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Clotrimazole Lozenges

DEFINITION
Clotrimazole Lozenges contain NLT 90.0% and NMT 110.0% of the labeled amount of clotrimazole ($C_{22}H_{17}ClN_2$) in a suitable molded base.

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: 0.3 g/L of anhydrous monobasic sodium phosphate and 0.35 g/L of anhydrous dibasic sodium phosphate in water. The resulting solution has a pH of 6.6–7.0.

Mobile phase: Acetonitrile and *Buffer* (1:1)

Diluent: Acetonitrile and water (1:1)

Standard solution: 0.2 mg/mL of USP Clotrimazole RS in *Diluent*

Sample solution: Nominally 0.2 mg/mL of clotrimazole in *Diluent* prepared as follows. Transfer a portion of powdered Lozenges (from NLT 20 Lozenges) equivalent to 5 mg of clotrimazole to a 25-mL volumetric flask. Dilute with *Diluent* to volume. Sonicate for about 10 min, and centrifuge at 3500 rpm for about 15 min at ambient temperature to obtain a clear supernatant. Use the clear supernatant for injection.

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

Mode: LC

Detector: UV 206 nm. For *Identification* test *B* use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L85

Flow rate: 1 mL/min

Injection volume: 8 µL

Run time: 1.25 times the retention time of clotrimazole

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clotrimazole ($C_{22}H_{17}ClN_2$) in the portion of Lozenges taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 2: 50 rpm

Time: 45 min

Determine the amount of clotrimazole ($C_{22}H_{17}ClN_2$) dissolved by using the following method.

Buffer A: 4.4 mg/mL of dibasic potassium phosphate in water

Buffer B: 17.4 mg/mL of dibasic potassium phosphate in water

Mobile phase: Methanol and *Buffer A* (4:1)

Diluent: Methanol and *Buffer B* (60:40)

Standard stock solution: 0.02 mg/mL of USP Clotrimazole RS in *Medium*

Standard solution: 4 µg/mL from the *Standard stock solution* in *Diluent*

Sample solution: Withdraw 25 mL of the solution under test from the vessel. Pass through a polyvinylidene difluoride filter of 0.45-µm pore size, and discard the first 10 mL of the filtrate. Transfer 5.0 mL of filtrate to a 25-mL volumetric flask, and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 3.9-mm × 7.5-cm; packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 µL

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 clotrimazole ($C_{22}H_{17}ClN_2$) dissolved:

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

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)

L = label claim of clotrimazole (mg/Lozenge)

D = dilution factor for the *Sample solution*, 5

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (Q) of the labeled amount of clotrimazole ($C_{22}H_{17}ClN_2$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

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

Standard solution: 1 µg/mL each of USP Clotrimazole RS, USP Clotrimazole Related Compound A RS, and USP Imidazole RS in *Diluent*

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 4.0 between clotrimazole related compound A and imidazole peaks; NLT 4.0 between clotrimazole and clotrimazole related compound A peaks

Relative standard deviation: NMT 2.0% for clotrimazole, clotrimazole related compound A, and imidazole

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified impurity in the portion of Lozenges taken:

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

r_U = peak response of the corresponding specified impurity from the *Sample solution*

r_S = peak response of the corresponding specified impurity from the *Standard solution*

C_S = concentration of the corresponding USP Reference Standard in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Lozenges taken:

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

r_U = peak response of any unspecified impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*. Disregard any impurity peak less than 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Imidazole	0.5	0.5
Clotrimazole related compound A	0.7	0.5
Clotrimazole	1.0	—
Any unspecified impurity	—	0.2
Total impurities	—	2.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩

USP Clotrimazole RS

USP Clotrimazole Related Compound A RS

(*o*-Chlorophenyl)diphenylmethanol.

$C_{19}H_{15}ClO$ 294.78

USP Imidazole RS

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

Topic/Question	Contact	Expert Committee
CLOTRIMAZOLE LOZENGES	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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