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Add the following:

▲Liothyronine Sodium Injection

DEFINITION

Liothyronine Sodium Injection contains an amount of liothyronine sodium ($C_{15}H_{11}I_3NNaO_4$) equivalent to NLT 90.0% and NMT 115.0% of the labeled amount of liothyronine ($C_{15}H_{12}I_3NO_4$).

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**

Solutions containing liothyronine should be protected from light.

Buffer: 5.8 g/L of dibasic sodium phosphate anhydrous and 3.5 g/L of monobasic potassium phosphate, anhydrous in water. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (55:45)

Diluent: Dilute hydrochloric acid in water (1:50), and then add the same volume of methanol.

Standard solution: 1 µg/mL of USP Liothyronine RS in *Diluent*

Sample solution: Nominally 1 µg/mL of liothyronine from Injection in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 225 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4-mm × 8-cm; 5-µm packing L7

Flow rate: 1.25 mL/min

Injection volume: 20 µL

Run time: NLT 2.5 times the retention time of liothyronine

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 liothyronine ($C_{15}H_{12}I_3NO_4$) in the portion of Injection taken:

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

r_U = peak response of liothyronine from the *Sample solution*

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

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

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

Acceptance criteria: 90.0%–115.0%

IMPURITIES

• **Organic Impurities**

Solutions containing liothyronine should be protected from light.

Solution A: 4.9 g/L of sulfamic acid and 0.8 g/L of sodium hydroxide in water. Adjust with 10 N sodium hydroxide TS to a pH of 2.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
3	90	10
6	70	30
14	70	30
44	20	80
54	20	80
56	90	10
60	90	10

Diluent: 0.175 g/L of citric acid, anhydrous, 71.5 mL/L of absolute alcohol, and 8.5 mL/L of ammonium hydroxide in water prepared as follows. Transfer an appropriate amount of citric acid, anhydrous to a suitable flask and dissolve in 20% of the flask volume of water. To this solution, add appropriate amounts of absolute alcohol and ammonium hydroxide, and then dilute with water to volume.

Standard solution: 0.03 µg/mL of USP Liothyronine RS in *Diluent*. Sonicate to dissolve, if necessary.

Sensitivity solution: 0.01 µg/mL of USP Liothyronine RS from the *Standard solution* in *Diluent*

Sample solution: Nominally 10 µg/mL of liothyronine from Injection

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4-mm × 15-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 150 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[Note—The relative retention times in *Table 2* are provided as information that could aid in peak assignment.]

Table 2

Name	Relative Retention Time
Diiodotyrosine[a]	0.4
Diiodothyronine[b]	0.6
Liothyronine	1.0

Name	Relative Retention Time
Levothyroxine[c]	1.2
Triiodothyroacetic acid[d]	1.7
Tetraiodothyroacetic acid[e]	1.9

[a] 3,5-Diiodo-L-tyrosine.

[b] *O*-(4-Hydroxyphenyl)-3,5-diiodo-L-tyrosine.

[c] *O*-(4-Hydroxy-3,5-diiodophenyl)-3,5-diiodo-L-tyrosine.

[d] [4-(4-Hydroxy-3-iodophenoxy)-3,5-diiodophenyl]acetic acid.

[e] [4-(4-Hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl]acetic acid.

Suitability requirements

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Injection taken:

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

r_U = peak response of each degradation product from the *Sample solution*

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

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

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

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.1%.

Table 3

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Diiodotyrosine	0.77	10.0
Triiodothyroacetic acid	1.25	0.5
Any unspecified degradation product	1.0	1.0
Total impurities[a]	—	5.0

[a] Total impurities excludes diiodotyrosine.

SPECIFIC TESTS

- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 9.5–11.5
- **Bacterial Endotoxins Test ⟨85⟩:** Meets the requirements
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose light-resistant containers. Store in a refrigerator.

• **USP Reference Standards** ⟨11⟩
USP Liothyronine RS

L-3-[4-(4-Hydroxy-3-iodophenoxy)-3,5-diiodophenyl]alanine.
$C_{15}H_{12}I_3NO_4$ 650.98▲ (USP 1-May-2024)

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

Topic/Question	Contact	Expert Committee
LIOTHYRONINE SODIUM INJECTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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