Valacyclovir Tablets

**DEFINITION**
Valacyclovir Tablets contain an amount of Valacyclovir Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of valacyclovir (C13H20N6O4).

**IDENTIFICATION**
- **A. Identification**
  - The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.
- **B. IDENTIFICATION TESTS—GENERAL, Chloride (191)**: Meet the requirements

**ASSAY**
- **PROCEDURE**

  **Diluent**: 0.1% (v/v) phosphoric acid in water

  **Mobile phase**: Methanol and Diluent (5:95)

  **Standard solution**: 0.1 mg/mL of USP Valacyclovir Hydrochloride RS in Diluent. [NOTE—USP Valacyclovir Hydrochloride RS contains a detectable quantity of D-valacyclovir.]

  **Sample solution**: Transfer NLT 5 Tablets into a suitable volumetric flask, and add 0.1 M hydrochloric acid (approximately 80% of the volume of the flask). Mechanically shake the sample until the Tablets disintegrate into a fine suspension (60 min), and sonicate for 10 min. Cool to ambient temperature, dilute with 0.1 M hydrochloric acid to volume, and mix to obtain a solution having a concentration of 2.5 mg/mL. Dilute a portion of the sample with Diluent to obtain a nominal concentration of 0.1 mg/mL of valacyclovir, and mix. Pass a portion of this solution through a membrane filter of 0.45-µm or finer pore size, and use the filtrate.

  **Chromatographic system**
  (See Chromatography (621), System Suitability.)

  **Mode**: LC

  **Detector**: UV 254 nm

  **Column**: 4-mm × 15-cm; 5-µm packing L66

  **Column temperature**: 10°

  **Flow rate**: 0.75 mL/min

  **Injection volume**: 10 µL

  **System suitability**
  - **Sample**: Standard solution
  - **Suitability requirements**
    - **Resolution**: NLT 1.3 between the D-valacyclovir and valacyclovir peaks
    - **Tailing factor**: NMT 2.0 for the valacyclovir peak
  - **Relative standard deviation**: NMT 2.0%

  **Analysis**
  - **Samples**: Standard solution and Sample solution
  - Calculate the percentage of the labeled amount of valacyclovir (C13H20N6O4) in the portion of Tablets taken:

    \[
    \text{Result} = \left(\frac{r_U}{r_s}\right) \times \left(\frac{C_U}{C_s}\right) \times \left(\frac{M_1}{M_2}\right) \
    \]

    \[\times 100\]

    where:
    - \(r_U\) = peak response from the Sample solution
    - \(r_s\) = peak response from the Standard solution
    - \(C_s\) = concentration of USP Valacyclovir Hydrochloride RS in the Standard solution (mg/mL)
    - \(C_U\) = nominal concentration of valacyclovir in the Sample solution (mg/mL)
    - \(M_1\) = molecular weight of valacyclovir, 324.34
    - \(M_2\) = molecular weight of valacyclovir hydrochloride, 360.80

  **Acceptance criteria**: 90.0%–110.0%

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution (711)**
  - **Test 1**: (RB 1-May-2012)
    - **Medium**: 0.1 N hydrochloric acid; 900 mL
    - **Apparatus 2**: 50 rpm
    - **Time**: 45 min
  - **Diluent**: Prepare as directed in the Assay.

  **Mobile phase**: Acetonitrile and Diluent (5:95)

  **Standard solution**: Prepare a solution in Diluent containing USP Valacyclovir Hydrochloride RS equivalent to 0.044 mg/mL of valacyclovir free base.

  **Sample solution**: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with Diluent to obtain a final concentration of about 0.044 mg/mL of valacyclovir free base considering complete dissolution of the Tablet label claim.

  **Chromatographic system**
  (See Chromatography (621), System Suitability.)

  **Mode**: LC

  **Detector**: UV 254 nm

  **Column**: 4.6-mm × 5-cm, 5-µm packing L1

  **Flow rate**: 2.0 mL/min

  **Injection volume**: 10 µL

  **System suitability**
  - **Sample**: Standard solution
  - **Suitability requirements**
    - **Tailing factor**: NMT 2.0
    - **Relative standard deviation**: NMT 2.0%

  **Analysis**
  - **Samples**: Standard solution and Sample solution
  - Calculate the percentage of the labeled amount of valacyclovir (C13H20N6O4) dissolved:

    \[
    \text{Result} = \left(\frac{r_U}{r_s}\right) \times \left(\frac{V}{M_1}\right) \times \left(\frac{M_1}{M_2}\right) \times (1/L) \times D \times 100
    \]

