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Epirubicin Hydrochloride Injection

DEFINITION

Epirubicin Hydrochloride Injection contains NLT 90.0% and NMT 110.0% of the labeled amount of epirubicin hydrochloride ($C_{27}H_{29}NO_{11} \cdot HCl$).

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 absorption spectrum of the major peak of the *Sample solution* and the *Standard solution* as obtained in the *Assay* exhibit maxima and minima at the same wavelengths.

ASSAY

• **Procedure**

Solution A: Dissolve 2.9 g of sodium lauryl sulfate in 950 mL of water. To the resulting solution add 1.4 mL of phosphoric acid and dilute with water to 1 L.

Mobile phase: Acetonitrile and *Solution A* (50:50)

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

Sample solution: Nominally 1 mg/mL of epirubicin hydrochloride from Injection

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. When this procedure is used for *Identification* test *B*, use a diode array detector set at 200–400 nm.

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

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of epirubicin hydrochloride ($C_{27}H_{29}NO_{11} \cdot HCl$) in the portion of Injection 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 USP Epirubicin Hydrochloride RS in the *Standard solution* (mg/mL)

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

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

Solution A: Dissolve 3.7 g of sodium lauryl sulfate in 950 mL of water. To the resulting solution add 28 mL of phosphoric acid and dilute with water to 1 L.

Solution B: Dilute 28 mL of phosphoric acid with water to 1 L.

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

Diluent: Acetonitrile, methanol, and *Solution B* (29:17:27)

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

Peak identification solution: Dissolve 10 mg of USP Doxorubicin Hydrochloride RS in a mixture of 5 mL of water and 5 mL of phosphoric acid. Allow to stand for 30 min. Adjust with 2 M sodium hydroxide to a pH of 2.6. Add 15 mL of acetonitrile and 10 mL of methanol, and mix.

Standard stock solution: 0.5 mg/mL of USP Epirubicin Hydrochloride RS in *Mobile phase*

Standard solution: 0.01 mg/mL of USP Epirubicin Hydrochloride RS from *Standard stock solution* in *Diluent*

Sample solution: Nominally 1 mg/mL of epirubicin hydrochloride from Injection in *Diluent*. Store at room temperature and use within 4 h.

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

For the Standard solution: About 2 times the retention time of the epirubicin peak

For the System suitability solution, Peak identification solution, and **Sample solution:** About 4.5 times the retention time of the epirubicin peak

System suitability

Samples: *System suitability solution*, *Peak identification solution*, and *Standard solution*. [NOTE—Use the *Peak identification solution* to identify the doxorubicinone peak.]

Suitability requirements

Resolution: NLT 2.0 between epirubicin and doxorubicin, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Injection 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 = nominal 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	1.8
Daunorubicinone[b]	0.4	1.0	0.5
Doxorubicin	0.8	1.0	1.0

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Epirubicin	1.0	—	—
Dihydro daunorubicin[c]	1.1	1.0	0.5
Daunorubicin	1.5	1.0	0.5
Epidaunorubicin[d,e]	1.7	1.0	—
Epirubicin dimer[e,f]	2.1	1.0	—
Any other individual impurity	—	1.0	0.5
Total impurities	—	—	3.9

[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.

[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] These impurities do not have individual limits; they are included in total impurities.

[f] 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}.

SPECIFIC TESTS

- **pH ⟨791⟩:** 2.5–3.5
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **Bacterial Endotoxins Test ⟨85⟩:** NMT 1.61 USP Endotoxin Units/mg of epirubicin
- **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in light-resistant containers. Store in a refrigerator.
- **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 INJECTION	Documentary Standards Support	SM12020 Small Molecules 1

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