

Nitrofurantoin

Nitrofurantoin is a widely used drug for the treatment of urinary tract infections.

Nitrofurantoin 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

- Hypothesis-generating cohort screening study for drug-cancer associations: Selby *et al.* (1989)
- Case report of benign liver tumor: Anttinen *et al.* (1982)

Animal carcinogenicity data

Long-term feed studies

- Two-year studies in mice
 - Male and female B6C3F₁ mice: NTP (1989)
 - Male and female BDF₁ mice: Ito *et al.* (1983), as cited by NTP (1989, p. 21)
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- Twenty-two-month studies in male and female Swiss mice: Butler *et al.* (1990)
- Two-year studies in rats
 - Female Sprague-Dawley rats: Wang *et al.* (1984)
 - Male and female F344/N rats: NTP (1989)

Transplacental administration studies

- Subcutaneous injection to pregnant ICR female mice (offspring sacrificed 32 weeks after birth): Nomura *et al.* (1984), as cited by IARC (1990, p. 215)

Other relevant data

- Genotoxicity
 - *Salmonella typhimurium* mutagenicity assays: NTP (1989)
 - Mouse lymphoma cell mutagenicity assay: NTP (1989)
 - Chinese hamster ovary (CHO) cell assay for sister chromatid exchange: NTP (1989)
 - CHO cell assay for chromosomal aberrations: NTP (1989)
 - Sex-linked recessive lethal assay in *Drosophila*: NTP (1989)
 - Reviews: NTP (1989, pp. 21-22), IARC (1990) and CCRIS (2006)

- Structure activity considerations: Similar in structure to furan and nitrofurazone, which are Proposition 65 carcinogens.

Reviews

- IARC (1990)

References¹

Anttinen H, Ahonen A, Leinonen A, Kallioinen M, Heikkinen ES (1982). Diagnostic imaging of focal nodular hyperplasia of the liver developing during nitrofurantoin therapy. *Acta Med Scand* **211**(3): 227-232.

Butler WH, Graham TC, Sutton ML (1990). Oncogenicity study of Macrochantin in Swiss Mice. *Fd Chem Toxic* **1**: 49-54.

Chemical Carcinogenesis Research Information System (CCRIS, 2006)
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International Agency for Research on Cancer (IARC, 1990). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*. Vol. 50: Nitrofurantoin. IARC, World Health Organization, Lyon, France.

National Toxicology Program (NTP, 1989). Toxicology and carcinogenesis studies of nitrofurantoin in F344/N rats and B6C3F₁ mice (feed studies). U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, Technical Report Series No. 341.

Selby JV, Friedman GD, Fireman BH (1989). Screening Prescription Drugs for Possible Carcinogenicity: Eleven to Fifteen Years of Follow-up. *Cancer Research* **49**:5736-5747.

Wang CY, Croft WA, Bryan GT (1984). Tumor production in germ-free rats fed 5-nitrofurans. *Cancer Letters* **21**: 303-308.

¹ Copies of these listed references, as either the abstract, the relevant sections of the publication, or the complete publication, have been provided to members of the Carcinogen Identification Committee. These references have been provided in the order in which they are discussed in this document.