55A2F6A3_4_en-US
DOI: https://doi.org/10.31003/USPNF_M21670_04_01
DOI Ref: s8mub

© 2025 USPC
Do not distribute

Cyproheptadine Hydrochloride



$C_{21}H_{21}N \cdot HCl \cdot 1\frac{1}{2}H_2O$ 350.88
 $C_{21}H_{21}N \cdot HCl$ 323.87
Piperidine, 4-(5H-dibenzo[a,d]cyclohepten-5-ylidene)-1-methyl-, hydrochloride, sesquihydrate;
4-(5H-Dibenzo[a,d]cyclohepten-5-ylidene)-1-methylpiperidine hydrochloride sesquihydrate CAS RN®: 41354-29-4; UNII: NJ82J0F8QC.
Anhydrous CAS RN®: 969-33-5; UNII: 0S9323MCT0.

DEFINITION
Cyproheptadine Hydrochloride contains NLT 98.0% and NMT 102.0% of cyproheptadine hydrochloride ($C_{21}H_{21}N \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#) ▲ (CN 1-MAY-2020)
- **B.** The retention time of the cyproheptadine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• **PROCEDURE**

Solution A: 1 mL/L of [trifluoroacetic acid](#) in [water](#)
Solution B: [Acetonitrile](#) and *Solution A* (38:62)
Solution C: [Acetonitrile](#)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution B (%)	Solution C (%)
0.0	100	0
6.0	100	0
6.1	15	85
9.0	15	85
9.1	100	0
12	100	0

Diluent: [Acetonitrile](#) and [water](#) (38:62)
Standard solution: 40 µg/mL of [USP Cyproheptadine Hydrochloride RS](#) in *Diluent*. Sonication may be used to aid dissolution.
Sample solution: 40 µg/mL of Cyproheptadine Hydrochloride in *Diluent*. Sonication may be used to aid dissolution.
Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 266 nm

Column: 4.6-mm × 15-cm; 2.7-μm packing [L60](#)

Flow rate: 1 mL/min

Injection volume: 15 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cyproheptadine hydrochloride ($C_{21}H_{21}N \cdot HCl$) in the portion of Cyproheptadine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Cyproheptadine Hydrochloride RS](#) in the *Standard solution* (μg/mL)

C_U = concentration of Cyproheptadine Hydrochloride in the *Sample solution* (μg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• ORGANIC IMPURITIES

Solution A, Solution B, Solution C, Mobile phase, Diluent, and Chromatographic system: Proceed as directed in the Assay.

Standard stock solution: 50 μg/mL each of [USP Cyproheptadine Hydrochloride RS](#), [USP Cyproheptadine Related Compound A RS](#), [USP Amitriptyline Related Compound A RS](#), and [USP Cyproheptadine Related Compound C RS](#), prepared as follows. Transfer a suitable quantity of each Reference Standard to an appropriate volumetric flask. Add 38% of the total flask volume of [acetonitrile](#) to dissolve, and then dilute with [water](#) to volume.

Standard solution: 0.75 μg/mL each of [USP Cyproheptadine Hydrochloride RS](#), [USP Cyproheptadine Related Compound A RS](#), [USP Amitriptyline Related Compound A RS](#), and [USP Cyproheptadine Related Compound C RS](#) from the *Standard stock solution* in *Diluent*

Sensitivity solution: 0.25 μg/mL each of [USP Cyproheptadine Hydrochloride RS](#), [USP Cyproheptadine Related Compound A RS](#), [USP Amitriptyline Related Compound A RS](#), and [USP Cyproheptadine Related Compound C RS](#) from the *Standard stock solution* in *Diluent*

Sample solution: 500 μg/mL of Cyproheptadine Hydrochloride in *Diluent*. Sonication may be used to aid dissolution.

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[NOTE—See [Table 2](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between amitriptyline related compound A and cyproheptadine related compound A, *Standard solution*

Relative standard deviation: NMT 5.0% for cyproheptadine, cyproheptadine related compound A, amitriptyline related compound A, and cyproheptadine related compound C, *Standard solution*

Signal-to-noise ratio: NLT 10 for cyproheptadine hydrochloride, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cyproheptadine related compound A, amitriptyline related compound A, and cyproheptadine related compound C in the portion of Cyproheptadine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each related compound from the *Sample solution*

r_S = peak response of each related compound from the *Standard solution*

C_S = concentration of the appropriate USP Reference Standard in the *Standard solution* (μg/mL)

C_U = concentration of Cyproheptadine Hydrochloride in the *Sample solution* (μg/mL)

Calculate the percentage of any individual unknown impurity in the portion of Cyproheptadine Hydrochloride taken: