Valsartan Tablets

Type of Posting	Revision Bulletin
Posting Date	17–Nov–2017
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Expert Committee	Chemical Medicines Monographs 2
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Expert Committee 2 has revised the Valsartan Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA approved drug products. In addition, the chemical name for USP Valsartan Related Compound B is corrected.

Minor editorial changes have been made to update the monograph to the current *USP* style.

Valsartan Tablets Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated in the *Second Supplement* to *USP41–NF36*.

Should you have any questions, please contact Donald Min Ph.D., Senior Scientific Liaison (301–230–7457 or ddm@USP.org).

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 (50:50)

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: Nominally 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
Samples: *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 of valsartan 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* (mg/mL)
C_U = nominal concentration of valsartan the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

•**Test 1**• (RB 1-Dec-2017)
Medium: pH 6.8 phosphate buffer prepared as follows. Dissolve 6.805 g of monobasic potassium phosphate and 0.896 g of sodium hydroxide in and dilute with water to 1000 mL. Adjust with 0.2 M sodium hydroxide or 1 M phosphoric acid as required to a pH of 6.8; 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.

•**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.
Medium: 0.067 M phosphate buffer prepared as follows. Dissolve 91.2 g of monobasic potassium phosphate and 12 g of sodium hydroxide in 10 L of water. Adjust with 1 N sodium hydroxide or 1 N orthophosphoric acid to a pH of 6.8; 1000 mL.
Apparatus 2: 50 rpm
Time: 30 min
Standard stock solution: 0.4 mg/mL of USP Valsartan RS prepared as follows. Transfer an appropriate quantity of USP Valsartan RS into a suitable volumetric flask, and add methanol to about 5% of the volume of the flask. Sonicate to dissolve. Dilute with *Medium* to volume.
Standard solution: 0.02 mg/mL of USP Valsartan RS in *Medium* from *Standard stock solution*
Sample solution: Withdraw 10 mL of the solution under test and pass through a suitable filter. Dilute a portion of the solution with *Medium* to the concentration similar to that in the *Standard solution*.

Instrumental conditions
Mode: UV-Vis
Analytical wavelength: 250 nm
Cell: 1.0 cm
Blank: *Medium*
System suitability
Sample: *Standard solution*
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of valsartan ($C_{24}H_{29}N_5O_3$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

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)
V = volume of *Medium*, 1000 mL
D = dilution factor
L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of valsartan ($C_{24}H_{29}N_5O_3$) is dissolved.● (RB 1-Dec-2017)

- **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
Samples: *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
Samples: *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.

Add the following:

●• **LABELING:** When more than one test for *Dissolution* is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.● (RB 1-Dec-2017)

Change to read:

- **USP REFERENCE STANDARDS ⟨11⟩**

USP Valsartan RS
USP Valsartan Related Compound B RS
●*N*-Butyryl-*N*-{[2′-(1*H*-tetrazole-5-yl)biphenyl-4-yl]methyl}-L-valine.● (RB 1-Dec-2017)
$C_{23}H_{27}N_5O_3$ 421.49