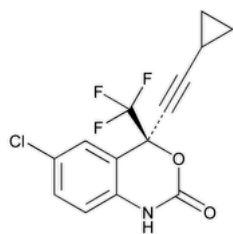


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Efavirenz



C₁₄H₉ClF₃NO₂ 315.67
1H-Benzo[d][1,3]oxazin-2(4H)-one, 6-chloro-4-cyclopropylethynyl-4-trifluoromethyl;
(S)-6-Chloro-4-(cyclopropylethynyl)-1,4-dihydro-4-(trifluoromethyl)-2H-3,1-benzoxazin-2-one CAS RN®: 154598-52-4; UNII: JE6H2O27P8.

DEFINITION
Efavirenz contains NLT 98.0% and NMT 102.0% of C₁₄H₉ClF₃NO₂, calculated on the anhydrous, solvent-free basis.

IDENTIFICATION

Change to read:

- A. ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#) ▲ (CN 1-MAY-2020)

Sample: Dry at 105° for 30 min, and cool in dessicator.

Change to read:

- B. ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy: 197U](#) ▲ (CN 1-MAY-2020)

Solvent: Methanol

Standard solution: 10 µg/mL of [USP Efavirenz RS](#) in Solvent

Sample solution: 10 µg/mL of Efavirenz in Solvent

Acceptance criteria: Meets the requirements

ASSAY

• PROCEDURE

[NOTE—Protect solutions of efavirenz from light. Use of polypropylene HPLC vials is recommended to avoid possible degradation from certain types of glass vials.]

Diluent: Acetonitrile and water (1:1)

Solution A: Methanol, trifluoroacetic acid, and water (1:0.005:9). [NOTE—Use only freshly-opened trifluoroacetic acid, ≤6 months.]

Solution B: Methanol, trifluoroacetic acid, and water (9:0.005:1). [NOTE—Use only freshly-opened trifluoroacetic acid, ≤6 months.]

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	60	40
16	50	50
23	35	65
28	30	70
29	20	80
31	20	80
32	60	

Time (min)	Solution A (%)	Solution B (%)
40	60	40

Standard solution: 250 µg/mL of [USP Efavirenz RS](#) and 1.0 µg/mL of [USP Efavirenz Related Compound B RS](#) in *Diluent*. [NOTE—Dissolve in about 65% of the flask volume in *Diluent* and shake for 30 min or until dissolved before diluting with *Diluent* to volume.]

Sample solution: 250 µg/mL of Efavirenz in *Diluent*. [NOTE—Dissolve in about 65% of the flask volume of *Diluent*, and shake for 30 min or until dissolved before diluting with *Diluent* to volume.]

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 15-cm; 5-µm packing L10

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection size: 35 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.2 between efavirenz related compound B and efavirenz

Relative standard deviation: NMT 1.0% for efavirenz

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{14}H_9ClF_3NO_2$ in the portion of Efavirenz taken:

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

r_U = peak response for efavirenz from the *Sample solution*

r_S = peak response for efavirenz from the *Standard solution*

C_S = concentration of [USP Efavirenz RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the anhydrous, solvent-free basis

IMPURITIES

INORGANIC IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%, use a platinum crucible

ORGANIC IMPURITIES

PROCEDURE 1

Diluent, Solution A, Solution B, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

System suitability solution: Use the *Standard solution* prepared as directed in the Assay.

Standard solution: 1.25 µg/mL of [USP Efavirenz RS](#) in *Diluent*, prepared from the *System suitability solution*

System suitability

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

Suitability requirements

Resolution: NLT 1.2 between efavirenz related compound B and efavirenz, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Efavirenz taken:

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

r_U = peak response for any individual impurity from the *Sample solution*

r_S = peak response for efavirenz from the *Standard solution*

C_S = concentration of [USP Efavirenz RS](#) in the *Standard solution* (mg/mL)

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