Add the following:

Terbinafine Hydrochloride

C₃₁H₄₅N₂·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.
(2E)-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 C₃₁H₄₅N₂·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 ignition (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.]

Method–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°C. The chromatogram is programmed as follows.

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
<th>Elution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>100</td>
<td>0</td>
<td>isocratic</td>
</tr>
<tr>
<td>4–25</td>
<td>100–0</td>
<td>0–100</td>
<td>linear gradient</td>
</tr>
<tr>
<td>25–30</td>
<td>0</td>
<td>100</td>
<td>isocratic</td>
</tr>
<tr>
<td>30–30.1</td>
<td>0–100</td>
<td>100–0</td>
<td>linear gradient</td>
</tr>
<tr>
<td>30.1–38</td>
<td>100</td>
<td>0</td>
<td>re-equilibration</td>
</tr>
</tbody>
</table>

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:

\[(2H/h)\frac{F}{h}
\]

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:

\[100 \left(1/F \times C_{S} / C_{T}\right) \left(r_{2} / r_{S}\right)\]

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_{2} 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

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor (F)</th>
<th>Limit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-Methyl-C-(naphthalen-1-yl)methanamine</td>
<td>0.1</td>
<td>1.7</td>
<td>0.1</td>
</tr>
<tr>
<td>trans-Isotherbinafine&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.92</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>cis-Terbinafine&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.94</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>1.0</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>4-Methylterbinafine&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1.1</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Terbinafine dimer&lt;sup&gt;4&lt;/sup&gt;</td>
<td>1.7</td>
<td>2.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Any other individual impurity</td>
<td>n/a</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Total impurities</td>
<td>n/a</td>
<td>n/a</td>
<td>0.3</td>
</tr>
</tbody>
</table>

<sup>1</sup>(2E)-N,6,6-Trimethyl-N-(naphthalen-2-ylmethyl)hept-2-en-4-yn-1-amine.

<sup>2</sup>(2Z)-N,6,6-Trimethyl-N-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine.

<sup>3</sup>(2E)-N,6,6-Trimethyl-N-{[4-methyl(naphthalen-1-yl)methyl]hept-2-en-4-yn-1-amine.

<sup>4</sup>(2E,4E)-4-(4,4-Dimethylpent-2-ynylidene)-N,N'-dimethyl-N,N'-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<sub>21</sub>H<sub>25</sub>N·HCl<sub>2</sub> VS (USP31).