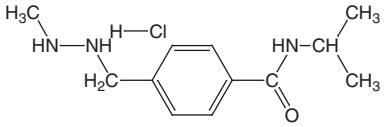
Procarbazine Hydrochloride
CAS No. 366-70-1

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



Carcinogenicity

Procarbazine hydrochloride is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (NCI 1979, IARC 1981, 1982, 1987). The generic name procarbazine is used interchangeably with procarbazine hydrochloride in the literature, and since only procarbazine hydrochloride is produced, it was assumed to be procarbazine hydrochloride under study. When administered by repeated intraperitoneal injection, procarbazine hydrochloride induced olfactory neuroblastomas, adenocarcinomas of the mammary gland, and malignant lymphomas in rats of both sexes. Olfactory neuroblastomas were induced in mice of both sexes, and uterine adenocarcinomas were induced in female mice. When administered by gavage, the compound induced leukemia and benign tumors of the lung in mice of both sexes and adenocarcinomas or carcinomas of the mammary gland in female rats, but not in male rats. When administered by repeated intravenous injections, the compound induced three renal sarcomas and two intra-abdominal spindle cell sarcomas in male rats. Male and female monkeys, including Rhesus, cynomolgus, and African green monkeys, were given procarbazine hydrochloride by subcutaneous, intravenous, and oral routes. Rhesus monkeys developed acute myelogenous leukemia. Cynomolgus monkeys developed leukemia or lymphoma, and multiple hemangiosarcomas. The rarity of neoplasms, and in particular leukemias (none in control monkeys in that colony), strongly suggests that procarbazine induced the tumors.

There is inadequate evidence for the carcinogenicity of procarbazine in humans (IARC 1987). In various combinations with other chemotherapeutic agents given for Hodgkin's disease, procarbazine use has repeatedly been shown to lead to the appearance of acute nonlymphocytic leukemia. These combinations typically also include nitrogen mustard, an alkylating agent that is also a potent animal carcinogen, and these observations do not permit conclusions about the independent effect of either drug.

Properties

Procarbazine hydrochloride is a white to pale yellow crystalline powder with a slight odor. It is sensitive to oxidation. It is very soluble in water and methanol and freely soluble in chloroform and diethyl ether (IARC 1981).

Use

Procarbazine hydrochloride is used in human medicine as an antineoplastic and chemotherapeutic agent. It is used in combination with other antineoplastic agents to treat Hodgkin's disease, malignant melanoma, non-Hodgkin's lymphoma, and small-cell carcinomas of the lung (IARC 1981). Procarbazine hydrochloride is marketed in 50 mg capsules (HSDB 2000).

Production

Procarbazine hydrochloride is not commercially produced in the United States (HSDB 2000). The USITC identified two U.S. producers of procarbazine hydrochloride in 1988, but no production data were reported (USITC 1989). No other production, import, or export data were located.

Exposure

The primary routes of potential human exposure to procarbazine hydrochloride are ingestion, inhalation, and dermal contact (HSDB 2000). For patients receiving the drug, the typical initial dose of procarbazine hydrochloride is 2 to 4 mg/kg body weight daily given orally in divided doses for 1 week, then 4 to 6 mg/kg body weight daily, until signs of bone marrow depression occur. After bone marrow recovery, treatment is resumed at a dose level of 1 to 2 mg/kg body weight per day (IARC 1981). Potential occupational exposure to procarbazine hydrochloride could occur during the manufacture, formulation, and packaging of the drug. The National Occupational Exposure Survey (1981-1983) indicated that 1,329 workers, including 289 women, potentially were exposed to procarbazine hydrochloride (NIOSH 1984). This estimate was derived from observations of the actual use of the compound (89% of total observations) and of trade name products known to contain the compound (11%). Health professionals such as physicians, nurses, and pharmacists are potentially exposed to the pharmaceuticals during preparation, administration, and cleanup.

Regulations

CPSC

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

FDA

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

REFERENCES

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