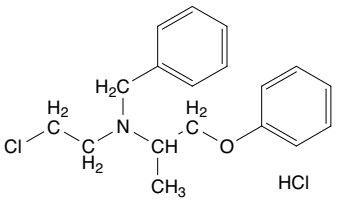
Phenoxybenzamine Hydrochloride

CAS No. 63-92-3

Reasonably anticipated to be a human carcinogen

First listed in the *Fifth Annual Report on Carcinogens* (1989)



Carcinogenicity

Phenoxybenzamine hydrochloride is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Exposure to phenoxybenzamine hydrochloride by injection caused tumors in two rodent species and at two different tissue sites. Intraperitoneal injection of phenoxybenzamine hydrochloride caused cancer of the abdominal cavity (sarcoma of the peritoneum) in mice and rats of both sexes (NCI 1978, IARC 1980). In strain A mice (a strain with a high spontaneous incidence of lung cancer), intraperitoneal injection of phenoxybenzamine (the free amine) increased the incidence of lung tumors in both sexes (IARC 1980).

Cancer Studies in Humans

The data available from epidemiological studies for phenoxybenzamine hydrochloride are inadequate to evaluate the relationship between human cancer and exposure specifically to phenoxybenzamine hydrochloride. Since phenoxybenzamine hydrochloride was listed in the *Fifth Annual Report on Carcinogens,* two case reports of patients receiving long-term treatment with phenoxybenzamine have been identified. Chronic lymphocytic leukemia and urinary-bladder cancer (small-cell and squamous-cell carcinoma) were reported in one case (Vaidyanathan *et al.* 2006) and cancer of the esophagus (squamous-cell carcinoma) in the other case (Nettesheim *et al.* 2003).

Properties

Phenoxybenzamine hydrochloride is the hydrochloride salt of a haloalkylamine (closely related chemically to the nitrogen mustards) that exists as a white crystalline powder at room temperature (Akron 2009). It is sparingly soluble in water, soluble in ethanol, chloroform, and propylene glycol, and insoluble in diethyl ether (IARC 1980). It is unstable in neutral and alkaline solutions and is sensitive to oxidation and photodegradation. Physical and chemical properties of phenoxybenzamine hydrochloride are listed in the following table.

Property	Information
Molecular weight	340.3
Melting point	137.5°C to 140°C
Log K_{ow}	3.12
Water solubility	15.2 mg/L at 25°C
Vapor pressure	5.56×10^{-12} mm Hg at 25°C

Source: ChemIDplus 2009.

Use

Phenoxybenzamine hydrochloride is an α-adrenergic receptor blocking agent that was used in the past to treat peripheral vascular disorders such as Raynaud's disease, to control hypertension, and to treat phlebitis, phlebothrombosis, diabetic gangrene, causalgia, chronic skin ulcers, and shock (NCI 1978, IARC 1980). It is now used primarily to treat hypertension and sweating caused by pheochromocytoma (MedlinePlus 2009). It may also be used to treat urinary-bladder problems such as urgency and frequency of urination and inability to control urination in patients with neurogenic bladder, functional outlet obstruction, or partial prostatic obstruction.

Production

Phenoxybenzamine hydrochloride has been produced commercially in the United States by one company since 1953 (IARC 1980). In 2009, it was available from 11 U.S. suppliers (ChemSources 2009). No data on amounts of U.S. production, imports, or exports of phenoxybenzamine hydrochloride were found.

Exposure

The only potential route of human exposure to phenoxybenzamine hydrochloride is ingestion during its medical use. The usual adult dosage is 10 mg twice a day, increasing to 20 to 40 mg two or three times a day, as long as there are no adverse effects on blood pressure (Mayo Clinic 2009). For children, the dose is based on body weight and typically begins at 0.2 mg/kg of body weight once a day, but may increase to 0.4 to 1.2 mg/kg given daily in three or four divided doses. The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 797 workers, including 406 women, potentially were exposed to phenoxybenzamine hydrochloride (NIOSH 1990).

Regulations

Consumer Product Safety Commission (CPSC)

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

Food and Drug Administration (FDA)

Phenoxybenzamine hydrochloride is regulated as a prescription drug subject to labeling and other requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

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