Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Sep-2022
Document Type: USP Monographs
DocId: GUID-D5E569FD-6848-4E35-A5A3-B492E5BC6B50_5_en-US
DOI: https://doi.org/10.31003/USPNF_M42489_05_01
DOI Ref: 6ph6q

Irinotecan Hydrochloride Injection

Change to read:

DEFINITION

Irinotecan Hydrochloride Injection is a sterile solution of Irinotecan Hydrochloride in Water for Injection. It contains ▲NLT▲ (ERR 1-Sep-2022) 90.0% and NMT 110.0% of the labeled amount of irinotecan hydrochloride ($C_{33}H_{38}N_4O_6 \cdot HCl \cdot 3H_2O$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

  Sample solution: 4 µg/mL

  Medium: Methanol

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

  Buffer: Dissolve 2 g of sodium 1-hexanesulfonate and 2 mL of triethylamine in 1 L of water.

  Mobile phase: Acetonitrile and *Buffer* (34:66). Adjust with phosphoric acid to a pH of 2.5.

  Standard solution: 0.04 mg/mL of USP Irinotecan Hydrochloride RS in *Mobile phase*. Sonication and shaking may be used to aid dissolution.

  Sample solution: 0.04 mg/mL of irinotecan hydrochloride in *Mobile phase* from Injection

  Chromatographic system

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

  Mode: LC

  Detector: UV 254 nm

  Column: 4.6-mm × 25-cm; 5-µm packing L7

  Flow rate: 1 mL/min

  Injection volume: 10 µL

  System suitability

  Sample: *Standard solution*

  Suitability requirements

  Tailing factor: NMT 2.5

  Relative standard deviation: NMT 1.0%

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of irinotecan hydrochloride ($C_{33}H_{38}N_4O_6 \cdot HCl \cdot 3H_2O$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

  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 = nominal concentration of irinotecan hydrochloride in the *Sample solution* (mg/mL)

  M_{r1} = molecular weight of irinotecan hydrochloride ($C_{33}H_{38}N_4O_6 \cdot HCl \cdot 3H_2O$), 677.18

  M_{r2} = molecular weight of irinotecan hydrochloride, anhydrous ($C_{33}H_{38}N_4O_6 \cdot HCl$), 623.14

  Acceptance criteria: 90.0%–110.0%

IMPURITIES

- **Organic Impurities**

  Solution A: Dissolve 2 g of sodium 1-hexanesulfonate and 1 mL of triethylamine in 1 L of water. Adjust with phosphoric acid to a pH of 2.5.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
20	80	20
50	65	35
63	50	50
64	80	20
70	80	20

Diluent: Acetonitrile, phosphoric acid, and *Solution A* (500:15:500)

System suitability solution: 0.2 mg/mL of USP Irinotecan Hydrochloride RS and 0.4 µg/mL of irinotecan related compound E in *Diluent*, added stepwise, if necessary. Sonication may be used to aid dissolution.

Sample solution: 0.2 mg/mL of irinotecan hydrochloride in *Diluent* from Injection

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 1 mL/min

Temperatures

Column: 55°

Sample: 15°

Injection volume: 25 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 4.0 between irinotecan and irinotecan related compound E

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Irinotecan Hydrochloride Injection taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak area of each impurity from the *Sample solution*

r_T = sum of the peak areas from the *Sample solution*

F = relative response factor for each individual impurity (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Irinotecan related compound B[a]	0.53	0.74	0.2
Camptothecin[b,d]	0.65	—	—
Irinotecan	1.00	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
7-Ethylcamptothecin[c,d]	1.16	—	—
Any unspecified impurity	—	1.0	0.2
Total impurities	—	—	1.0

[a] (*S*)-4,11-Diethyl-4,9-dihydroxy-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*,12*H*)-dione.

[b] (*S*)-4-Ethyl-4-hydroxy-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*,12*H*)-dione. It is a process impurity and is controlled in the API monograph.

[c] Irinotecan related compound E. It is a process impurity and is controlled in the API monograph.

[d] These process impurities are included in the table for identification only and are not included in the *Total impurities*.

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.83 USP Endotoxin Units/mg of irinotecan hydrochloride

• **Sterility Tests ⟨71⟩:** Meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined*, *Membrane Filtration*

• **pH ⟨791⟩:** 3.0–3.8

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections

• **Other Requirements:** Meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose vials, protected from light. Store at controlled room temperature.

• **Labeling:** Label it to indicate that it is to be diluted with either 5% dextrose solution (USP) or 0.9% Sodium Chloride Injection (USP) prior to intravenous infusion.

• **USP Reference Standards ⟨11⟩**

USP Irinotecan Hydrochloride RS

USP Irinotecan Related Compound E RS

(*S*)-4,11-Diethyl-4-hydroxy-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*,12*H*)-dione.

$C_{22}H_{20}N_2O_4$ 376.41

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

Topic/Question	Contact	Expert Committee
IRINOTECAN HYDROCHLORIDE INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 38(2)

Current DocID: GUID-D5E569FD-6848-4E35-A5A3-B492E5BC6B50_5_en-US

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