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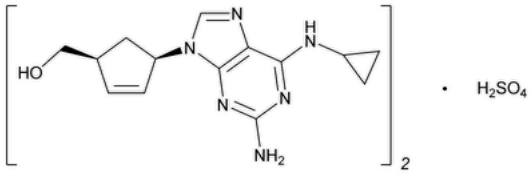
# Abacavir Sulfate



$(C_{14}H_{18}N_6O)_2 \cdot H_2SO_4$ 670.74

2-Cyclopentene-1-methanol, 4-[2-amino-6-(cyclopropyl amino)-9*H*-purin-9-yl]-, (1*S-cis*)-, sulfate (salt) (2:1);

(1*S*,4*R*)-4-[2-Amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol sulfate (salt) (2:1) CAS RN®: 188062-50-2; UNII: J220T4J9Q2.

**DEFINITION**

Abacavir Sulfate contains NLT 97.0% and NMT 102.0% of $(C_{14}H_{18}N_6O)_2 \cdot H_2SO_4$, calculated on the anhydrous and solvent-free basis.

**IDENTIFICATION**

***Change to read:***

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, obtained as directed in the test for *Organic Impurities, Procedure 2*.

• **C.** **Identification Tests—General, *Sulfate* ⟨191⟩**

**Sample solution:** 5 mg/mL

**ASSAY**

• **Procedure**

**Mobile phase:** Acetonitrile, phosphoric acid, and water (20:1:180)

**Standard solution:** 0.04 mg/mL of USP Abacavir Sulfate RS in water

**Sample solution:** 0.04 mg/mL of Abacavir Sulfate in water

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 254 nm

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

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection size:** 20 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Relative standard deviation:** NMT 1.5%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of $(C_{14}H_{18}N_6O)_2 \cdot H_2SO_4$ in the portion of Abacavir Sulfate taken:

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

$r_U$ = peak area of abacavir from the *Sample solution*

$r_S$ = peak area of abacavir from the *Standard solution*

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

$C_U$ = concentration of Abacavir Sulfate in the *Sample solution* (mg/mL)

**Acceptance criteria:** 97.0%–102.0% on the anhydrous and solvent-free basis

## IMPURITIES

### Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.2%

### Organic Impurities

- **Procedure 1: Related Compounds**

**Solution A:** Trifluoroacetic acid and water (0.05:99.95)

**Solution B:** Methanol and water (17:3)

**Mobile phase:** See the gradient table below.

| Time (min) | *Solution A* (%) | *Solution B* (%) |
|---|---|---|
| 0 | 95 | 5 |
| 20 | 70 | 30 |
| 35 | 10 | 90 |
| 35.1 | 95 | 5 |
| 50 | 95 | 5 |

**System suitability solution:** 0.25 mg/mL of USP Abacavir Related Compounds Mixture RS in water

**Sample solution:** 0.25 mg/mL of Abacavir Sulfate in water

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 254 nm

**Column:** 3.9-mm × 15-cm; 5-µm packing L1

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection size:** 20 µL

**System suitability**

**Sample:** *System suitability solution*

**Suitability requirements**

**Resolution:** NLT 1.5 between abacavir and *trans*-abacavir

**Analysis**

**Sample:** *Sample solution*

Calculate the percentage of each impurity in the portion of Abacavir Sulfate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

$r_U$ = peak area of each impurity from the *Sample solution*

$r_T$ = sum of the areas of all the peaks from the *Sample solution*

**Acceptance criteria**

**Individual impurities:** See *Impurity Table 1*.

**Total impurities:** NMT 0.8%

**Impurity Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Descyclopropyl abacavir[a] | 0.65 | 0.2 |
| Abacavir | 1.00 | — |
| *trans*-Abacavir[b] | 1.04 | 0.2 |

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| *O*-Pyrimidine derivative abacavir[c] | 1.33 | 0.2 |
| *t*-Butyl derivative abacavir[d] | 1.67 | 0.2 |
| Any unspecified impurity | — | 0.1 |

[a] [(1*S*,4*R*)-4-(2,6-Diamino-9*H*-purin-9-yl)cyclopent-2-enyl]methanol.

