Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Jan-2020
Document Type: USP Monographs
DocId: GUID-4EA641D5-79DD-4B38-9F76-30523199B95B_4_en-US
DOI: https://doi.org/10.31003/USPNF_M21700_04_01
DOI Ref: cfi0v

Cyproheptadine Hydrochloride Oral Solution

DEFINITION

Cyproheptadine Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of cyproheptadine hydrochloride ($C_{21}H_{21}N \cdot HCl$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major 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: Nominally 40 µg/mL of cyproheptadine hydrochloride from Oral Solution in *Diluent* prepared as follows. Transfer an appropriate volume of Oral Solution to a suitable volumetric flask and dilute with *Diluent* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 266 nm. For *Identification B*, use a diode array detector in the range of 210–400 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 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cyproheptadine hydrochloride ($C_{21}H_{21}N \cdot HCl$) in the portion of Oral Solution 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 = nominal concentration of cyproheptadine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

• **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: 0.6 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*▲ (ERR 1-Jan-2020)

Sample solution: Oral Solution

System suitability

Sample: *Standard 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

Relative standard deviation: NMT 5.0% for cyproheptadine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual unspecified degradation product in the portion of Oral Solution taken:

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

r_U = peak response of any individual unspecified degradation product from the *Sample solution*

r_S = peak response of cyproheptadine hydrochloride from the *Standard solution*

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

C_U = nominal concentration of cyproheptadine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.10%.

Table 2

[a] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance and are not to be reported or included in the total impurities for the drug product.

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 3.5–4.5

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cyproheptadine related compound C[a]	0.7	—
Cyproheptadine	1.0	—
Amitriptyline related compound A[a]	2.5	—
Cyproheptadine related compound A[a]	2.6	—
Any individual unspecified degradation product	—	0.20
Total degradation products	—	0.5

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Amitriptyline Related Compound A RS

Dibenzosuberone.

$C_{15}H_{12}O$ 208.26

USP Cyproheptadine Hydrochloride RS

USP Cyproheptadine Related Compound A RS

5*H*-Dibenzo[*a*,*d*]cycloheptene.

$C_{15}H_{12}$ 192.26

USP Cyproheptadine Related Compound C RS

5-(1-Methyl-piperidin-4-yl)-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol.

$C_{21}H_{23}NO$ 305.41

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
CYPROHEPTADINE HYDROCHLORIDE ORAL SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(3)

Current DocID: GUID-4EA641D5-79DD-4B38-9F76-30523199B95B_4_en-US

DOI: https://doi.org/10.31003/USPNF_M21700_04_01

DOI ref: cfi0v