

Status: Currently Official on 14-Feb-2025

Official Date: Official as of 01-May-2020

Document Type: USP Monographs

DocId: GUID-66B3EF7A-4395-4BAB-8410-DCB2CC7089F4_5_en-US

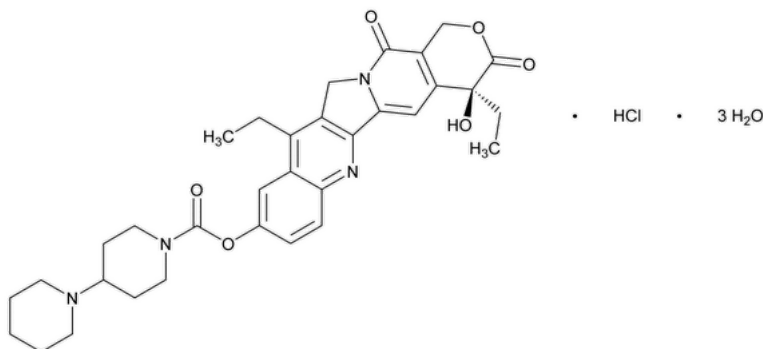
DOI: https://doi.org/10.31003/USPNF_M42485_05_01

DOI Ref: h5pva

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Irinotecan Hydrochloride

 $C_{33}H_{38}N_4O_6 \cdot HCl \cdot 3H_2O$

Anhydrous: 623.14

Trihydrate: 677.18

[1,4'-Bipiperidine]-1'-carboxylic acid, 4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride, trihydrate, (S)-;

(+)-7-Ethyl-10-hydroxycamptothecin 10-[1,4'-bipiperidine]-1'-carboxylate, monohydrochloride, trihydrate CAS RN®: 136572-09-3; UNII: 042LAQ1IIS.

DEFINITION

Irinotecan Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{33}H_{38}N_4O_6 \cdot HCl$, 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 major peak of the *Sample solution* corresponds to the irinotecan (S-enantiomer) peak in the *Identification solution*, as obtained in the test for *Limit of Irinotecan Hydrochloride Enantiomer*.
- **C.** [IDENTIFICATION TESTS—GENERAL, Chloride \(191\)](#): A 2-mg/mL solution meets the requirements of the tests.

ASSAY

PROCEDURE

Solution A: 2.8 g/L of monobasic sodium phosphate monohydrate and 1.8 g/L of 1-octanesulfonic acid sodium salt monohydrate in water

Mobile phase: Acetonitrile, methanol, and *Solution A* (17:24:59)

Diluent: Use *Mobile phase* adjusted with diluted hydrochloric acid to a pH of 3.65 ± 0.15 .

Standard solution: 1 mg/mL of [USP Irinotecan Hydrochloride RS](#) in *Diluent*

Sample solution: 1 mg/mL of Irinotecan Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 255 nm

Column: 4.6-mm × 25-cm; 5-μm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection size: 15 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of irinotecan hydrochloride ($C_{33}H_{38}N_4O_6 \cdot HCl$) in the portion of Irinotecan Hydrochloride taken.

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

C_U = concentration of Irinotecan Hydrochloride in the *Sample solution* (mg/mL)

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

IMPURITIES

- **RESIDUE ON IGNITION (281):** NMT 0.1%

- **LIMIT OF IRINOTECAN HYDROCHLORIDE ENANTIOMER**

Mobile phase: Hexane, dehydrated alcohol, and diethylamine (250:250:1)

Diluent: Dehydrated alcohol and diethylamine (250:1)

System suitability solution: 0.1 mg/mL each of [USP Irinotecan Hydrochloride RS](#) and [USP Irinotecan Related Compound D RS](#) in *Diluent*

Identification solution: 1 mg/mL of [USP Irinotecan Hydrochloride RS](#) in *Diluent*. [NOTE—This solution is used for *Identification test B*.]

Standard solution: 1.5 µg/mL of [USP Irinotecan Related Compound D RS](#) in *Diluent*

Sensitivity solution: 0.5 µg/mL of [USP Irinotecan Related Compound D RS](#) in *Diluent*, from the *Standard solution*

Sample solution: 1 mg/mL of Irinotecan Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 370 nm

Column: 4.6-mm × 25-cm; 10-µm packing L40

Flow rate: 1.0 mL/min

Injection size: 20 µL

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

[NOTE—The relative retention times for irinotecan related compound D (*R*-enantiomer) and irinotecan (*S*-enantiomer) are 0.7 and 1.00, respectively.]

Suitability requirements

Resolution: NLT 2.5 between irinotecan related compound D and irinotecan, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Sensitivity: The irinotecan related compound D peak should be visible, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of irinotecan hydrochloride *R*-enantiomer in the portion of Irinotecan Hydrochloride taken:

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

r_U = peak area of irinotecan related compound D from the *Sample solution*

r_S = peak area of irinotecan related compound D from the *Standard solution*

C_S = concentration of [USP Irinotecan Related Compound D RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Irinotecan Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria

***R*-enantiomer:** NMT 0.15%

[NOTE—On the basis of the synthetic route, perform either *Organic Impurities Procedure 1* or *Organic Impurities Procedure 2*.]

- **ORGANIC IMPURITIES PROCEDURE 1 (FOR MATERIAL LABELED AS PRODUCED BY A SYNTHETIC PROCESS)**

Mobile phase, Diluent, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

System suitability stock solution: 0.01 mg/mL each of [USP Irinotecan Related Compound B RS](#) and [USP Irinotecan Related Compound C RS](#) in methanol

System suitability solution: 1.0 µg/mL each of [USP Irinotecan Related Compound B RS](#) and [USP Irinotecan Related Compound C RS](#) in *Diluent*, from *System suitability stock solution*

Standard solution: 2.0 µg/mL of [USP Irinotecan Hydrochloride RS](#) in *Diluent*

Sensitivity solution: 0.5 µg/mL of [USP Irinotecan Hydrochloride RS](#) in *Diluent*

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

Suitability requirements