

Valsartan Tablets

Type of Posting	Revision Bulletin
Posting Date	17–Nov–2017
Official Date	01–Dec–2017
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 μ g/mL of USP Valsartan Related Compound B RS and 20 μ g/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 \times 25-cm; 10- μ m packing L1

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection size: 20 μ L

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*.

2 Valsartan

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 (C₂₄H₂₉N₅O₃) 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 (C₂₄H₂₉N₅O₃) 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)
 C₂₃H₂₇N₅O₃ 421.49