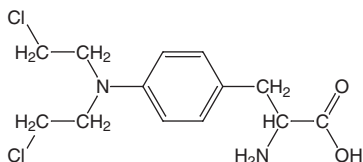


Melphalan

CAS No. 148-82-3

Known to be a human carcinogen

First Listed in the *First Annual Report on Carcinogens* (1980)



Carcinogenicity

Melphalan is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity in humans. Epidemiological studies found that patients treated with melphalan for breast cancer, ovarian cancer, and multiple myeloma (bone-marrow cancer) had an increased risk of leukemia (a relative risk greater than 100). The risk of leukemia increased with increasing dose of melphalan but was not affected by co-exposure to radiation therapy (IARC 1987).

There is sufficient evidence for the carcinogenicity of melphalan in experimental animals. When administered by intraperitoneal injection, melphalan caused lymphosarcoma in male mice, lung tumors in mice of both sexes, and peritoneal sarcoma in rats of both sexes (IARC 1975, 1987).

Properties

Melphalan is an alkylating agent and a derivative of nitrogen mustard. It is an odorless, white to buff-colored powder with a molecular weight of 305.2. It decomposes at its melting point, which is reported as 177°C to 182°C. Melphalan is practically insoluble in water but is soluble in ethanol, propylene glycol, alkaline solution, and dilute mineral acid (IARC 1975). Its log octanol-water partition coefficient is -0.52. When heated to decomposition, melphalan emits toxic fumes of hydrochloric acid, other chlorinated compounds, and nitrogen oxides (HSDB 2003).

Use

Melphalan is used as a drug to treat cancer and other medical conditions, including ovarian cancer, malignant melanoma, multiple myeloma (bone-marrow cancer), breast cancer, advanced prostate cancer, testicular cancer (seminoma), chronic myelogenous leukemia, osteogenic sarcoma (childhood bone cancer), polycythemia vera (overproliferation of blood cells), amyloidosis (accumulation of amyloid protein in tissues), and scleromyxedema (a rare skin disease). It also is used as an insect chemosterilant (IARC 1975, HSDB 2003, MEDLINEplus 2003).

Production

In 2003, one U.S. manufacturer (HSDB 2003), two U.S. suppliers of melphalan (ChemSources 2003), and one U.S. pharmaceutical company with drug products approved by the U.S. Food and Drug Administration (FDA) containing melphalan as the active ingredient were identified (FDA 2003). Imports of melphalan totaled 165 kg (364 lb) in 1983 (HSDB 2003). No other data on imports or exports were found.

Exposure

The general population is not expected to be exposed to melphalan, because its use is limited to medical treatment. Melphalan is available in 2-mg tablets and in an injectable form (melphalan hydrochloride, 50 mg/vial) (FDA 2003). The usual oral dose is 6 mg daily for two to

three weeks, followed by a rest period of about four weeks. Maintenance therapy is usually 2 to 4 mg per day. For intravenous therapy, the usual dose is 16 mg/m² infused over 15 to 20 minutes, repeated at two-week intervals for four doses and then at four-week intervals (Chabner *et al.* 2001).

Health professionals, such as pharmacists, nurses, and physicians, who handle melphalan could potentially be exposed during drug preparation, administration, or cleanup; however, exposure can be avoided through use of appropriate containment equipment and work practices (Zimmerman *et al.* 1981). One investigation reported that exposure of hospital personnel to melphalan could be reduced by treating excess solutions, spills, and urinals with chlorine bleach (Hansel *et al.* 1997). Occupational exposure also may occur during drug formulation or packaging. The National Occupational Exposure Survey (1981–1983) estimated that 2,418 workers, including 974 women, potentially were exposed to melphalan (NIOSH 1984).

Regulations

CPSC

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

EPA

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable Quantity (RQ) = 1 lb

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - U150

Listed as a Hazardous Constituent of Waste

FDA

Melphalan is a prescription drug subject to specific labeling requirements

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