Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Feb-2024
Document Type: USP Monographs
DocId: GUID-412473DF-D928-4FD4-B0C4-01CB7191152A_4_en-US
DOI: https://doi.org/10.31003/USPNF_M45446_04_01
DOI Ref: z8ww8

Linezolid Tablets

DEFINITION
Linezolid Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of linezolid ($C_{16}H_{20}FN_3O_4$).

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**

Buffer: 0.23 g/L of ammonium phosphate monobasic

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

Diluent: Methanol and *Buffer* (45:55)

Standard solution: 0.06 mg/mL of USP Linezolid RS in *Diluent*. Sonicate to dissolve as necessary.

Sample stock solution: Nominally 1.2 mg/mL of linezolid from Tablets prepared as follows. Finely powder Tablets (NLT 10) and transfer a suitable portion of the powder to a suitable volumetric flask. Add *Buffer* in small portions to disperse the powder. Use *Buffer* equivalent to 55% of the final volume. Shake for about 10 min. Add methanol, using 20% of the final volume, and sonicate for about 10 min. Allow this solution to stand for about 10 min. Dilute with methanol to volume.

Sample solution: Nominally 0.06 mg/mL of linezolid in *Diluent* from the *Sample stock solution*

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

Mode: LC

Detector: UV 251 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.6 times the retention time of linezolid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of linezolid ($C_{16}H_{20}FN_3O_4$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution ⟨711⟩**

Test 1

Medium: 0.05 M phosphate buffer pH 6.8; 900 mL, prepared as follows. Dissolve 6.8 g/L of potassium phosphate monobasic and 0.869 g/L of sodium hydroxide in water.

Apparatus 2: 50 rpm

Time: 60 min

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

Standard stock solution: 0.4 mg/mL of USP Linezolid RS in *Diluent*. Sonicate, as needed, to dissolve.

Standard solution: 0.04 mg/mL of USP Linezolid RS in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute the filtrate with *Medium* to obtain a final concentration similar to that of the *Standard solution*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of linezolid ($C_{16}H_{20}FN_3O_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \blacktriangle\times D\blacktriangle_{\text{(ERR 1-Feb-2024)}} \times 100$$

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

$\blacktriangle D$ = dilution factor of the *Sample solution*, as needed▲ (ERR 1-Feb-2024)

Tolerances: NLT 80% (*Q*) of the labeled amount of linezolid ($C_{16}H_{20}FN_3O_4$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.05 M phosphate buffer pH 6.8; 900 mL, prepared as follows. Dissolve 6.8 g of potassium phosphate monobasic in 1 L of water and adjust if needed with 2.5 N sodium hydroxide TS to a pH of 6.8.

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase: Acetonitrile and water (25:75)

Standard solution: 0.0264 mg/mL of USP Linezolid RS in *Medium*. Sonicate, as needed, to dissolve.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute the filtrate with *Medium* to obtain a final concentration similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.6 times the retention time of linezolid

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 linezolid ($C_{16}H_{20}FN_3O_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times D \times 100$$

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

D = dilution factor of the *Sample solution*, as needed

Tolerances: NLT 80% (*Q*) of the labeled amount of linezolid ($C_{16}H_{20}FN_3O_4$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements for *Weight Variation*

IMPURITIES

• **Organic Impurities**

Solution A: 6.8 g/L of potassium phosphate monobasic

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	65	35
5	65	35
35	35	65
40	65	35
50	65	35

Diluent: *Solution A* and *Solution B* (55:45)

System suitability stock solution: 0.05 mg/mL each of USP Linezolid Related Compound A RS and USP Linezolid Related Compound B RS in methanol. Sonicate, if necessary, to dissolve.

System suitability solution: 1 mg/mL of USP Linezolid RS in *Diluent*. Add 1.5 µg/mL each of USP Linezolid Related Compound A RS and USP Linezolid Related Compound B RS from the *System suitability stock solution* in *Diluent*. Sonicate, if necessary, to dissolve.

Standard solution: 0.002 mg/mL of USP Linezolid RS in *Diluent*. Sonicate, if necessary, to dissolve.

Sensitivity solution: 0.5 µg/mL of USP Linezolid RS from *Standard solution* in *Diluent*

Sample solution: Nominally 1 mg/mL of linezolid from Tablets prepared as follows. Finely powder Tablets (NLT 10) and transfer a suitable portion of the powder to a suitable volumetric flask, add *Buffer* in small portions to a total of 55% of the final volume. Shake for about 10 min. Add methanol equivalent to 30% of the final volume, and sonicate for about 10 min with intermittent shaking. Allow to stand for 10 min, and dilute with methanol to volume.

Chromatographic system

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

Mode: LC

Detector: UV 251 nm

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

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between linezolid related compound A and linezolid related compound B, *System suitability solution*

Tailing factor: NMT 2.0 for the linezolid peak, *System suitability solution*

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 impurity in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Linezolid related compound C[a]	0.40	0.2
Linezolid	1.0	—
Linezolid related compound B	1.70	—
Linezolid related compound A	1.80	—
Any individual unspecified impurity	—	0.17
Total impurities	—	1.00

[a] (*S*)-5-(Aminomethyl)-3-(3-fluoro-4-morpholinophenyl)oxazolidin-2-one.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Linezolid RS

USP Linezolid Related Compound A RS

(*R*)-5-(Azidomethyl)-3-(3-fluoro-4-morpholinophenyl)oxazolidin-2-one.

$C_{14}H_{16}FN_5O_3$ 321.31

USP Linezolid Related Compound B RS

(*S*)-*N*-{[3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl]methyl}thioacetamide.

$C_{16}H_{20}FN_3O_3S$ 353.41

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

Topic/Question	Contact	Expert Committee
LINEZOLID TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(3)

Current DocID: GUID-412473DF-D928-4FD4-B0C4-01CB7191152A_4_en-US

DOI: https://doi.org/10.31003/USPNF_M45446_04_01

DOI ref: z8ww8