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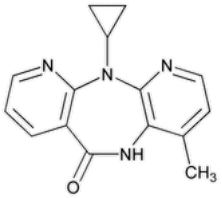
Nevirapine



$C_{15}H_{14}N_4O$ 266.30
6*H*-Dipyrido[3,2-*b*:2',3'-e][1,4]diazepin-6-one, 11-cyclopropyl-5,11-dihydro-4-methyl-;
11-Cyclopropyl-5,11-dihydro-4-methyl-6*H*-dipyrido[3,2-*b*:2',3'-e][1,4]diazepin-6-one CAS RN®: 129618-40-2; UNII: 99DK7FVK1H.
Hemihydrate 275.31

DEFINITION

Nevirapine is anhydrous or contains one-half molecule of water of hydration. It contains NLT 98.0% and NMT 102.0% of $C_{15}H_{14}N_4O$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K.**▲ (CN 1-May-2020) Do not dry the specimens.

• **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: 0.025 M of monobasic ammonium phosphate in water prepared as follows. Dissolve 2.9 g of monobasic ammonium phosphate in 800 mL of water. Adjust with 1 N sodium hydroxide to a pH of 5.0, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile and *Buffer* (1:4)

Standard stock solution A: 0.24 mg/mL of USP Nevirapine Anhydrous RS prepared as follows. Dissolve a quantity of USP Nevirapine Anhydrous RS in Acetonitrile and *Mobile phase* (1:20). Sonicate for at least 15 min, allow to cool to room temperature, and dilute with *Mobile phase* to volume. [Note—Do not use after 78 h.]

Standard stock solution B: 0.24 mg/mL of USP Nevirapine Related Compound A RS prepared as follows. Dissolve a quantity of USP Nevirapine Related Compound A RS in a volume of a mixture of acetonitrile and *Mobile phase* (1:3). Sonicate for at least 15 min, allow to cool to room temperature, and dilute with *Mobile phase* to volume.

Standard stock solution C: 0.06 mg/mL of USP Nevirapine Related Compound B RS prepared as follows. Dissolve a quantity of USP Nevirapine Related Compound B RS in a volume of a mixture of acetonitrile and *Mobile phase* (10:22). Sonicate for at least 30 min, allow to cool to room temperature, and dilute with *Mobile phase* to volume.

System suitability solution: 0.03 mg/mL each of USP Nevirapine Anhydrous RS and USP Nevirapine Related Compound A RS and 0.015 mg/mL of USP Nevirapine Related Compound B RS from suitable volumes of *Standard stock solution A*, *Standard stock solution B*, and *Standard stock solution C*, respectively, in *Mobile phase*. [Note—Do not use after 78 h.]

Standard solution: 0.03 mg/mL of USP Nevirapine Anhydrous RS in *Mobile phase* from *Standard stock solution A*. [Note—Do not use after 78 h.]

Sample stock solution: 0.24 mg/mL of Nevirapine in *Mobile phase* prepared as follows. Transfer the required amount of Nevirapine to a suitable volumetric flask, and add 4% of the final volume with acetonitrile and 80% of the final volume with *Mobile phase*. Sonicate for at least 15 min, allow to cool to room temperature, and dilute with *Mobile phase* to volume.

Sample solution: 0.03 mg/mL of nevirapine anhydrous in *Mobile phase* from the *Sample stock solution*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-µm packing L60

Column temperature: 35°

Flow rate: 1 mL/min

Injection size: 25 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times are shown in *Table 1*.]

Suitability requirements

Resolution: NLT 5.0 between nevirapine related compound B and nevirapine, and NLT 7.4 between nevirapine and nevirapine related compound A; *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nevirapine ($C_{15}H_{14}N_4O$) in the portion of Nevirapine 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 Nevirapine Anhydrous RS in the *Standard solution* (mg/mL)

C_U = concentration of Nevirapine in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **ORGANIC IMPURITIES**

Buffer, Mobile phase, System suitability solution, and **Standard stock solution A:** Proceed as directed in the *Assay*.

Standard solution: 0.2 µg/mL of USP Nevirapine Anhydrous RS in *Mobile phase* from *Standard stock solution A*

Sample solution: 0.24 mg/mL of Nevirapine in *Mobile phase* prepared as follows. Transfer the required amount of Nevirapine to a suitable volumetric flask, and add 4% of the final volume with acetonitrile and 80% of the final volume with *Mobile phase*. Sonicate for at least 15 min, allow to cool to room temperature, and dilute with *Mobile phase* to volume.

Chromatographic system: Proceed as directed in the *Assay*, except for *Run time* and *Injection size*.

Run time: At least 80 min

Injection size: 25 µL for *System suitability*; 50 µL for *Analysis*

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times are shown in *Table 1*.]

Suitability requirements

Resolution: NLT 5.0 between nevirapine related compound B and nevirapine, and NLT 7.4 between nevirapine and nevirapine related compound A; *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Nevirapine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of nevirapine from the *Standard solution*

C_S = concentration of USP Nevirapine Anhydrous RS in the *Standard solution* (µg/mL)

C_U = concentration of nevirapine anhydrous in the *Sample solution* (µg/mL)

F = relative response factor for each impurity (see *Table 1*)

Acceptance criteria See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Nevirapine related compound B	0.7	1.3	0.2
Nevirapine	1.0	1.0	—
Nevirapine related compound A	1.5	1.0	0.2
Nevirapine impurity C	2.8	1.0	0.2
Any other individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.6

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩

For Nevirapine anhydrous: NMT 0.2%

For Nevirapine hemihydrate: 3.1%–3.9%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **Labeling:** Label to indicate whether it is anhydrous or the hemihydrate.

• **USP Reference Standards** ⟨11⟩

USP Nevirapine Anhydrous RS

USP Nevirapine Hemihydrate RS

USP Nevirapine Related Compound A RS

5,11-Dihydro-6*H*-11-ethyl-4-methyl- dipyrido[3,2-*b*:2',3'-*e*][1,4]diazepin-6-one.

$C_{14}H_{14}N_4O$ 254.29

USP Nevirapine Related Compound B RS

5,11-Dihydro-4-methyl-6*H*-dipyrido[3,2-*b*:2',3'-*e*][1,4]diazepin-6-one.

$C_{12}H_{10}N_4O$ 226.23

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
NEVIRAPINE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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