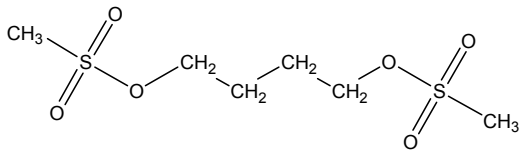
1,4-BUTANEDIOL DIMETHANESULFONATE (MYLERAN®)
CAS No. 55-98-1

First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

1,4-Butanediol dimethanesulfonate (Myleran®; busulfan) is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity in humans (IARC 1982, 1987). Patients receiving 1,4-butanediol dimethanesulfonate treatment developed leukemia as well as cytological and hematological abnormalities.

An IARC Working Group reported that there is limited evidence of carcinogenicity of 1,4-butanediol dimethanesulfonate in experimental animals (IARC 1982, 1987). When administered intraperitoneally, one study reported that 1,4-butanediol dimethanesulfonate induced T-cell lymphomas in male mice; two other studies reported that it did not increase the incidence of tumors. When administered by intravenous injection, 1,4-butanediol dimethanesulfonate increased the incidence of thymic lymphomas and ovarian tumors in female mice (IARC 1974, 1982, 1987). One study reported that pulmonary lesions developed in mice treated with 1,4-butanediol dimethanesulfonate, but the route of administration was not specified. 1,4-Butanediol dimethanesulfonate administered intravenously induced a variety of tumors in male rats, but an IARC Working Group reported that the experiments could not be evaluated due to a lack of information.

PROPERTIES

1,4-Butanediol dimethanesulfonate is a white crystalline powder that is practically insoluble in water, but is soluble in acetone; however, it is sensitive to moisture and readily hydrolyzes in water. When burned, it emits toxic fumes of sulfur oxides, carbon monoxide, and carbon dioxide. The commercial product contains a minimum of 98% 1,4-butanediol dimethanesulfonate (IARC 1974, Aldrich Chemical 1997, NTP 2001).

USE

1,4-Butanediol dimethanesulfonate is used as a chemotherapeutic agent to treat some forms of leukemia, particularly chronic myelocytic leukemia (IARC 1974, 1982). It also may be used in combination with cyclophosphamide as a conditioning regimen prior to bone marrow transplants for chronic myelogenous leukemia. 1,4-Butanediol dimethanesulfonate is given in tablets or by intravenous injection (MEDLINEplus 2001, RxList 2001).

PRODUCTION

One U.S. company has produced 1,4-butanediol dimethanesulfonate since 1954 (IARC 1974, SRI 1992). Total annual production was believed to be less than 500 kg (1,100 lb) (IARC 1974). Five current U.S. suppliers were listed by Chem Sources (2001). No data on imports or exports were available.

EXPOSURE

Patients may be exposed to 1,4-butanediol dimethanesulfonate during its use in chemotherapeutic treatment by ingestion or intravenous administration. The typical dosage level (tablet form) is 4 to 8 mg daily (IARC 1974). The recommended intravenous dose given prior to bone marrow transplant is 0.8 mg/kg body weight given as a two hour infusion every six hours for four days (RxList 2001). Potential occupational exposure may occur for workers formulating or packaging the tablets and for health care professionals administering the drug. The National Occupational Exposure Survey (1981-1983) estimated that a total of 1,763 workers, including 893 females, potentially were exposed to 1,4-butanediol dimethanesulfonate (NIOSH 1984).

REGULATIONS

1,4-Butanediol dimethanesulfonate is a pharmaceutical and is used in relatively small amounts; therefore, it is of little regulatory concern to EPA. However, there may be a small pollution problem relative to hospital wastes.

FDA regulates 1,4-butanediol dimethanesulfonate under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug approved for human use. FDA requires warning labels on drugs containing 1,4-butanediol dimethanesulfonate concerning potential carcinogenicity, mutagenicity, teratogenicity, and/or impairment of fertility.

OSHA regulates 1,4-butanediol dimethanesulfonate as a chemical hazard in laboratories under the Hazard Communication Standard. Regulations are summarized in Volume II, Table 26.

REFERENCES

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