Hydralazine and Its Salts

Hydralazine and its salts are antihypertensive agents that act to dilate arterial smooth muscle. Hydralazine chloride is a prescription drug.

Hydralazine and its salts passed the human and animal data screens, 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

- Case-control study as reviewed in IARC (1980, pp. 94-95)
  - Elevated relative risk estimate (not significant) for breast cancer in National Breast-Cancer Screening project: Williams (1978)

- Cohort studies (no increased risk) as reviewed in IARC (1987, pp. 222-223)
  - all cancers: Rogers (1984)
  - breast cancers: Kaufman (1987)

- Case report as reviewed in IARC (1980, pp. 94-95)
  - Four of 24 patients with hydralazine toxicity developed cancer (2 breast carcinomas and 2 lung carcinomas). One of 92 patients without hydralazine toxicity developed cancer: Perry (1963)

Animal carcinogenicity data

- Lifetime drinking water studies
  - Male and female Swiss mice: Toth (1978)
    - Increase in lung tumors (by pairwise comparison) in male and female mice
  - Male and female Swiss mice: Drozdz et al. (1987)
    - Increase in lung tumors (by pairwise comparison) in male and female mice

- Long-term diet studies
  - 2-year gavage studies in male and female Sprague-Dawley rats: FDA (1985)
    - Increase in benign interstitial cell tumors (by pairwise comparison) in testes of males
    - Increase in benign hepatic neoplastic nodules (by pairwise comparison) in males and females
87-week diet study in male Sprague-Dawley rats: Gershbein (1992) as reviewed in CCRIS (1996)
- No treatment-related findings

Subcutaneous study
- No treatment-related findings

Other relevant data

- Genotoxicity: as reviewed by IARC or FDA (1986) or cited in CCRIS (1996)
  - Mutagenicity in *Salmonella typhimurium* strain TA100, TA102, TA1530, and TA 1535 (*positive*)
  - Mutagenicity in *Salmonella typhimurium* strain TA1537, TA 1538, TA 98 (*negative*): Tosk et al (1979)
  - *In vitro* poly A test (*positive*)
  - *Salmonella* intrasанquilne host mediated assay/NMRI mouse in tester strains TA100, TA1535, TA1537 (*positive*)
  - Sister chromatid exchange in Chinese hamster (*negative*)
  - BALB/3T3 cell formation assay (*negative*)
  - DNA repair test in rat hepatocytes (*positive and negative*)
  - DNA repair test inhuman fibroblasts (*negative*)
  - DNA repair test in rabbit hepatocytes (*positive in slow acetylator hepatocytes; negative in fast acetylator hepatocytes*)
  - Unscheduled DNA synthesis in rat hepatocytes (*negative*)
  - Unscheduled DNA synthesis in rat liver (*positive*)

- Mechanistic considerations
  - Decrease of superoxide dismutase and increase of free radicals in lung tissue: Drozdz et al. (1987)

Reviews

- IARC (1980)
- IARC (1987)
References


FDA (1986). NDA 8303: Review and Evaluation of Nonclinical Data (suppl). New correspondence; corresp. date 4/16/86.


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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.