

## Abacavir and Its Salts

Abacavir is an antiviral drug for the treatment of Human immunodeficiency virus (HIV) infection. The drug is given as abacavir sulfate, which dissociates to produce abacavir. Abacavir is a carboxylic nucleoside analogue that inhibits HIV 1 in peripheral blood lymphocytes, macrophages and MT4 cells.

Abacavir and its salts passed the animal data screen, underwent a preliminary toxicological evaluation, and are being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

### Epidemiological data

No cancer epidemiology studies were identified.

### Animal carcinogenicity data

- Two-year oral gavage studies in rats
  - Male and female Han Wistar rats treated by gavage twice a day for two years: FDA (2001, pp. 8-9, 18)
    - *Increase in preputial gland squamous cell carcinoma (by pairwise comparison and trend) in males*
    - *Increase in clitoral gland squamous cell carcinoma (rare tumor), hepatocellular carcinoma, hepatocellular adenoma/carcinoma combined, thyroid follicular cell adenoma (by pairwise comparison and trend for each type of neoplasms) in females*
- Two-year oral gavage studies in mice
  - Male and female CD-1 mice administered by gavage twice a day for two years: FDA (2001, pp. 16, 18)
    - *Increase in preputial gland squamous cell carcinoma (by pairwise comparison and trend) in males*
    - *No treatment-related tumor findings in females*

## Other relevant data

- Genotoxicity as reviewed in FDA (2001, pp. 19, 42-45) and FDA approved Epzicom drug label (2011, p. 21)
  - *In vitro* chromosome aberration in human peripheral lymphocytes in the presence and absence of metabolic activation (*positive*)
  - *In vivo* bone marrow micronucleus assays in male and female CD-1 mice dosed orally (*positive in males and negative in females*)
  - Mouse lymphoma assays in the absence of metabolic activation (*positive*)
  - Mouse lymphoma assays in the presence of metabolic activation (*negative*)
  - Mutagenicity assays in *Salmonella typhimurium* (*negative*)
- Structure activity considerations
  - Abacavir belongs to the group of nucleoside analogues. Several chemicals in this group are Proposition 65 carcinogens, such as Ganciclovir, Zalcitabine and Zidovudine.

## Reviews

- FDA (2001)

## References<sup>1</sup>

FDA NDA review (NDA number: 20977). Pharmacologist's review. August 16, 2001.

FDA approved drug label for Epzicom (abacavir sulfate and lamivudine) tablets (2011).

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<sup>1</sup> Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.