

BRIEFING

Efavirenz Capsules. A new USP Pending Monograph is being proposed based on submitted data. 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

Add the following:

►Efavirenz Capsules

Draft 1

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 column; 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*.)

2 / **Efavirenz Capsules**

Mode: LC
Detector: UV 252 nm
Column: 4.6-mm × 25-cm column; 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*

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	—
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 \blacktriangleleft (1-Nov-2009)