

BRIEFING

Abacavir Tablets. This monograph has been posted on the USP Pending Monographs Web page for review and public comment for more than 90 days. The MD-AA Expert Committee has approved the monograph as an Authorized USP Pending Monograph. The following is a summary of the comments and the Expert Committee's decisions.

Comment 1: Commenter suggested correcting the preparation of the *Standard solution* in the *Assay* to include preparation of the *Standard stock solution* in the *Diluent* and the *Standard solution* in the *Mobile phase*.
Response: Comment was incorporated.

Comment 2: Commenter suggested clarifying the preparation of the *Buffer* in the test for *Organic Impurities* by specifying the final volume of solution.
Response: Comment was incorporated.

Comment 3: Commenter suggested deleting the run time to ensure that all organic impurities are eluted from the HPLC column in products not manufactured by the same process.
Response: Comment was incorporated.

Comment 4: Commenter suggested changing the solvent used in the dilution of the *Sample solution* in the test for *Organic Impurities* from the *Diluent* to the *Mobile phase*.
Response: Comment was incorporated.

Comment 5: Commenter suggested correcting the chemical names of abacavir related compounds in *Impurity Table 1*.
Response: Comment was incorporated.

The HPLC procedures in the *Assay* and in the test for *Organic Impurities* are based on analyses performed using an Inertsil ODS-3V brand of L1 column. The typical retention time of the abacavir peak is about 10.0 min for *Organic Impurities* and 6.5 min for the *Assay*.

(MD-AA: L. Santos, B. Davani. BPC: M. Marques.) RTS—
C63866

Abacavir Tablets

v.1 Authorized November 1, 2009

DEFINITION

Abacavir Tablets contain abacavir sulfate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of abacavir (C₁₄H₁₈N₆O).

IDENTIFICATION

- A. ULTRAVIOLET ABSORPTION (197U)**
Wavelength range: 250–350 nm
Sample solution: 13.2 µg/mL of abacavir in 0.1 N hydrochloric acid
- B.** The retention time of the abacavir peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

PROCEDURE

Buffer: 1.15 mg/mL of ammonium dihydrogen phosphate and 2 mg/mL of tetrabutyl ammonium hydrogen sulfate in water. Adjust with triethylamine to a pH of 6.00 ± 0.05. Pass the solution through a suitable 0.45-µm filter.

Mobile phase: Acetonitrile and *Buffer* (3:17)

Diluent: 0.1 N hydrochloric acid

Standard stock solution: 0.88 mg/mL of USP Abacavir Sulfate RS in *Diluent*

Standard solution: 88 µg/mL of USP Abacavir Sulfate RS in *Mobile phase*. Pass the solution through a suitable 0.45-µm filter.

Sample stock solution: Transfer an equivalent to 750 mg of abacavir from finely powdered Tablets (NLT 20) to a 1000-mL volumetric flask. Add about 800 mL of *Diluent*, and sonicate for about 10 min. Allow the solution to cool to room temperature. Dilute with *Diluent* to volume and mix.

Sample solution: 75 µg/mL of abacavir in *Mobile phase*. Pass the solution through a suitable 0.45-µm filter.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

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

Flow rate: 2 mL/min

Injection size: 20 µL

Column temperature: 30 ± 2°

Run time: 12 min

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3500 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of C₁₄H₁₈N₆O in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of abacavir multiplied by 2, 572.66

M_{r2} = molecular weight of abacavir sulfate, 670.74

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

DISSOLUTION (711)

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm

Time: 15 min

Standard solution: 15.6 µg/mL of USP Abacavir Sulfate RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable 0.45-µm filter.

Spectrometric conditions

Mode: UV absorption spectroscopy

Analytical wavelength: UV 297 nm

Blank: *Medium*

Calculate the percentage of abacavir dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times V \times D \times 100$$

A_U = absorbance of abacavir from the *Sample solution*

A_S = absorbance of abacavir from the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

D = dilution factor of solution under test

M_{r1} = molecular weight of abacavir multiplied by 2, 572.66

M_{r2} = molecular weight of abacavir sulfate, 670.74

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

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

IMPURITIES

Organic Impurities

PROCEDURE

Buffer: 1.15 mg/mL of ammonium dihydrogen phosphate and 2 mg/mL of tetrabutyl ammonium hydrogen sulfate in water. Add 2 mL of triethylamine in 1000 mL of solution, and adjust with orthophosphoric acid to a pH of 6.00 ± 0.05. Pass the solution through a suitable 0.45-µm filter.

2 / Abacavir Tablets

Mobile phase: Acetonitrile and Buffer (3:17)
Standard solution: 2.9 µg/mL of USP Abacavir Sulfate RS in Mobile phase
Sample solution: Transfer an equivalent to 50 mg of abacavir from finely powdered Tablets (NLT 20) to a 100-mL volumetric flask. Add about 80 mL of Mobile phase, and sonicate for about 10 min. Allow the solution to cool to room temperature. Dilute with Mobile phase to volume and mix.

Chromatographic system

(See Chromatography <621>, System Suitability.)

Mode: LC

Detector: UV 214 nm

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

Flow rate: 1.2 mL/min

Injection size: 20 µL

Sample temperature: 5°

Column temperature: 30 ± 2°

System suitability

Sample: Standard solution

Suitability requirements

Column efficiency: NLT 3000 theoretical plates for the abacavir peak

Tailing factor: NMT 2.0 for the abacavir peak

Relative standard deviation: NMT 5.0%

Analysis

Samples: Standard solution and Sample solution

[NOTE—The relative retention times are listed in Impurity Table 1.]

Calculate the percentage of each impurity and unknown impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = response of each impurity peak in the Sample solution

r_S = response of abacavir in the Standard solution
 C_S = concentration of USP Abacavir Sulfate RS in the Standard solution (mg/mL)
 C_U = nominal concentration of abacavir in the Sample solution (mg/mL)
 M_{r1} = molecular weight of abacavir multiplied by 2, 572.66
 M_{r2} = molecular weight of abacavir sulfate, 670.74

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Abacavir related compound A ^a	0.38	0.2
Abacavir related compound B ^b	0.71	0.2
Abacavir related compound C ^c	0.79	0.2
Abacavir	1.00	—
Any unknown impurity	—	0.2

^a 4-(2,6-Diamino-9H-purin-9-yl)cyclopent-2-ene-yl-methanol.

^b [4-(2,5-Diamino-6-chloropyrimidin-4-ylamino)cyclopent-2-enyl]methanol.

^c [(1S,4R)-4-(2-Amino-6-chloro-9H-purin-9-yl)cyclopent-2-enyl]methanol.

Acceptance criteria

Total impurities: NMT 1.0%

ADDITIONAL REQUIREMENTS

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