[b] {(1*R*,4*R*)-4-[2-Amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-cyclopent-2-enyl}methanol.

[c] $N^6$-Cyclopropyl-9-{(1*R*,4*S*)-4-[(2,5-diamino-6-chloropyrimidin-4-yl oxy)methyl]cyclopent-2-enyl}-9*H*-purine-2,6-diamine.

[d] 9-[(1*R*,4*S*)-4-(*tert*-Butoxymethyl)cyclopent-2-enyl]-$N^6$-cyclopropyl-9*H*-purine-2,6-diamine.

- **Procedure 2: Enantiomeric Purity**

**Solution A:** Heptane, 2-propanol, and diethylamine (850:150:1).

**Solution B:** Heptane and 2-propanol (1:1)

**Mobile phase:** See the gradient table below.

| Time (min) | *Solution A* (%) | *Solution B* (%) | Flow Rate (mL/min) |
|---|---|---|---|
| 0 | 100 | 0 | 1.0 |
| 25 | 100 | 0 | 1.0 |
| 27 | 0 | 100 | 0.8 |
| 37 | 0 | 100 | 0.8 |
| 39 | 100 | 0 | 1.0 |
| 55 | 100 | 0 | 1.0 |

**Diluent:** Methanol and trifluoroacetic acid (200:1)

**System suitability solution:** Transfer a quantity of USP Abacavir Stereoisomers Mixture RS to a suitable volumetric flask, add a volume of *Diluent* equivalent to 30% of the final volume, and sonicate until the solid is fully dissolved. Add a volume of 2-propanol equivalent to about 30% of the final volume, mix, and dilute with heptane to volume to obtain 0.4 mg/mL of USP Abacavir Stereoisomers Mixture RS.

**Sample solution:** Transfer 4 mg of Abacavir Sulfate to a 10-mL volumetric flask. Add 3 mL of *Diluent*, and sonicate until the solid is fully dissolved. Add 3 mL of 2-propanol, mix, and dilute with heptane to volume.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 286 nm

**Column:** 4.6-mm × 25-cm; 10-µm packing L51

**Column temperature:** 30°

**Injection size:** 20 µL

**System suitability**

[Note—The relative retention times for *trans*-abacavir, abacavir enantiomer, and abacavir are 0.8, 0.9, and 1.0, respectively.]

**Sample:** *System suitability solution*

**Suitability requirements**

**Resolution:** NLT 1.0 between *trans*-abacavir and abacavir enantiomer; NLT 1.5 between abacavir enantiomer and abacavir

**Analysis**

**Sample:** *Sample solution*

Calculate the percentage of abacavir enantiomer in the portion of Abacavir Sulfate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

$r_U$ = peak area of abacavir enantiomer from the *Sample solution*

$r_T$ = total peak areas of abacavir and abacavir enantiomer from the *Sample solution*

**Acceptance criteria**

**Individual impurities:** NMT 0.3% of abacavir enantiomer

### SPECIFIC TESTS

• **Water Determination, *Method Ic*⟨921⟩:** NMT 0.5%

### ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Abacavir Sulfate RS

USP Abacavir Stereoisomers Mixture RS

A mixture of abacavir sulfate, abacavir enantiomer, and *trans*-abacavir.

USP Abacavir Related Compounds Mixture RS

A mixture of abacavir glutarate, *O*-pyrimidine derivative abacavir, descyclopropyl abacavir, *trans*-abacavir, and *t*-butyl derivative abacavir.

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| ABACAVIR SULFATE | Documentary Standards Support | SM12020 Small Molecules 1 |

**Chromatographic Database Information:** Chromatographic Database

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