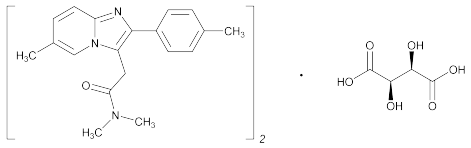
the test solution and the Standard solution to the plate, and allow the spots to dry. Place the plate in a saturated chamber containing a solvent system consisting of a mixture of toluene, acetone, and ammonium hydroxide (75:18:7), and lined with filter paper. Develop the chromatogram until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, allow the plate to air-dry. Spray the plate with *Modified Dragendorff's reagent*, and examine the plate: no individual secondary spot observed in the chromatogram obtained from the test solution is greater in size or intensity than the principal spot observed in the chromatogram obtained from the Standard solution, corresponding to 2%, and the total of any such spots observed does not exceed 3%.

Chloride content—Transfer about 400 mg of it, accurately weighed, to a conical flask, add 5 mL of water, 5 mL of glacial acetic acid, and 50 mL of methanol, and swirl to dissolve. Add 1 drop of eosin Y TS, and titrate with 0.1 N silver nitrate VS to the endpoint when the granular precipitate first turns to a permanent pink color. Each mL of 0.1 N silver nitrate is equivalent to 3.545 mg of chloride: between 10.5% and 11.5% is found.

Assay—Transfer about 480 mg of Zolazepam Hydrochloride, accurately weighed, to a conical flask, add 70 mL of glacial acetic acid, 10 mL of mercuric acetate TS, and swirl to dissolve. Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 32.28 mg of $C_{15}H_{15}FN_4O \cdot HCl$.

Zolpidem Tartrate



$(C_{19}H_{21}N_3O)_2 \cdot C_4H_6O_6$ 764.87

Imidazo[1,2-*a*]pyridine-3-acetamide, *N,N,*6-trimethyl-2-(4-methylphenyl)-, [*R-(R*,R*)*]-2,3-dihydroxybutanedioate; *N,N,*6-Trimethyl-2-*p*-tolylimidazo[1,2-*a*]pyridine-3-acetamide L-(+)-tartrate [99294-93-6].

DEFINITION

Zolpidem Tartrate contains NLT 98.5% and NMT 101.0% of $C_{42}H_{48}N_6O_8$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨**197K**⟩
  Sample: Dissolve 0.10 g in 10 mL of 0.1 M hydrochloric acid. Add 10 mL of water. Add dropwise with stirring 1 mL of dilute ammonia. Filter and collect the resulting precipitate. Wash the precipitate with water, and then dry at 100°–105° for 2 h. Use 2 mg of the dried residue to make the KBr pellet.
  Analysis: The IR spectrum of the free base thus obtained corresponds to the IR spectrum of a similarly prepared KBr pellet with 2 mg of USP Zolpidem RS free base.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Organic Impurities*.
- **C. Reaction of Tartrates**
  Sample: 0.1 g of Zolpidem Tartrate
  Analysis: Dissolve the *Sample* in 1 mL of methanol with gentle heating. To 0.1 mL of the solution, add 0.1 mL of a 100-g/L solution of potassium bromide, 0.1 mL of a 20-g/L solution of resorcinol, and 3 mL of sulfuric acid. Heat on a water bath for 5–10 min. A dark blue color develops. Allow to cool, then pour the solution into water.
  Acceptance criteria: The dark blue color changes to red.

ASSAY

- **Procedure**
  Sample solution: Dissolve 0.300 g of Zolpidem Tartrate in a mixture of 20 mL of anhydrous acetic acid and 20 mL of acetic anhydride.
  Titrimetric system
  (See *Titrimetry* ⟨541⟩.)
  Mode: Direct titration
  Titrant: 0.1 N perchloric acid VS
  Endpoint detection: Potentiometric
  Analysis
  Sample: *Sample solution*
  Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Carry out a blank titration.
  Calculate the percentage of $C_{42}H_{48}N_6O_8$ in the portion of Zolpidem Tartrate taken:

$$\text{Result} = [(V - B) \times N \times F/W] \times 100$$

  V = sample titrant volume (mL)
  B = blank titrant volume (mL)
  N = titrant normality (meq/mL)
  F = 382.4 mg/meq
  W = sample weight (mg)
  Acceptance criteria: 98.5%–101.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition** ⟨**281**⟩**:** NMT 0.1%
- **Heavy Metals,** *Method II* ⟨**231**⟩**:** 20 ppm

Organic Impurities

- **Procedure**
  Buffer: 5.6 g/L phosphoric acid in water. Adjust with triethylamine to a pH of 5.5.
  Mobile phase: Methanol, acetonitrile, and *Buffer* (23:18:59)
  System suitability solution: 0.05 mg/mL each of USP Zolpidem Tartrate RS and USP Zolpidem Related Compound A RS in *Mobile phase*
  Standard solution: 1 µg/mL of USP Zolpidem Tartrate RS in *Mobile phase*
  Sample solution: 0.5 mg/mL of Zolpidem Tartrate in *Mobile phase*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: 3.9-mm × 15-cm; 4-µm packing L1
  Flow rate: 1.5 mL/min
  Injection size: 20 µL
  System suitability
  Samples: *System suitability solution* and *Standard solution*
  Suitability requirements
  Resolution: NLT 2.0 between zolpidem tartrate related compound A and zolpidem tartrate, *System suitability solution*
  Relative standard deviation: NMT 10.0%, *Standard solution*
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of each impurity in the portion of Zolpidem Tartrate taken:

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

  r_U = peak response for each impurity from the *Sample solution*
  r_S = peak response for 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
Individual impurities: NMT 0.10%
Total impurities: NMT 0.2%
[NOTE—Disregard any peak with an area less than 0.25 times that of the principal peak from the *Standard solution* (0.05%) and any peak with a relative retention time of 0.16, which is due to tartaric acid.]

SPECIFIC TESTS
- **WATER DETERMINATION,** *Method Ia* ⟨**921**⟩**:** NMT 3.0%

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Zolpidem RS
USP Zolpidem Related Compound A RS
N,N,7-trimethyl-2-(4-methylphenyl)imidazo[1,2-*a*]pyridine-3-acetamide.
$C_{19}H_{21}N_3O$ 307.39
USP Zolpidem Tartrate RS

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 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
- **DISSOLUTION** ⟨**711**⟩
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 $C_{42}H_{48}N_6O_8$ 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 = Tablet label claim (mg)
V = volume of *Medium* (mL), 900
Tolerance: NLT 80% (Q) of the labeled amount of $C_{42}H_{48}N_6O_8$ is dissolved.
- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES
Organic Impurities
- **PROCEDURE**
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 Tartrate 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*