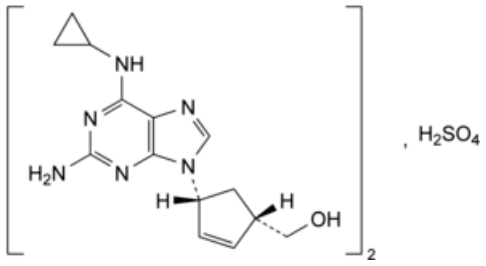
Edition: BP 2025 (Ph. Eur. 11.6 update)

Abacavir Sulfate

General Notices

(Ph. Eur. monograph 2589)



$C_{28}H_{38}N_{12}O_6S$ 671 *188062-50-2*

Action and use

Nucleoside reverse transcriptase inhibitor; antiviral (HIV).

Preparations

Abacavir Oral Solution

Abacavir Tablets

Abacavir, Zidovudine and Lamivudine Tablets

Abacavir and Lamivudine Tablets

Ph Eur

DEFINITION

Bis[[(1*S*,4*R*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]cyclopent-2-enyl]methanol] sulfate.

Content

99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white powder.

Solubility

Soluble in water, practically insoluble in ethanol (96 per cent) and in methylene chloride.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *abacavir sulfate CRS*.

B. Enantiomeric purity (see Tests).
C. Solution S (see Tests) gives reaction (a) of sulfates (2.3.1).

TESTS

Solution S

Dissolve 0.250 g in *water R* and dilute to 25.0 mL with the same solvent.

Enantiomeric purity

Liquid chromatography (2.2.29).

Solution A Mix 0.5 mL of *trifluoroacetic acid R* and 100 mL of *methanol R*.

Solution B Mix 30 volumes of *methanol R*, 30 volumes of *2-propanol R* and 40 volumes of *heptane R*.

Test solution Dissolve 40 mg of the substance to be examined in 30 mL of solution A. Sonicate until dissolution is complete. Add 30 mL of *2-propanol R* and dilute to 100.0 mL with *heptane R*.

Reference solution (a) Dissolve 2 mg of *abacavir for system suitability CRS* (containing impurities A and D) in 1.5 mL of solution A. Sonicate until dissolution is complete. Add 1.5 mL of *2-propanol R* and dilute to 5.0 mL with *heptane R*.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with solution B. Dilute 1.0 mL of this solution to 10.0 mL with solution B.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *amylose derivative of silica gel for chiral separation R* (10 µm);

— *temperature*: 30 °C.

Mobile phase:

— *mobile phase A*: *diethylamine R*, *2-propanol R*, *heptane R* (0.1:15:85 *V/V/V*);

— *mobile phase B*: *heptane R*, *2-propanol R* (50:50 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 25	100	0
25 - 27	100 → 0	0 → 100
27 - 37	0	100

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 286 nm.

Injection 20 µL.

Identification of impurities Use the chromatogram supplied with *abacavir for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A and D.

Relative retention With reference to abacavir (retention time = about 17 min): impurity D = about 0.8; impurity A = about 0.9.

System suitability Reference solution (a):

— *resolution*: minimum 1.5 between the peaks due to impurities D and A; minimum 1.5 between the peaks due to impurity A and abacavir.

Limit:

— *impurity A*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent).

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use and transfer them to low-adsorption, inert glass vials.*

Test solution Dissolve 25 mg of the substance to be examined in *water R* and dilute to 100.0 mL with the same solvent. Sonicate until dissolution is complete.

Reference solution (a) Dissolve 2.5 mg of *abacavir for peak identification CRS* (containing impurities B and D) in 10.0 mL of *water R*.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with *water R*. Dilute 1.0 mL of this solution to 10.0 mL with *water R*.

Column:

— *size*: *l* = 0.15 m, *Ø* = 3.9 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 µm);

— *temperature*: 30 °C.

