

BRIEFING

Terbinafine Tablets. This monograph has been posted on the USP Pending Monographs Web page for review and public comment for more than 90 days. The MD-AA Expert Committee approved the monograph as an Authorized USP Pending Monograph.

Comment: Comments were received to revise the limits for impurities and the *Buffer* preparation in the test for *Dissolution*.

Response: Since the commenter has received FDA approval for its specifications, these comments will be considered for the Terbinafine Tablets proposal that is scheduled to appear in a future issue of *PF*.

The proposed liquid chromatographic procedure in the test for *Organic Impurities* is based on analyses performed with the Waters Symmetry C18 brand of L1 column. The typical retention time for the terbinafine peak is 22 min. The liquid chromatographic procedure in the *Assay* is based on analyses performed with the Kromacil C18 brand of L1 column. The retention time of the terbinafine peak is 5 min.

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C50810

Terbinafine Tablets

v. 1 Authorized November 1, 2009

DEFINITION

Terbinafine Tablets contain Terbinafine Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of terbinafine free base (C₂₁H₂₅N).

IDENTIFICATION

• **A. ULTRAVIOLET ABSORPTION (197U)**

Medium: Methanol

Standard solution: 5 µg/mL of USP Terbinafine Hydrochloride RS in methanol. [NOTE—Sonicate for 15 min.]

Sample solution: Transfer finely ground Tablets, equivalent to 250 mg of terbinafine hydrochloride, to a 500-mL volumetric flask. Add 250 mL of methanol, sonicate for 15 min, and dilute with methanol to volume. Dilute 10 mL of this solution with methanol to 100 mL. Further dilute 10 mL with methanol to 100 mL.

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **PROCEDURE**

Solution A: Acetonitrile and tetrahydrofuran (25:8)

Solution B: 11.5 mg/mL of ammonium dihydrogen phosphate. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: *Solution A* and *Solution B* (9:11)

Diluent: Acetonitrile and *Solution B* (9:11)

Standard solution: 28 µg/mL of USP Terbinafine Hydrochloride RS in *Diluent* (equivalent to 25 µg/mL of terbinafine)

Sample stock solution: 0.5 mg/mL of terbinafine in *Diluent*, from crushed, finely powdered Tablets. [NOTE—Sonicate for 30 min with intermittent shaking.]

Sample solution: 25 µg/mL of terbinafine in *Diluent*, from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Temperature: 30°

Flow rate: 1 mL/min

Injection size: 10 µL

Run time: 2 times the retention time of the terbinafine peak

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 4000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of C₂₁H₂₅N in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of terbinafine, 291.44

M_{r2} = molecular weight of terbinafine hydrochloride, 327.90

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **DISSOLUTION (711)**

Buffer: Dissolve 21 g of monohydrate citric acid and 8 g of sodium hydroxide in 1 L of water. Adjust with hydrochloric acid to a pH of 3.0.

Medium: *Buffer*; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: 28 µg/mL USP Terbinafine Hydrochloride RS prepared as follows: Transfer USP Terbinafine Hydrochloride RS to a suitable volumetric flask. Dissolve first in methanol with 10% of the final volume, and then dilute with *Medium* to volume. Further dilute a portion of this solution with *Medium* to obtain the final concentration.

Sample solution: Pass a portion of the solution under test through a suitable 0.45-µm filter. Dilute with *Medium* to obtain a solution with a concentration of L/10,000 mg/mL, where L is the Tablet label claim, in mg.

Detection: UV 283 nm

Blank: *Medium*

Calculate the percentage of C₂₁H₂₅N dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = Tablet label claim (mg)

M_{r1} = molecular weight of terbinafine, 291.44

M_{r2} = molecular weight of terbinafine hydrochloride, 327.90

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (Q) of the labeled amount of terbinafine is dissolved.

• **UNIFORMITY OF DOSAGE UNITS (905):** Meet the requirements

IMPURITIES

Organic Impurities

• **PROCEDURE**

Buffer: Use *Solution B* from the *Assay*.

Mobile phase: Methanol, tetrahydrofuran, and *Buffer* (40:8:52)

Standard solution: 0.004 mg/mL of USP Terbinafine Hydrochloride RS in *Mobile phase*

2 / Terbinafine Tablets

Sample solution: 2 mg/mL of terbinafine in *Mobile phase* from crushed, finely powdered Tablets. [NOTE—Sonicate for 10 min, and cool to room temperature.]

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Temperature: 35°

Flow rate: 1 mL/min

Injection size: 20 μL

Run time: 3 times the retention time of the terbinafine peak

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Column efficiency: NLT 5000 theoretical plates

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

r_u = peak response of each individual impurity from the *Sample solution*

r_s = peak response of terbinafine from the *Standard solution*

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

C_u = nominal concentration of terbinafine in the *Sample solution* (mg/mL)

F = relative response factor, as given in *Impurity Table 1*

M_{r1} = molecular weight of terbinafine, 291.44

M_{r2} = molecular weight of terbinafine hydrochloride, 327.90

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.75%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
<i>N</i> -Methyl-1-(naphthalen-1-yl)methanamine	0.2	0.46	0.2
<i>cis</i> -Terbinafine ^a	0.9	0.87	0.2
Terbinafine	1.0	—	—
Any other individual impurity	—	1.0	0.2

^a (*Z*)-*N*,6,6-Trimethyl-*N*-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, protected from light, and stored at room temperature.
- **USP REFERENCE STANDARDS <11>**
USP Terbinafine Hydrochloride RS