Abacavir tablets (Abacaviri compressi)

Category. Antiretroviral (Nucleoside Reverse Transcriptase Inhibitor).

Storage. Abacavir tablets should be kept in a well-closed container.

Labelling. The designation of the container of Abacavir tablets should state that the active ingredient is in the sulfate form and the quantity should be indicated in terms of the equivalent amount of abacavir.

Additional information. Strength in the current WHO Model list of essential medicines: 300 mg of abacavir. Strength in the current WHO Model list of essential medicines for children: 300 mg of abacavir.

Requirements

Comply with the monograph for "Tablets".

Definition. Abacavir tablets contain Abacavir sulfate. They contain not less than 90.0% and not more than 110.0% of the amount of abacavir ($C_{14}H_{18}N_6O$) stated on the label.

Identity tests

• Either tests A, C and D, or tests B, C and D may be applied.

A. Carry out test A.1 or, where UV detection is not available, test A.2.

A.1 Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica R6 as the coating substance and a mixture of 8 volumes of dichloromethane R, 2 volumes of 2-propanol R as the mobile phase. Apply separately to the plate

5 µl of each of the following 2 solutions in methanol R. For solution (A) shake a quantity of the tablets containing the equivalent of 25 mg of abacavir with 5 mL, filter, and use the clear filtrate. For solution (B) use 6 mg of abacavir sulfate RS per mL. After removing the plate from the chromatographic chamber, allow it to dry exhaustively in air or in a current of cool air. Examine the chromatogram in ultraviolet light (254 nm).

The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

A.2. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using the conditions described above under test A.1 but using silica gel R5 as the coating substance. Spray with vanillin/sulfuric acid TS1. Heat the plate for a few minutes at 120°C. Examine the chromatogram in daylight.

The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

B. See method A described under Assay. The retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that in the chromatogram obtained with solution (2).

C. To a quantity of powdered tablets containing the equivalent of 15 mg abacavir add 100 mL of water R, shake and filter. Dilute 5 mL of the filtrate to 50 mL with the same solvent. The absorption spectrum (1.6) of the resulting solution, when observed between 220 nm and 320 nm, exhibits a maximum at about 291 nm.

D. To a quantity of the powdered tablets containing the equivalent of about 20 mg of abacavir add 5 mL of water R and shake. The resulting solution yields reaction A described under 2.1 General identification tests as characteristic of sulfates.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, using the chromatographic conditions as described under Assay method A.

Prepare the following solutions in the dissolution solvent prepared by diluting 1 mL of phosphoric acid (~ 1440 g/l) TS in 1 litre of water R.

For solution (1) transfer a quantity of the powdered tablets containing the equivalent of 10 mg of abacavir in the dissolution solvent and dilute to 50.0 mL with the same solvent. For solution (2) dilute 5.0 mL of solution (1) to 50.0 mL with the dissolution solvent. Then dilute 5.0 mL of this solution to 50.0 mL with the same solvent. For solution (3) dissolve 5 mg of abacavir sulfate for system suitability RS (containing abacavir sulfate and impurities B to F) in the dissolution solvent and dilute to 25 mL with the same solvent.

Inject separately 20 µl each of solution (1), (2) and (3) and of dissolution solvent in the chromatographic system. Examine the blank chromatogram for any extraneous peaks and disregard the corresponding peaks observed in the chromatogram obtained with solution (1).

In the chromatogram obtained with solution (3), the impurity peaks are eluted at the following relative retention with reference to abacavir (retention time about 19 minutes): impurity C about 0.7; impurity D about 1.05; impurity E about 1.10; impurity B about 1.3; impurity F about 1.7. The test is not valid unless the resolution between the peaks due to abacavir and impurity D is at least 1.5.

In the chromatogram obtained with solution (1) the area of any peak corresponding to impurity C is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%); the area of any peak with a relative retention less than that of impurity C (impurity G) is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%); the area of any other peak, apart from the principal peak, is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%). The sum of the areas of all peaks, other than the principal peak, is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2.0%). Disregard any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

Assay

• Either method A or method B my be applied

A. Weigh and powder 20 tablets. Carry out the test under *1.14.1 Chromatography*, High-performance liquid chromatography using a stainless steel column (15 cm x 4.6 mm), packed with octadecylsilyl silica gel for chromatography (5 µm).

The mobile phases for gradient elution consist of a mixture of Mobile phase A and Mobile phase B, using the following conditions:

Mobile phase A: 0.05% solution of trifluoroacetic acid R in water R.

Mobile phase B: 85 volumes of methanol R and 15 volumes of water R.

Time (min)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comments
0 - 20	95 - 70	5 to 30	Linear gradient
20 - 35	70 - 10	30 to 90	Linear gradient
35 - 40	10 - 95	90 to 5	Return to initial composition
40 - 45	95	5	Re-equilibration

Operate with a flow rate of 0.8 mL per minute and the column oven temperature at 30 °C. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 254 nm. Prepare the following solutions in the dissolution solvent prepared by diluting 1 mL of phosphoric acid (~ 1440 g/l) TS in 1 litre of water R.

For solution (1) transfer a quantity of the powdered tablets containing the equivalent of about 20 mg of abacavir, accurately weighed, to a 100-mL volumetric flask. Add about 80 mL of dissolution solvent, sonicate for about 5 minutes, allow to cool at room temperature, and make up to volume using the same solvent. Filter a portion of this solution through a 0.45-µm filter, discarding the first few mL of the filtrate. For solution (2) use 0.23 mg of abacavir sulfate RS per mL of dissolution solvent.

Inject alternatively 20 µl each of solution (1) and (2) and record the chromatograms.

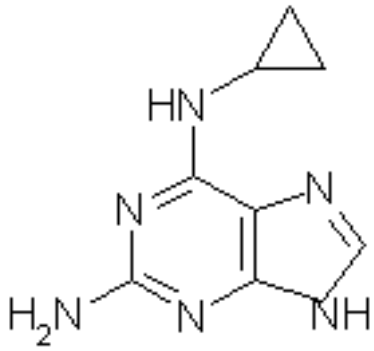
Measure the areas of the peak responses obtained in the chromatograms from solution (1) and (2), and calculate the content of abacavir ($C_{14}H_{18}N_6O$) in the tablets using the declared content of $(C_{14}H_{18}N_6O)_2,H_2SO_4$ in abacavir sulfate RS. Each mg of $(C_{14}H_{18}N_6O)_2,H_2SO_4$ is equivalent to 0.8537 mg of $C_{14}H_{18}N_6O$.

B. Weigh and powder 20 tablets. Transfer a quantity of the powdered tablets containing the equivalent of about 15 mg of abacavir, accurately weighed, to a 100-mL volumetric flask. Add about 25 mL of water R, sonicate for about 5 minutes, allow to cool to room temperature, and make up to volume using the same solvent. Filter a portion of this solution through a 0.45-µm filter, discarding the first few mL of the filtrate. Dilute 5.0 mL of the filtrate to 50.0 mL with the same solvent. Measure the absorbance (1.6) of this solution in a 1-cm layer at the maximum at about 291 nm against a solvent cell containing water R.

Calculate the content of abacavir ($C_{14}H_{18}N_6O$) in the tablets using an absorptivity value of 42 ($A^{1\%}_{1cm}$ = 420).

Impurities

The impurities limited by the requirements of this monograph include those listed in the monograph for Abacavir sulfate and the following:



G. (N^6-cyclopropyl-3*H*-purine-2,6-diamine)