Add the following:

■Zolpidem Tartrate Tablets

DEFINITION

Zolpidem Tartrate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of zolpidem tartrate ($C_{42}H_{48}N_6O_8$).

IDENTIFICATION

- **A. ULTRAVIOLET ABSORPTION ⟨197U⟩:** The spectrum of the *Sample solution* in the test for *Dissolution* matches that of the *Standard solution*.
- **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**

Buffer: 3.4 g/L of monobasic potassium phosphate in water, adjusted with ammonium hydroxide to a pH of 5.5
Mobile phase: Acetonitrile, methanol, and *Buffer* (3:2:5)
Standard stock solution: 0.8 mg/mL of USP Zolpidem Tartrate RS in 0.01 M hydrochloric acid
Standard solution: 0.16 mg/mL of USP Zolpidem Tartrate RS in *Mobile phase* from the *Standard stock solution*
Sample stock solution: Transfer NLT 20 Tablets to a suitable volumetric flask to obtain a solution having a concentration of 0.4 mg/mL of zolpidem tartrate. Add 40% of the flask volume of 0.125 N hydrochloric acid. Mix well until the Tablets disintegrate, then add 50% of the flask volume of *Mobile phase*. Dilute with water to volume, and stir for 30 min using a magnetic stirrer. Allow solid particles to settle, and pass the supernatant through a suitable filter (e.g. Whatman No. 40 filter or equivalent).
Sample solution: 0.16 mg/mL of zolpidem tartrate from the filtered *Sample stock solution* and *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Flow rate: 1.2 mL/min
Injection size: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 3.0 for zolpidem
Relative standard deviation: NMT 2.0% for zolpidem
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{42}H_{48}N_6O_8$ in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Zolpidem Tartrate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION ⟨711⟩**

●**Test 1**● (RB 1-Feb-2011)
Medium: 0.01 N hydrochloric acid; 900 mL, deaerated
Apparatus 2: 50 rpm
Time: 15 min
Sample solution: Pass a portion of the solution through a suitable filter of 0.45-µm pore size.
Standard solution: (*L*/1000) mg/mL of USP Zolpidem Tartrate RS in *Medium*, where *L* is the Tablet label claim in mg
Detection: UV 295 nm
Blank: *Medium*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of zolpidem tartrate ($C_{42}H_{48}N_6O_8$) dissolved:

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

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 (mL)

Tolerance: NLT 80% (*Q*) of the labeled amount of zolpidem tartrate ($C_{42}H_{48}N_6O_8$) is dissolved.

●**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 20 min
Sample solution: Pass a portion of the solution under test through a suitable filter.
Standard solution: (*L*/900) mg/mL of USP Zolpidem Tartrate RS in *Medium*, where *L* is the Tablet label claim in mg
Detection: UV 295 nm
Blank: *Medium*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of zolpidem tartrate ($C_{42}H_{48}N_6O_8$) dissolved:

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

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 (mL)

Tolerance: NLT 80% (*Q*) of the labeled amount of zolpidem tartrate ($C_{42}H_{48}N_6O_8$) is dissolved.● (RB 1-Feb-2011)

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

- **ORGANIC IMPURITIES**

Buffer, Mobile phase, Standard stock solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
System suitability solution: 2 mg/mL of USP Zolpidem Impurities Mixture RS, prepared by dissolving the weighed amount of USP Zolpidem Impurities Mixture RS in 10% of the flask volume of 0.01 N hydrochloric acid, and diluting with *Mobile phase* to volume

Standard solution: 8 µg/mL of USP Zolpidem Hydrochloride RS in *Mobile phase* from the *Standard stock solution*
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 1.5 between zolpidem related compound B and zolpidem related compound C, *System suitability solution*
Tailing factor: NMT 2.0 for the zolpidem peak, *Standard solution*
Relative standard deviation: NMT 10.0% for the zolpidem peak, *Standard 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 zolpidem from the *Standard solution*
C_S = concentration of USP Zolpidem Tartrate RS in the *Standard solution* (mg/mL)
C_U = concentration of zolpidem tartrate in the *Sample solution* (mg/mL)
Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Zolpidem acid[a]	0.23	0.3
Zolpidem related compound B[b]	0.58	0.3
Zolpidem related compound C[c]	0.70	0.3
Zolpidem tartrate	1.0	—
Zolpidem carbaldehyde[d]	1.45	0.3
Any individual unspecified degradation product	—	0.2
Total impurities	—	0.5

[a] 2-(6-Methyl-2-*p*-tolylimidazo[1,2-α]pyridin-3-yl)acetic acid.
[b] *N,N*-Dimethyl-2-(6-methyl-2-*p*-tolylimidazo[1,2-a]pyridin-3-yl)-2-oxoacetamide.
[c] 4-Methyl-*N*-(5-methylpyridin-2-yl)benzamide.
[d] 6-Methyl-2-*p*-tolylimidazo[1,2-α]pyridine-3-carbaldehyde.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.

Add the following:

•• **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.• (RB 01-Feb-2011)

- **USP REFERENCE STANDARDS** ⟨11⟩

USP Zolpidem Impurities Mixture RS—
Contains at least 98.5% of zolpidem tartrate; 0.2% of zolpidem tartrate related compound B (*N,N,6*-trimethyl-2-(4-methylphenyl)imidazo[1,2-*a*]pyridine-3-(2-oxoacetamide)); and 0.2% of zolpidem tartrate related compound C (5-methyl-2-(4-methylbenzamido)pyridine).
USP Zolpidem Tartrate RS■2S *(USP33)*