  - **Instrumental conditions**
    - (See Spectrophotometry and Light-Scattering (851).)
    - **Analytical wavelength**: 252 nm
    - **Cell**: 0.02 cm
    - **Blank**: Medium

  **Standard solution**
  For Tablets labeled to contain 500 mg: 0.6 mg/mL of USP Valacyclovir Hydrochloride RS in Medium. A small volume of methanol, not exceeding 5% of the final volume, may be used to help solubilize valacyclovir.
UNIFORMITY OF DOSAGE UNITS

• Change to read:

For Tablets labeled to contain 1000 mg: 1.2 mg/mL of USP Valacyclovir Hydrochloride RS in Medium. A small volume of methanol, not exceeding 5% of the final volume, may be used to help solubilize valacyclovir.

Sample solution: Pass a portion of the solution under test through a filter of 0.45-µm pore size. Discard the first 3 mL of sample filtrate.

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of valacyclovir (C₁₃H₂₀N₆O₄) dissolved:

\[
\text{Result} = \left( \frac{r_0}{r_s} \right) \times \left( \frac{C_s}{C_U} \right) \times \left( \frac{V}{M_{12}} \right) \times \left( \frac{M_{12}}{M_{11}} \right) \times \left( \frac{1}{D} \right) \times \left( \frac{1}{L} \right) \times 100
\]

\( r_0 \) = absorbance of the Sample solution
\( r_s \) = absorbance of the Standard solution
\( C_s \) = concentration of USP Valacyclovir Hydrochloride RS in the Standard solution (mg/mL)
\( V \) = volume of Medium, 900 mL
\( M_{11} \) = molecular weight of valacyclovir, 324.34
\( M_{12} \) = molecular weight of valacyclovir hydrochloride, 360.80
\( L \) = label claim (mg/Tablet)
\( D \) = dilution factor of the Sample solution

Tolerances: NLT 80% (Q) of the labeled amount of valacyclovir (C₁₃H₂₀N₆O₄) is dissolved. (RB 1-May-2012)

Change to read:

• UNIFORMITY OF DOSAGE UNITS (905)

Procedure for content uniformity

[NOTE—All of the concentrations are expressed as valacyclovir free base.]

Diluent: Prepare as directed in the Assay.

Mobile phase: Acetonitrile and Diluent (3:95)

Standard solution: Prepare a solution of USP Valacyclovir Hydrochloride RS, equivalent to 0.04 mg/mL of valacyclovir, in Diluent.

Sample solution: Transfer 1 Tablet into a suitable volumetric flask. Add Diluent (approximately 60% of the volume of the flask), add a sufficient volume of Mobile phase to dissolve the tablets, and make the solution volume 18 mL. Dilute a portion of each sample with Diluent to obtain a nominal concentration of 0.04 mg/mL of valacyclovir. Pass a portion of each sample through a membrane filter of 0.45-µm pore size, and use the filtrate.

Chromatographic system and System suitability: Proceed as directed in Dissolution. Test 1. (RB 1-May-2012)

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of valacyclovir (C₁₃H₂₀N₆O₄) in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_0}{r_s} \right) \times \left( \frac{C_s}{C_U} \right) \times \left( \frac{M_{12}}{M_{11}} \right) \times \left( 1/L \right) \times D \times 100
\]

\( r_0 \) = peak response from the Sample solution
\( r_s \) = peak response from the Standard solution
\( C_s \) = concentration of USP Valacyclovir Hydrochloride RS in the Standard solution (mg/mL)

IMPURITIES

• ORGANIC IMPURITIES

Diluent, Mobile phase, Standard solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of D-valacyclovir and acyclovir in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_0}{r_s} \right) \times \left( \frac{C_s}{C_U} \right) \times \left( \frac{M_{12}}{M_{11}} \right) \times \left( 1/L \right) \times D \times 100
\]

\( r_0 \) = peak response of D-valacyclovir or acyclovir from the Sample solution
\( r_s \) = peak response of USP Valacyclovir Hydrochloride RS from the Standard solution
\( C_s \) = concentration of valacyclovir hydrochloride in the Standard solution (mg/mL)

Acceptance criteria:

Acceptance criteria: Meet the requirements

Individual impurities: See Table 1.

ADDITIONAL REQUIREMENTS

• PACKAGING AND STORAGE: Preserve in tight containers. Store at controlled room temperature.

ADD the following:

• LABELING: When more than one Dissolution test is given, the labeling states the test used only if Test 1 is not used. (RB 1-May-2012)

• USP REFERENCE STANDARDS (11)

USP Valacyclovir Hydrochloride RS

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