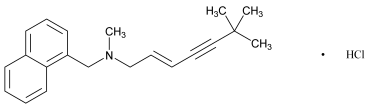
Add the following:

■Terbinafine Hydrochloride



$C_{21}H_{25}N \cdot HCl$ 327.90

1-Naphthalenemethanamine, *N*-(6,6-dimethyl-2-hepten-4-ynyl)-*N*-methyl-, (*E*)-, hydrochloride.

(*E*)-*N*-(6,6-Dimethyl-2-hepten-4-ynyl)-*N*-methyl-1-naphthalenemethylamine, hydrochloride.

(2*E*)-*N*,6,6-Trimethyl-*N*-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine hydrochloride [*78628-80-5*].

» Terbinafine Hydrochloride contains not less than 99.0 percent and not more than 101.0 percent of $C_{21}H_{25}N \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers, protected from light. Store at room temperature.

USP Reference standards ⟨11⟩—*USP Terbinafine Hydrochloride RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: It meets the requirements of the test for *Chloride* ⟨191⟩ when using dehydrated alcohol as a solvent.

Delete the following:

•**Melting range** ⟨741⟩**:** between 204° and 208°.• (RB 1-Apr-2009)

Loss on drying ⟨731⟩**—**Dry it at 105° to constant weight: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Related compounds—[NOTE—Protect all solutions containing Terbinafine Hydrochloride from light.]

Methanol–acetonitrile mixture—Prepare a mixture of methanol and acetonitrile (60 : 40).

Buffer pH 7.5—Prepare a solution in water containing 2.0 mL of triethylamine per L. Adjust with diluted acetic acid to a pH of 7.5.

Solution A—Prepare a mixture of *Methanol–acetonitrile mixture* and *Buffer pH 7.5* (70 : 30).

Solution B—Prepare a mixture of *Methanol–acetonitrile mixture* and *Buffer pH 7.5* (95 : 5).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of acetonitrile and water (50 : 50).

Test solution—Dissolve an accurately weighed quantity of Terbinafine Hydrochloride in *Diluent* to obtain a solution having a known concentration of about 0.5 mg per mL.

Standard solution—Dissolve an accurately weighed quantity of USP Terbinafine Hydrochloride RS in *Diluent* to obtain a solution having a known concentration of about 0.5 µg per mL.

System suitability solution—Prepare a solution in *Diluent* containing about 1 mg of terbinafine hydrochloride per mL, and expose it to UV light at 254 nm for 1 hour.

Sensitivity solution—Dilute a portion of the *Standard solution* with *Diluent* to obtain a solution having a concentration of about 0.25 µg of terbinafine hydrochloride per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 3.0-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 0.8 mL per minute. The column temperature is maintained at 40°. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–4	100	0	isocratic
4–25	100→0	0→100	linear gradient
25–30	0	100	isocratic
30–30.1	0→100	100→0	linear gradient
30.1–38	100	0	re-equilibration

Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the resolution, *R*, between *cis*-terbinafine and terbinafine is not less than 2.0. Chromatograph the *Standard solution*, and record the peak response as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 10%. Chromatograph the *Sensitivity solution*, and calculate the signal-to-noise ratio, *S/N*, by the formula:

$$(2H)/h$$

in which *H* is the measured height of the terbinafine peak; and *h* is the amplitude of the average measured baseline noise. The *S/N* ratio is not less than 10.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, identify the peaks based on their relative retention times as given in *Table 1*, and measure the peak responses. Calculate the percentage of each impurity in the portion of Terbinafine Hydrochloride taken by the formula:

$$100(1/F)(0.001 \times C_S / C_T)(r_U / r_S)$$

in which *F* is the relative response factor as listed in *Table 1;* 0.001 is the conversion factor from µg per mL to mg per mL; C_S is the concentration, in µg per mL, of terbinafine hydrochloride in the *Standard solution;* C_T is the concentration, in mg per mL, of terbinafine hydrochloride in the *Test solution;* r_U is the peak response for each impurity obtained from the *Test solution;* and r_S is the peak response for the terbinafine peak obtained from the *Standard solution*. Disregard any peak observed in the blank, and any peak less than 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor (*F*)	Limit (%)
N-Methyl-*C*-(naphthalen-1-yl)methanamine	0.1	1.7	0.1
trans-Isoterbinafine[1]	0.92	1.0	0.1
cis-Terbinafine[2]	0.94	1.0	0.1
Terbinafine	1.0	n/a	n/a
4-Methylterbinafine[3]	1.1	1.0	0.1
Terbinafine dimer[4]	1.7	2.5	0.05
Any other individual impurity	n/a	1.0	0.1
Total impurities	n/a	n/a	0.3

[1](2*E*)-*N*,6,6-Trimethyl-*N*-(naphthalen-2-ylmethyl)hept-2-en-4-yn-1-amine.
[2](2*Z*)-*N*,6,6-Trimethyl-*N*-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine.
[3](2*E*)-*N*,6,6-Trimethyl-*N*-[(4-methylnaphthalen-1-yl)methyl]hept-2-en-4-yn-1-amine.
[4](2*E*,4*E*)-4-(4,4-Dimethylpent-2-ynylidene)-N^1,N^5-dimethyl-N^1,N^5-bis(naphthalen-1-ylmethyl)pent-2-ene-1,5-diamine.

Assay—Dissolve about 250 mg of Terbinafine Hydrochloride in 50 mL of alcohol, and add 5 mL of 0.01 N hydrochloric acid VS. Titrate with 0.1 N sodium hydroxide VS, determining the endpoint potentiometrically. Read the volume added between the two points of inflexion: 1 mL of 0.1 N sodium hydroxide is equivalent to 32.79 mg of $C_{21}H_{25}N \cdot HCl$.■1S (*USP31*)