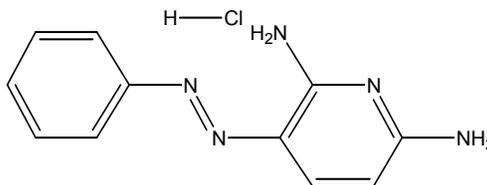


PHENAZOPYRIDINE HYDROCHLORIDE

CAS No. 136-40-3

First Listed in the *Second Annual Report on Carcinogens*



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 and ethanol, 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; the free base is not available commercially. Phenazopyridine hydrochloride decomposes at 235°C and emits toxic fumes of nitrogen oxides and hydrochloric acid. It is sensitive to air and light (HSDB 2001, NTP 2001).

USE

Phenazopyridine hydrochloride has been used for over 60 years as an analgesic drug to reduce pain, burning, and discomfort associated with urinary tract infection or irritation. It is also frequently used in combination with sulfonamides to treat infections of the urinary tract, mouth, and conjunctiva. Although it is not an antibiotic, it was used in the past as a urinary tract antiseptic (IARC 1975, HSDB 2001, MEDLINEplus 2001, NTP 2001).

PRODUCTION

Commercial production of phenazopyridine hydrochloride in the U.S. 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

EPA has proposed that phenazopyridine hydrochloride be subject to handling and reporting and record-keeping requirements under the Resource Conservation and Recovery Act (RCRA).

FDA has approved the use of phenazopyridine hydrochloride as a prescription drug for human use for symptomatic relief of pain and other discomforts arising from irritation of the lower urinary tract. FDA is considering labeling requirements for this drug concerning possible carcinogenicity and dose duration limitations.

OSHA regulates phenazopyridine hydrochloride under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 144.

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