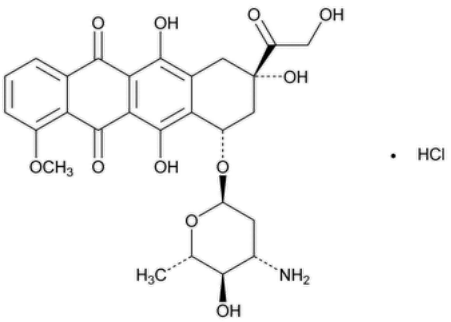
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-94FF5724-CF3C-498C-8A86-2C622B82F83D_4_en-US
DOI: https://doi.org/10.31003/USPNF_M29694_04_01
DOI Ref: 2v1fv

Epirubicin Hydrochloride



$C_{27}H_{29}NO_{11} \cdot HCl$ 579.98

5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-α-L-*arabino*-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, hydrochloride, (8*S*-*cis*)-;
(1*S*,3*S*)-3-Glycoloyl-1,2,3,4,6,11-hexahydro-3,5,12-trihydroxy-10-methoxy-6,11-dioxo-1-naphthacenyl-3-amino-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside hydrochloride CAS RN®: 56390-09-1; UNII: 22966TX7J5.

DEFINITION

Epirubicin Hydrochloride contains NLT 97.0% and NMT 102.0% of epirubicin hydrochloride ($C_{27}H_{29}NO_{11} \cdot HCl$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.
- **C.** **Identification Tests—General, *Chloride*⟨191⟩**

Solution A: Nitric acid and water (1:1)

Sample solution: 10 mg/mL in *Solution A*

Acceptance criteria: Meets the requirements

ASSAY

- **Procedure**

Allow the *System suitability solution*, *Standard solution*, and *Sample solution* to stand for 3 h before use.

Solution A: Dilute 10 mL of phosphoric acid with water to 100 mL.

Solution B:

Dissolve 3.7 g of sodium lauryl sulfate in 950 mL of water. To the resulting solution, add 28 mL of *Solution A*, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile, methanol, and *Solution B* (29:17:54)

System suitability solution: 0.1 mg/mL each of USP Epirubicin Hydrochloride RS and USP Doxorubicin Hydrochloride RS in *Mobile phase*

Standard solution: 1 mg/mL of USP Epirubicin Hydrochloride RS in *Mobile phase*

Sample solution: 1 mg/mL of Epirubicin Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L13

Column temperature: 35°

Flow rate: 2.5 mL/min

Injection volume: 10 µL

Run time: About 3.5 times the retention time of the epirubicin peak

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.0 between doxorubicin and epirubicin

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of epirubicin hydrochloride ($C_{27}H_{29}NO_{11} \cdot HCl$) in the portion of Epirubicin Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

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

P = potency of epirubicin hydrochloride in USP Epirubicin Hydrochloride RS (mg/mg)

Acceptance criteria: 97.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• **Organic Impurities**

Allow the *System suitability solution*, *Sample solution*, and *Standard solution* to stand for 3 h before use.

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

Standard solution: 0.01 mg/mL of USP Epirubicin Hydrochloride RS in *Mobile phase*

Peak identification solution: Dissolve 10 mg of USP Doxorubicin Hydrochloride RS in 10 mL of a mixture of water and phosphoric acid (1:1). Allow to stand for 30 min. Adjust with 2 N sodium hydroxide solution to a pH of 2.6. Add 15 mL of acetonitrile and 10 mL of methanol, and mix.

Analysis

Samples: *Sample solution*, *Standard solution*, and *Peak identification solution*

[Note—Use the *Peak identification solution* to identify the doxorubicinone peak.]

Calculate the percentage of each impurity in the portion of Epirubicin Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times (1/F) \times 100$$

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

r_S = peak response of epirubicin from the *Standard solution*

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

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

P = potency of epirubicin hydrochloride in USP Epirubicin Hydrochloride RS (mg/mg)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05% of the area of the epirubicin peak in the *Standard solution*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Doxorubicinone[a]	0.3	1.4	1.0
Daunorubicinone[b]	0.4	1.0	0.5
Doxorubicin	0.8	1.0	1.0
Epirubicin	1.0	—	—
Dihydro daunorubicin[c]	1.1	1.0	0.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Daunorubicin	1.5	1.0	0.5
Epidaunorubicin[d]	1.7	1.0	1.0
Epirubicin dimer[e]	2.1	1.0	1.0
Individual unspecified impurity	—	1.0	0.5
Total impurities	—	—	3.0

[a] (8*S*,10*S*)-6,8,10,11-Tetrahydroxy-8-(hydroxyacetyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.

[b] (8*S*,10*S*)-8-Acetyl-6,8,10,11-tetrahydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.

[c] Dihydrodaunorubicin; (8*S*,10*S*)-10-[(3-Amino-2,3,6-trideoxy-α-L-*lyxo*-hexopyranosyl)oxy]-6,8,11-trihydroxy-8-(1-hydroxyethyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione hydrochloride.

[d] (8*S*,10*S*)-8-Acetyl-10-[(3-amino-2,3,6-trideoxy-α-L-*arabino*-hexopyranosyl)oxy]-6,8,11-trihydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione.

[e] 8,8'-[(2*R*,4*R*)-4-Hydroxy-2-(hydroxymethyl)-1,3-dioxolan-2,4-diyl]bis{(8*S*,10*S*)-10-[(3-amino-2,3,6-trideoxy-α-L-*arabino*-hexopyranosyl)oxy]-6,8,11-trihydroxy-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione}.

• **Limit of Acetone**

Analysis: See *Residual Solvents* ⟨467⟩.

Acceptance criteria: NMT 1.5%

SPECIFIC TESTS

• **Water Determination,** *Method Ic*⟨921⟩**:** NMT 4.0%

• **pH** ⟨791⟩

Sample solution: 5 mg/mL

Acceptance criteria: 4.0–5.5

• **Bacterial Endotoxins Test** ⟨85⟩**:** NMT 1.1 USP Endotoxin Units/mg, where the label states that Epirubicin Hydrochloride is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

• **Sterility Tests** ⟨71⟩**:** Meets the requirements where the label states that Epirubicin Hydrochloride is sterile.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store in airtight containers, protected from light. Store as per labeling instructions. Possible storage conditions could include the following: Store at a temperature between 2° and 8°. Store at room temperature. If the substance is sterile, store in a sterile, airtight, tamper-proof container.

• **USP Reference Standards** ⟨11⟩

USP Doxorubicin Hydrochloride RS

USP Epirubicin Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
EPIRUBICIN HYDROCHLORIDE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(2)

Current DocID: GUID-94FF5724-CF3C-498C-8A86-2C622B82F83D_4_en-US

DOI: https://doi.org/10.31003/USPNF_M29694_04_01

DOI ref: 2v1fv