Abacavir

\[ t_{1/2} : \text{0.9–3.7 h} \]
\[ V_d : \text{0.7–1.0 L/kg} \]
\[ F_b : \text{0.50} \]
\[ pK_a : \text{5.0 (base)} \]
\[ b/p : \text{1.0} \]
\[ CAS : \text{136470-78-5} \]
\[ MW : \text{286.33 (C}_{14}\text{H}_{18}\text{N}_6\text{O)} \]

Occurrence and Usage. Abacavir (Ziagen, ingredient of Epzicom, Kivexa, Trizivir) is a nucleoside analogue and reverse transcriptase inhibitor used in the treatment of HIV infections, often in combination with other antiviral agents, since 1998. It is available as the sulfate salt in 300–600 mg tablets and a 20 mg/mL solution for oral administration. It is also available in combination with lamivudine as a single tablet for once-daily dosing (Epzicom) and with lamivudine and zidovudine as a single tablet for twice-daily dosing (Trizivir). The recommended adult dose is 300 mg given twice daily or 600 mg once daily.

Blood Concentrations. A single oral 300 mg dose given to 18 adult HIV patients resulted in an average peak plasma abacavir concentration of 2.6 mg/L (range, 2.3–2.9) occurring at 0.4–1.1 hours and declining with an elimination half-life averaging 1.4 hours. The oral bioavailability of abacavir averages 83% (Chittick et al., 1999). A single oral 600 mg dose in 8 adult patients yielded an average peak plasma level of 4.7 mg/L at 1.7 hours, with a 1.7 hour elimination half-life (Kumar et al., 1999). Adult patients receiving twice-daily 300 mg oral doses for 12 weeks exhibited peak plasma levels averaging 3.0 mg/L (range, 2.4–3.7) at the end of the study (McDowell et al., 2000). Neither renal dysfunction (Izzedine et al., 2001) nor co-administration of lamivudine or zidovudine (Wang et al., 1999) was found to significantly alter the pharmacokinetics of abacavir.

Metabolism and Excretion. A single oral labeled abacavir dose is eliminated in the urine (83%) and feces (16%) over a 10 day period. Urinary elimination products include the 5'-glucuronide conjugate (36% of a dose), 5'-COOH-abacavir (30%) and unchanged drug (1.9%). None of the known metabolites has significant pharmacologic activity (Chittick et al., 1999; McDowell et al., 1999; PDR, 2001).

Toxicity. The adverse effects associated with abacavir therapy include nausea, vomiting, diarrhea, loss of appetite and insomnia. A hypersensitivity syndrome, potentially fatal, has been described that is often manifested by fatigue, myalgia, fever, dyspnea, headache, edema, paresthesia and skin rash. Genetic screening for the HLA-B*5701 allele, present in 6% of the population, has been recommended to preclude use of the drug in susceptible persons (Mallal et al., 2008). Two young women developed reversible hepatitis within 1–3 months of beginning therapy (Soni et al., 2008). A 47 year old man exhibited manic behavior one week after initiation of therapy with the drug (Brouilette and Routy, 2007). Anaphylaxis has occurred after temporary interruption of therapy, and at least one case of agranulocytosis has been described (Tikhomirov et al., 1999; Walensky et al., 1999; Frissen et al., 2001).

Analysis. Abacavir has been determined in biological fluids by liquid chromatography with ultraviolet (Veldkamp et al., 1999; Ravitch and Moseley, 2001; Sparidans et al., 2001; Ferrer et al., 2004) or mass spectrometric detection (Le Saux et al., 2008; Yadav et al., 2010).

Abacavir was stable in plasma for 4.5 hours at 60 °C (heat inactivation), 3 days at room temperature (Veldkamp et al., 1999) and 11 months at -20 or -80 °C (Sparidans et al., 2001). It was stable in urine for 5 hours at 58 °C and 6 weeks at -20 °C (Ravitch and Moseley, 2001).

References

Abamectin


Abamectin

Abamectin (avermectin B₁, Abba, Affirm, Avid, Zephyr) is an antimicrobial substance, produced by Streptomyces avermitilis, that has been used since 1980 as an insecticide and veterinary anthelmintic agent. It is supplied as the neutral substance, a mixture of at least 80% abamectin B₁b and 20% or less abamectin B₁a, in a 0.01% bait or spray, 0.5% solution, 2% concentrate and 46–92% technical chemical for insecticidal purposes and in a 5 mg/mL topical solution, 80 mg extended-release oral capsule or a 1% injectable solution for administration to large animals.

Blood Concentrations. Blood or plasma levels of abamectin have not been determined in exposed, asymptomatic humans. A single oral 0.2 mg/kg dose in horses led to an average peak plasma abamectin concentration of 35 µg/L after 1.5 days, declining with a 5.6 day elimination half-life (Echeverria et al., 2001). A single subcutaneous 0.25 mg/kg dose in cattle produced an average peak plasma level of 54 µg/L after 3.0 days, with a 2.8 day elimination half-life (Borges et al., 2007). A single subcutaneous 0.2 mg/kg dose in deer yielded a peak plasma level that averaged 110 µg/L at 20 hours; the elimination half-life averaged 5.0 days (Zele et al., 2011).

Metabolism and Excretion. A single oral labeled abamectin dose in rats was eliminated over 7 days in urine (0.4% of the dose) and feces (94%). Biotransformation occurred via hydroxymethyl formation or O-demethylation, resulting in two minor metabolites (FAO, 1992). Very similar results were obtained in goats (Maynard et al., 1989).