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Add the following:

▲Etravirine Tablets

DEFINITION
Etravirine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of etravirine ($C_{20}H_{15}BrN_6O$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K or 197A

• **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**

Protect solutions containing etravirine from light.

Buffer: 10 mM ammonium formate in water

Diluent: Acetonitrile and *Buffer* (50:50, v/v)

Solution A: 50 mM formic acid in *Buffer*

Solution B: Acetonitrile

Solution C: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	60	30	10
35	0	0	100
37	60	30	10
45	60	30	10

Standard solution: 0.10 mg/mL of USP Etravirine RS prepared as follows. Transfer a suitable amount of USP Etravirine RS to a suitable volumetric flask and dissolve in 5% of the total volume of 1-methyl-2-pyrrolidone. Dilute with *Diluent* to volume.

Sample solution: Nominally 0.10 mg/mL of etravirine in *Diluent* prepared as follows. Transfer a portion equivalent to NLT 50 mg of etravirine from finely powdered Tablets (NLT 20) to a suitable volumetric flask. Add 5% of the flask volume of *Diluent* and shake for 5 min. Add 5% of the flask volume of 1-methyl-2-pyrrolidone and shake for 30 min. Dilute with *Diluent* to volume. Allow the solution to stand for 4 h at room temperature. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, and use the clear filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 310 nm

Column: 3.0-mm × 15-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 0.6 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of etravirine ($C_{20}H_{15}BrN_6O$) in the portion of Tablets taken:

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

r_U = peak response of etravirine from the *Sample solution*

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Protect solutions containing etravirine from light.

Solution A: 0.01 M hydrochloric acid

Solution B: 2.25% sodium lauryl sulfate in *Solution A*

Medium

For Tablets labeled to contain 25 and 100 mg: 500 mL of *Solution A* and 400 mL of *Solution B*

For Tablets labeled to contain 200 mg: 1000 mL of *Solution A* and 800 mL of *Solution B*

Apparatus 2

For Tablets labeled to contain 25 and 100 mg: 50 rpm

For Tablets labeled to contain 200 mg: 70 rpm

Time

For Tablets labeled to contain 25 and 100 mg: 45 min

For Tablets labeled to contain 200 mg: 30 min

Mobile phase: Acetonitrile and 0.5% phosphoric acid (65:35)

Standard solution: 0.111 mg/mL of USP Etravirine RS in *Medium* for Tablets labeled to contain 100 and 200 mg; 0.0278 mg/mL of USP Etravirine RS in *Medium* for Tablets labeled to contain 25 mg, prepared as follows. Transfer a suitable amount of USP Etravirine RS to a suitable volumetric flask and dissolve in 5% of the total volume of 1-methyl-2-pyrrolidone. Add acetonitrile to 50% of the total volume, equilibrate to room temperature, and dilute with *Solution B* to volume.

Sample solution: Place 1 Tablet in each vessel filled with a volume of *Solution A* as specified in *Medium*. After 10 min, add a volume of preheated *Solution B* as specified in *Medium* and reset the time to zero. Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 3.0-mm × 5.0-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 0.5 mL/min

Injection volume

For Tablets labeled to contain 25 mg: 40 µL

For Tablets labeled to contain 100 and 200 mg: 10 µL

Run time: NLT 2 times the retention time of etravirine

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 etravirine ($C_{20}H_{15}BrN_6O$) dissolved:

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

r_U = peak response of etravirine from the *Sample solution*

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*; 900 mL for Tablets labeled to contain 25 and 100 mg; 1800 mL for Tablets labeled to contain 200 mg

Tolerances: NLT 80% (Q) of the labeled amount of etravirine ($C_{20}H_{15}BrN_6O$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Protect solutions containing etravirine from light.

Buffer, Diluent, Solution A, Solution B, Solution C, Mobile phase, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 0.10 mg/mL of USP Etravirine System Suitability Mixture RS prepared as follows. Transfer a suitable amount of USP Etravirine System Suitability Mixture RS to a suitable volumetric flask and dissolve in 10% of the total volume of 1-methyl-2-pyrrolidone. Dilute with *Diluent* to volume.

Sensitivity solution: 0.05 µg/mL of USP Etravirine RS from the *Standard solution* in *Diluent*

System suitability

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

Suitability requirements

Resolution: NLT 4.3 between the etravirine amino analog (4-[(4-Amino-5-bromo-6-chloropyrimidin-2-yl)amino]benzonitrile) and desbromoetravirine (4-{[6-amino-2-{(4-cyanophenyl)amino}pyrimidin-4-yl]oxy}-3,5-dimethylbenzonitrile), with peaks at relative retention times of 0.66 and 0.73, respectively; *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: The reporting threshold is 0.1%.

Any unspecified degradation product: NMT 0.20%

Total degradation products: NMT 0.50%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Etravirine RS

USP Etravirine System Suitability Mixture RS▲ (USP 1-Dec-2022)

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

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

Chromatographic Database Information: Chromatographic Database

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