Budesonide

16,17-Butylidenebis(oxy)-11-,21-dihydroxypregna-1,4-diene-3,20-dione

Budesonide is a synthetic glucocorticoid steroid for the treatment of asthma, non-infectious rhinitis, and for treatment and prevention of nasal polyposis.

Budesonide passed the animal data screen, underwent a preliminary toxicological evaluation, and is 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 drinking water studies
  - Male and female Sprague-Dawley rats: FDA (2001, pp.36-37, pp. 66-67)
    - *Increases in brain gliomas and primary hepatocellular neoplasms in males and primary mammary neoplasms in females (by pairwise comparison and trend)*
  - Male Sprague-Dawley rats: Ryrfeldt *et al*. (1992)
    - *Increase in hepatocellular adenomas and carcinomas combined (by pairwise comparison)*
  - Male Fischer 344 rats: FDA (2001, pp. 42-44, p. 67)
    - *No treatment related tumor findings by gross pathological examination. FDA audit of study indicated several serious regulatory deficits.*

- 91-week drinking water studies
  - Male and female CD-1 mice: FDA (2001, pp, 33-34, p. 66)
    - *Increase in lung alveolar/bronchiolar carcinomas in males (by trend)*
    - *No treatment related tumor findings in females*
    - *Inadequate numbers of male and female animals at risk for late occurring tumors*

Other relevant data

- Genotoxicity
  - Review: FDA (2001, p. 48, p. 67)
    - *S. typhimurium* reverse mutation*, D. melanogaster* recessive lethal mutation, and mouse lymphoma assays *(negative)*
    - Chromosome aberrations in cultured human lymphocytes *(negative)*

        - Micronuclei in mouse bone marrow *(negative)*
        - Unscheduled DNA synthesis *in vitro (negative)*

- Metabolism: FDA (2001, pp. 48-52, pp. 63-64, p. 67-68)
    - Budesonide is metabolized *in vitro* by human and animal liver microsomes to 21-dehydrobudesonide, which is mutagenic in *S. typhimurium*
    - *In vitro* incubation of budesonide with rat liver and brain S9 fractions results in covalent binding to tissue macromolecules

References[1]

FDA (2001). *Budesonide pharmacology reviews*. New Drug Application (NDA) #21-324. FDA Center for Drug Evaluation and Research.

Ryrfeldt A, Squire RA, Ekman L (1992). Liver tumors in male rats following treatment with glucocorticosteroids. *Toxicol Pathol* **20**:115-7.

[1] 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.