

BRIEFING

Efavirenz Capsules. This monograph has been posted on the USP Pending Monographs Web page for review and public comment for more than 90 days. No comments were received. The MD-AA Expert Committee has approved the monograph as an Authorized USP Pending Monograph.

The HPLC procedures in the *Assay* and in the tests for *Dissolution* and *Organic Impurities* are based on analyses performed using a Hypersil BDS C18 brand of L1 column. The typical retention time for efavirenz in the *Assay* and in the test for *Dissolution* is about 8.5 min. The typical retention time for efavirenz in the test for *Organic Impurities* is about 16 min.

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C71172

Efavirenz Capsules

v.1 Authorized November 1, 2009

DEFINITION

Efavirenz Capsules contain NLT 92.0% and NMT 108.0% of the labeled amount of efavirenz (C₁₄H₉ClF₃NO₂).

IDENTIFICATION

- The retention time of the efavirenz peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

PROCEDURE

Solution A: 0.8 mg/mL of ammonium acetate in water. Adjust with 2% ammonium hydroxide solution to a pH of 7.50 ± 0.05. Pass the solution through a suitable 0.45-µm filter.

Mobile phase: Acetonitrile and *Solution A* (3:2)

Standard solution: 60 µg/mL of USP Efavirenz RS in *Mobile phase*

Sample stock solution: Transfer intact Capsules, equivalent to about 1000 mg of efavirenz, to a 500-mL volumetric flask.

Add about 100 mL of *Solution A* and sonicate for 30 min with frequent vigorous shaking. Add about 200 mL of *Mobile phase* and sonicate for 30 min. Allow the solution to cool to room temperature. Dilute with *Mobile phase* to volume, and centrifuge the solution.

Sample solution: 60 µg/mL of efavirenz in *Mobile phase*. Pass the solution through a suitable 0.45-µm filter.

Chromatographic system

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

Mode: LC

Detector: UV 252 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 5000 theoretical plates

Tailing factor: NMT 1.8

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of C₁₄H₉ClF₃NO₂ in the portion of Capsules taken:

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

r_U = peak response of efavirenz in the *Sample solution*

r_S = peak response of efavirenz in the *Standard solution*

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

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

Acceptance criteria: 92.0%–108.0%

PERFORMANCE TESTS

DISSOLUTION (711)

Medium: 1% sodium lauryl sulfate, 900 mL

Apparatus 2: 50 rpm with sinker (see *Dissolution* (711), Figure 2a)

Time: 45 min

Mobile phase: Proceed as directed in the *Assay*.

Standard stock solution: 0.5 mg/mL of efavirenz dissolved initially at 10% of final volume with methanol. Dilute with *Medium* to final volume.

Standard solution: 25 µg/mL of USP Efavirenz RS in *Mobile phase*

Sample solution: Dilute with *Mobile phase* to about 25 µg/mL. Pass the solution through a suitable 0.45-µm filter.

Mobile phase and Chromatographic system: Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity dissolved as a percentage of the labeled amounts of C₁₄H₉ClF₃NO₂ in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times D \times 100$$

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

D = dilution factor of solution under test

Tolerances: NLT 80% (Q) of the labeled amount of efavirenz is dissolved.

- UNIFORMITY OF DOSAGE UNITS (905):** Meet the requirements

IMPURITIES

Organic Impurities

PROCEDURE

Solution A and Sample stock solution: Proceed as directed in the *Assay*.

Solution B: Acetonitrile

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	50	50
25	50	50
40	20	80
55	20	80
60	50	50
65	50	50

Diluent: Acetonitrile and *Solution A* (3:2)

System suitability solution: 0.5 mg/mL of USP Efavirenz RS in *Diluent*

Standard solution: 1 µg/mL of USP Efavirenz RS in *Diluent*

Sample solution: 1 mg/mL of efavirenz in *Diluent*. Pass the solution through a suitable 0.45-µm filter.

Chromatographic system

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

Mode: LC

Detector: UV 252 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

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

Suitability requirements

Column efficiency: NLT 8000 theoretical plates, *System suitability solution*

Tailing factor: NMT 1.8, *System suitability solution*

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

2 / Efavirenz Capsules

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

- r_U = response of each impurity peak in the *Sample solution*
 r_S = response of efavirenz in 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

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.50%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Efavirenz aminoalcohol ^a	0.81	—
Efavirenz	1.00	—

^a (S)-2-(2-amino-5-chlorophenyl)-4-cyclopropyl-1,1,1-trifluorobut-3-yn-2-ol. [NOTE—For information only. This is a process impurity, which is controlled in the drug product.]

^b (S)-N-(4-chloro-2-(4-cyclopropyl-1,1,1-trifluoro-2-hydroxybut-3-yn-2-yl)phenyl)-4-methoxybenzamide. [NOTE—For information only. This is a process impurity, which is controlled in the drug product.]

Impurity Table 1 (continued)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Efavirenz benzylaminoalcohol ^b	1.90	—
Any individual unknown impurity	—	0.10

^a (S)-2-(2-amino-5-chlorophenyl)-4-cyclopropyl-1,1,1-trifluorobut-3-yn-2-ol. [NOTE—For information only. This is a process impurity, which is controlled in the drug product.]

^b (S)-N-(4-chloro-2-(4-cyclopropyl-1,1,1-trifluoro-2-hydroxybut-3-yn-2-yl)phenyl)-4-methoxybenzamide. [NOTE—For information only. This is a process impurity, which is controlled in the drug product.]

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS** <11>
USP Efavirenz RS