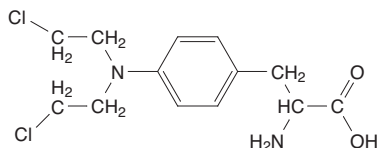


Melphalan

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 from studies in humans.

Cancer Studies in Humans

Epidemiological studies found that patients treated with melphalan for breast cancer, ovarian cancer, and bone-marrow cancer (multiple myeloma) had an increased risk of leukemia (relative risk > 100). The risk of leukemia increased with increasing dose of melphalan but was not affected by co-exposure to radiation therapy (IARC 1987).

Cancer Studies in Experimental Animals

There is sufficient evidence for the carcinogenicity of melphalan from studies in experimental animals. When administered by intraperitoneal injection, melphalan caused cancer of lymphatic tissue (lymphosarcoma) in male mice, lung tumors in mice of both sexes, and cancer of the abdominal cavity (sarcoma of the peritoneum) in rats of both sexes (IARC 1975, 1987).

Properties

Melphalan is an alkylating agent that is a white to buff odorless powder at room temperature. It is practically insoluble in water, insoluble in chloroform and ether, slightly soluble in methanol, and soluble in ethanol, propylene glycol, 2% carboxymethylcellulose, and alkaline and dilute acid solutions. It hydrolyzes in aqueous solution (IARC 1975). Physical and chemical properties of melphalan are listed in the following table.

Property	Information
Molecular weight	305.2 ^a
Melting point	182°C to 183°C (decomposes) ^a
Log K_{ow}	-0.52 (at pH 7) ^a
Water solubility	0.0457 g/L at 25°C ^b
Vapor pressure	3×10^{-10} mm Hg at 25°C ^b

Sources: ^aHSDB 2009, ^bChemIDplus 2009.

Use

Melphalan is used as a drug to treat cancer and other medical conditions, including ovarian cancer, malignant melanoma, multiple myeloma, breast cancer, advanced prostate cancer, testicular cancer, chronic myelogenous leukemia, osteogenic sarcoma, polycythemia vera, amyloidosis, and scleromyxedema (a rare skin disease). It is also used as an insect chemosterilant (IARC 1975, HSDB 2009, MedlinePlus 2009).

Production

In 2009, melphalan was produced by one U.S. manufacturer (HSDB 2009) and was available from 11 U.S. suppliers (ChemSources 2009), and drug products approved by the U.S. Food and Drug Administration containing melphalan as the active ingredient were produced by

one U.S. pharmaceutical company (FDA 2009). Imports of melphalan totaled 165 kg (364 lb) in 1983 (HSDB 2009). No other data on U.S. imports or exports of melphalan 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, in 50-mg vials) (FDA 2009). 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). In 2009, 428 clinical trials involving melphalan were in progress or recently completed (ClinicalTrials 2009).

Health professionals who handle melphalan, such as pharmacists, nurses, and physicians, 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 study 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 (conducted from 1981 to 1983) estimated that 2,418 workers, including 974 women, potentially were exposed to melphalan (NIOSH 1990).

Regulations

Consumer Product Safety Commission (CPSC)

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

Environmental Protection Agency (EPA)

Comprehensive Environmental Response, Compensation, and Liability Act
Reportable quantity (RQ) = 1 lb.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste code for which the listing is based wholly or partly on the presence of melphalan = U150.
Listed as a hazardous constituent of waste.

Food and Drug Administration (FDA, an HHS agency)

Melphalan is a prescription drug subject to specific labeling requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

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

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

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

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