ASSAY

Change to read:

- **PROCEDURE**

Diluent: Acetonitrile and water (45:55)
Buffer: 1.4 g/L monobasic potassium phosphate in water
Mobile phase: Acetonitrile and *Buffer* (45:55)
System suitability solution: 0.02 mg/mL each of USP Triazolam RS and USP Alprazolam Related Compound A RS in *Diluent*
Standard solution: 0.025 mg/mL of USP Triazolam RS in *Diluent*
Sample solution: 0.025 mg/mL of Triazolam in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 215 nm
Column: 4.6-mm × 15-cm; 3.5-µm packing L1
Column temperature: 40°
Flow rate: 1 mL/min
Injection size: 10 µL
Run time: 3 times the retention time of triazolam
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for alprazolam related compound A and triazolam are 0.77 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 4.0 between alprazolam related compound A and triazolam, *System suitability solution*
Tailing: NMT 1.5, *Standard solution*
Relative standard deviation: NMT 1.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of triazolam ($C_{17}H_{12}Cl_2N_4$) in the portion of Triazolam taken:

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

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

Acceptance criteria: 97.0%–103.0% on the dried basis■1S (*USP35*)

IMPURITIES

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.5%
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm

Change to read:

- **ORGANIC IMPURITIES**

Diluent, Buffer, Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 0.25 µg/mL of USP Triazolam RS in *Diluent*
Sample solution: 0.25 mg/mL of Triazolam in *Diluent*
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for alprazolam related compound A and triazolam are 0.77 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 4.0 between alprazolam related compound A and triazolam, *System suitability solution*
Tailing: NMT 1.5, *Standard solution*
Relative standard deviation: NMT 5.0%, *Standard solution*
Analysis
Sample: *Sample solution*
Calculate the total percentage of impurities in the portion of Triazolam taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = sum of the areas of each of the minor component peaks detected
r_T = sum of all minor component peak areas and the area of the major component peak

Acceptance criteria
Total impurities: NMT 1.5%■1S (*USP35*)

SPECIFIC TESTS

- **LOSS ON DRYING** ⟨**731**⟩**:** Dry a sample at 60° and at a pressure not exceeding 5 mm of mercury for 16 h: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

Change to read:

- **PACKAGING AND STORAGE:** Preserve in well-closed containers ■at room temperature.■1S (*USP35*)

Change to read:

- **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Triazolam RS
■USP Alprazolam Related Compound A RS
2-(2-Acetylhydrazino)-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine.
$C_{17}H_{15}ClN_4O$ 326.78■1S (*USP35*)

Add the following:

■Valsartan Tablets

DEFINITION

Valsartan Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of valsartan ($C_{24}H_{29}N_5O_3$).

IDENTIFICATION

- **A.** 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**

Mobile phase: Acetonitrile, water, and glacial acetic acid (50:50:0.1)
Diluent: Acetonitrile and water (1:1)
System suitability solution: 2 µg/mL of USP Valsartan Related Compound B RS and 20 µg/mL of USP Valsartan RS in *Diluent*
Standard solution: 0.20 mg/mL of USP Valsartan RS in *Diluent*
Sample stock solution: Place NLT 20 Tablets in a suitable volumetric flask, and initially add water (10% of the volume of the flask). Stir or shake until the Tablets disintegrate (about 5 min). Add acetonitrile (about 80% of

the volume of the flask). Stir or shake for 30 min, and sonicate for 10 min. Cool, and dilute with acetonitrile to volume, mix, and centrifuge a portion of the suspension.
Sample solution: 0.2 mg/mL of valsartan from the *Sample stock solution* in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 230 nm
Column: 4.6-mm × 25-cm; 10-µm packing L1
Column temperature: 30°
Flow rate: 1.0 mL/min
Injection size: 20 µL
System suitability
Sample: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 1.5 between valsartan related compound B and valsartan, *System suitability solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of valsartan ($C_{24}H_{29}N_5O_3$) 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 Valsartan RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩
Medium: pH 6.8 phosphate buffer; 1000 mL, degassed
Apparatus 2: 50 rpm
Time: 30 min
Standard solution: (*L*/1000) mg/mL of USP Valsartan RS in *Medium*, where *L* is the label claim, in mg/Tablet. [NOTE—Dilute with *Medium* as needed.]
Sample solution: Pass a portion of the solution under test through a suitable filter.
Analysis
Analytical wavelength: UV 250 nm
Blank: *Medium*
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of valsartan ($C_{24}H_{29}N_5O_3$) 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 USP Valsartan RS in the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 1000 mL
Tolerances: NLT 80% (*Q*) of the labeled amount of valsartan ($C_{24}H_{29}N_5O_3$) is dissolved.
• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **Organic Impurities**
Mobile phase, Diluent, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 0.4 µg/mL of USP Valsartan RS in *Diluent*
Sensitivity solution: 0.1 µg/mL of USP Valsartan RS in *Diluent*, from the *Standard solution*
System suitability
Sample: *Standard solution*, *Sensitivity solution*, and *System suitability solution*
Suitability requirements
Resolution: NLT 1.5 between valsartan related compound B and valsartan, *System suitability solution*
Relative standard deviation: NMT 10.0%, *Standard solution*
Signal-to-noise ratio: NLT 10, *Sensitivity solution*
Analysis
Sample: *Sample solution* and *Standard solution*
Calculate the percentage of each individual 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 valsartan from the *Standard solution*
C_S = concentration of USP Valsartan RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of valsartan in the *Sample solution* (µg/mL)
Acceptance criteria
Each individual impurity: NMT 0.2%
Total impurities: NMT 0.4%. [NOTE—Calculate the total impurities from the sum of all individual impurity peaks. Disregard any peak due to valsartan related compound B and any peaks ≤0.05%.]

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.
• **USP Reference Standards** ⟨11⟩
USP Valsartan RS
USP Valsartan Related Compound B RS
(*S*)-*N*-Butyryl-*N*-{[2′-(1-*H*-tetrazole-5-yl)-biphenyl-4-yl]-methyl}-valine.
$C_{23}H_{27}N_5O_3$ 421.49■1S *(USP35)*

Add the following:

■Verapamil Hydrochloride Extended-Release Capsules

DEFINITION

Verapamil Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$).

IDENTIFICATION

• **A.** 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: 0.01 N sodium acetate in water containing 33 mL/L of glacial acetic acid
Mobile phase: Acetonitrile, 2-aminoheptane, and *Solution A* (60:1:140)
System suitability solution: 0.12 mg/mL of USP Verapamil Hydrochloride RS and 0.1 mg/mL of USP Verapamil Related Compound B RS in *Mobile phase*
Standard solution: 0.12 mg/mL of USP Verapamil Hydrochloride RS in *Mobile phase*
Sample stock solution: 1.2 mg/mL of verapamil hydrochloride prepared as follows. Transfer an equivalent to 240 mg of verapamil hydrochloride, from the pool of Capsule contents (NLT 20), to a 200-mL volumetric flask.