Mobile phase:

— *mobile phase A*: dilute 0.5 mL of *trifluoroacetic acid R* in 1000 mL of *water R*;

— *mobile phase B*: *water R*, *methanol R* (15:85 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 5	95	5
5 - 25	95 → 70	5 → 30
25 - 40	70 → 10	30 → 90

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 20 µL.

Identification of impurities Use the chromatogram supplied with *abacavir for peak identification CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities B and D.

Relative retention With reference to abacavir (retention time = about 22 min): impurity D = about 1.04; impurity B = about 1.3.

System suitability Reference solution (a):

— *peak-to-valley ratio*: minimum 3.0, where H_p = height above the baseline of the peak due to impurity D and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to abacavir.

Limits:

— *impurity B*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Water (*2.5.32*)

Maximum 0.5 per cent, determined on 60.0 mg.

Sulfated ash (*2.4.14*)

Maximum 0.2 per cent, determined on 1.0 g.

ASSAY

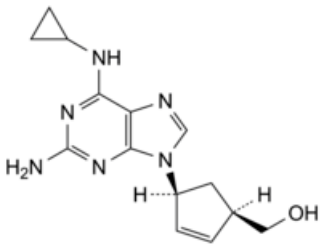
Dissolve 0.300 g in 50 mL of *water R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M sodium hydroxide* is equivalent to 33.54 mg of $C_{28}H_{38}N_{12}O_6S$.

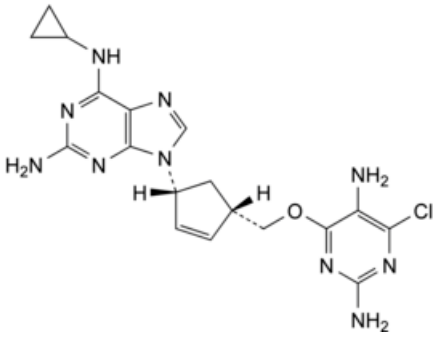
IMPURITIES

Specified impurities *A, B.*

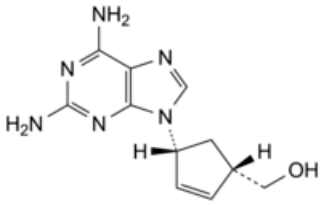
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *C, D, E, F.*



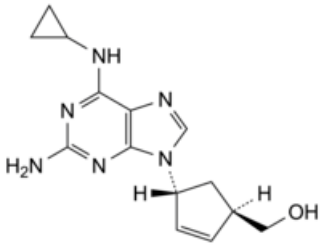
A. [(1*R*,4*S*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]cyclopent-2-enyl]methanol,



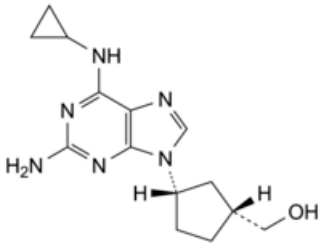
B. 6-(cyclopropylamino)-9-[(1*R*,4*S*)-4-[[(2,5-diamino-6-chloropyrimidin-4-yl)oxy]methyl]cyclopent-2-enyl]-9*H*-purine-2-amine,



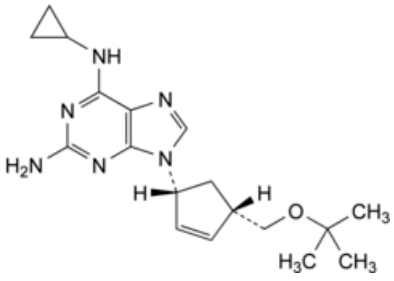
C. [(1*S*,4*R*)-4-(2,6-diamino-9*H*-purin-9-yl)cyclopent-2-enyl]methanol,



D. [(1*R*,4*R*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]cyclopent-2-enyl]methanol,



E. [(1*R*,3*S*)-3-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]cyclopentyl]methanol,



F. 6-(cyclopropylamino)-9-[(1*R*,4*S*)-4-[[(1,1-dimethylethyl)oxy]methyl]cyclopent-2-enyl]-9*H*-purine-2-amine.