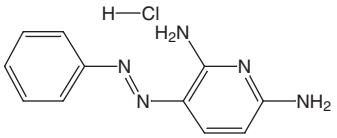
Phenazopyridine Hydrochloride
CAS No. 136-40-3

Reasonably anticipated to be a human carcinogen
First Listed in the *Second Annual Report on Carcinogens* (1981)



Carcinogenicity

Phenazopyridine hydrochloride is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1980, 1982, 1987, NCI 1978). When administered in the diet, phenazopyridine hydrochloride increased the incidences of hepatocellular adenomas and carcinomas in female mice and adenomas and adenocarcinomas of the colon and rectum in rats of both sexes.

There is inadequate evidence for the carcinogenicity of phenazopyridine hydrochloride in humans (IARC 1987). In one limited epidemiological study, no significant excess of any cancer was observed among 2,214 patients who received phenazopyridine hydrochloride and were followed for a minimum of 3 years.

Properties

Phenazopyridine hydrochloride occurs as brick-red microcrystals or powder with a violet luster and a slightly bitter taste. Aqueous solutions are yellow to brick-red and slightly acidic. It is slightly soluble in cold water, ethanol, and lanolin; soluble in boiling water, acetic acid, glycerol, ethylene glycol, and propylene glycol; and insoluble in acetone, benzene, chloroform, diethyl ether, and toluene. The commercial compound may contain some β,β-*N*-bis(phenylazo)-α,α′-diaminopyridine (HSDB 2001).

Use

Phenazopyridine hydrochloride has been used as an analgesic drug to reduce pain, burning, and discomfort associated with urinary tract infections or irritation. It is frequently used in combination with sulfonamides and antibiotics (IARC 1975, 1980, HSDB 2001, MEDLINEplus 2001).

Production

Commercial production of phenazopyridine hydrochloride in the United States began in 1944. By the early 1970s, only two companies reported producing this drug (IARC 1975). The USITC does not currently list any producers or production volumes for phenazopyridine hydrochloride. However, the Chem Sources USA directory identified three companies as producers and one as a supplier in the mid 1980's (Chem Sources 1984, 1986). Six current U.S. suppliers were listed (Chem Sources 2001). In 1980, domestic production was estimated to be 22,000 to 110,000 lb/year. In 1978, imports of the compound were reported by the USITC to total 15,400 lb (IARC 1980). In 1983, U.S. imports of phenazopyridine hydrochloride totaled over 17,000 lb (USITC 1984). No more recent production, import, or export data were located. Phenazopyridine hydrochloride was not included in the TSCA Inventory.

Exposure

Occupational exposure to phenazopyridine hydrochloride may occur through dermal contact or inhalation of dust during production, formulation, packaging, or administration. In the general population, exposure is most likely to occur from prescription medication (HSDB 2001). The typical adult oral dosage is 200 mg three times/day; the dosage for children is 4 mg/kg divided into three daily doses (MEDLINEplus 2001). Phenazopyridine hydrochloride was used in the past as a urinary antiseptic in a dose of 300 mg/day (IARC 1980). The National Occupational Exposure Survey (1981-1983) indicated that 2,547 workers, including 1,328 women, potentially were exposed to phenazopyridine hydrochloride (NIOSH 1984).

Regulations

CPSC

Any orally-administered, prescription drug for human use requires child-resistant packaging

FDA

Phenazopyridine hydrochloride is a prescription drug subject to labeling and other requirements

REFERENCES

ChemSources. 1984. Chem Sources, USA, 25th ed. Omond Beach, FL: Directories Publishing Company, Inc.
ChemSources. 1986. Chem Sources, USA, 27th ed. Omond Beach, FL: Directories Publishing Company, Inc.
ChemSources. 2001. Chemical Sources International, Inc. http://www.chemsources.com.
HSDB. 2001. Hazardous Substances Data Base. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.
IARC. 1975. Some Aromatic Azo Compounds. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 8. Lyon, France: International Agency for Research on Cancer. 357 pp.
IARC. 1980. Some Pharmaceutical Drugs. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 24. Lyon, France: International Agency for Research on Cancer. 337 pp.
IARC. 1982. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 4. Lyon, France: International Agency for Research on Cancer. 292 pp.
IARC. 1987. Overall Evaluations of Carcinogenicity. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 7. Lyon, France: International Agency for Research on Cancer. 440 pp.
MEDLINEplus. 2001. Phenazopyridine. National Library of Medicine. http://www.nlm.nih.gov/medlineplus/druginformation.html and search Phenazopyridine (Systemic).
NCI. 1978. Bioassay of Phenazopyridine Hydrochloride for Possible Carcinogenicity (CAS No. 136-40-3). Technical Report Series No 99. DHEW (NIH) Publication No. 78-1349. Bethesda, MD: National Institutes of Health. 115 pp.
NIOSH. 1984. National Occupational Exposure Survey (1981-83). Cincinnati, OH: U. S. Department of Health and Human Services. http://www.cdc.gov/noes/noes3/empl0003.html.
USITC. 1984. Imports of Benzenoid Chemicals and Products, 1983. USITC Publication No 1548. Washington, D.C.: U.S. Government Printing Office.