

# International Agency for Research on Cancer (IARC) - Summaries & Evaluations

## NITROGEN MUSTARD (Group 2A)

For definition of Groups, see [Preamble Evaluation](#).

**Supplement 7:** (1987) (p. 269)

**CAS No.:** 51-75-2

**Chem. Abstr. Name:** 2-Chloro-*N*-(2-chloroethyl)-*N*-methylethanamine

### A. Evidence for carcinogenicity to humans (*limited*)

No epidemiological study of nitrogen mustard as a single agent was available to the Working Group. However, it is the principal alkylating agent in leukaemogenic combination chemotherapy given for Hodgkin's disease, and other alkylating agents are clearly leukaemogenic. The many case reports of cancer following topical application of nitrogen mustard cannot be interpreted with certainty because concurrent treatment with radiation and other potent drugs has been the rule rather than the exception, and occasionally such associations would be expected by chance.

Squamous-cell carcinomas of the skin following long-term topical application of nitrogen mustard alone or in combination with systemic therapy for mycosis fungoides [ref: 1-4] and psoriasis [ref: 5-7] have been observed to appear on skin surfaces not exposed to the sun.

### B. Evidence for carcinogenicity to animals (*sufficient*)

Nitrogen mustard, administered mainly as the hydrochloride, has been tested for carcinogenicity in mice and rats by subcutaneous, intravenous and intraperitoneal administration and by skin painting. It produced mainly lung tumours and lymphomas in mice after subcutaneous, intravenous and intraperitoneal administration. Intravenous injection of nitrogen mustard to rats induced tumours in different organs [ref: 8]. Application by skin painting produced local tumours in mice in a dose-dependent manner [ref: 9,10].

### C. Other relevant data

Nitrogen mustard is a bifunctional alkylating agent. In one study, it induced chromosomal aberrations in lymphocytes of treated patients [ref: 11].

Nitrogen mustard induced dominant lethal mutations and micronuclei in bone-marrow cells of mice exposed *in vivo* and alkylated DNA of ascites cells in experimental animals treated *in vivo*. It induced chromosomal aberrations, sister chromatid exchanges and unscheduled DNA synthesis in human cells *in vitro*. In rodent cells *in vitro*, it induced sister chromatid exchanges, chromosomal aberrations and DNA damage; studies on the induction of mutation were inconclusive. It transformed mouse C3H 10T1/2 cells. Nitrogen mustard induced aneuploidy and somatic mutation and recombination in *Drosophila*, chromosomal aberrations in plants, mitotic recombination and mutation in fungi, and mutation and DNA damage in fungi [ref: 11].

## Overall evaluation

Nitrogen mustard is *probably carcinogenic to humans (Group 2A)*.

For definition of the italicized terms, see [Preamble Evaluation](#).

Also see previous evaluation: [Vol. 9 \(1975\)](#)

## References

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2. Kravitz, P.H. & McDonald, C.J. (1978) Topical nitrogen mustard induced carcinogenesis. Acta dermatol. venereol., 58, 421-425
3. Lee, L.A., Fritz, K.A., Golitz, L., Fritz, T.J. & Weston, W.L. (1982) Second cutaneous malignancies in patients with mycosis fungoides treated with topical nitrogen mustard. J. Am. Acad. Dermatol., 7, 590-598
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6. Ganor, S. (1983) Skin cancer in psoriatics treated with nitrogen mustard. J. Am. Acad. Dermatol., 8, 164
7. Halprin, K.M., Comerford, M. & Taylor, J.R. (1982) Skin cancer in psoriatics treated with nitrogen mustard. J. Am. Acad. Dermatol., 8, 164-165
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9. Zackheim, H.S. & Smuckler, E.A. (1980) Tumorigenic effect of topical mechlorethamine, BCNU and CCNU in mice. Experientia, 36, 1211-1212
10. Epstein, J.H. (1984) Nitrogen mustard (mechlorethamine) and UVB photocarcinogenesis: a dose response effect. J. invest. Dermatol., 83, 320-322
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## Synonyms

- *N,N'*-Bis(2-chloroethyl)-*N*-methylamine
- *N,N*-Bis(2-chloroethyl)methylamine
- Bis(2-chloroethyl)methylamine
- Bis( $\beta$ -chloroethyl)methylamine
- Caryolysin

- Chloramine
- Chlormethine
- Cloramin
- $\beta,\beta'$ -Dichlorodiethyl-N-methylamine
- Di(2-chloroethyl)methylamine
- 2,2'-Dichloro-*N*-methyl-diethylamine
- Embichin
- HN2
- MBA
- Mechlorethamine
- *N*-Methyl-bis(2-chloroethyl)amine
- *N*-Methyl-bis( $\beta$ -chloroethyl)amine
- Methylbis(beta-chloroethyl)amine
- Methylbis(chloroethylamine)
- *N*-Methyl-2,2'-dichlorodiethylamine
- Methyl-di(2-chloroethyl)amine
- Mustargen
- Mustine
- Mutagen

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## NITROGEN MUSTARD (HYDROCHLORIDE)

VOL.: 9 (1975) (p. 193)

CAS No.: 51-75-2

Chem. Abstr. Name: 2-Chloro-*N*-(2-chloroethyl)-*N*-methylethanimine

CAS No.: 55-86-7

Chem. Abstr. Name: 2-Chloro-*N*-(2-chloroethyl)-*N*-methylethanimine hydrochloride

### 5. Summary of Data Reported and Evaluation

#### 5.1 Animal carcinogenicity data

Nitrogen mustard, administered mainly as the hydrochloride, is carcinogenic in mice and rats. Following its subcutaneous, intraperitoneal or intravenous injection, it produced an increased incidence of lung tumours and thymic lymphomas in mice; it produced a variety of malignant tumours in rats following its intravenous injection.

#### 5.2 Human carcinogenicity data

No case reports or epidemiological studies referring to exposures to nitrogen mustard alone were available to the Working Group.

Subsequent evaluation: [Suppl. 7 \(1987\) \(Nitrogen mustard\)](#)

#### Synonyms for Nitrogen mustard

- *N,N*-Bis(2-chloroethyl)-*N*-methylamine
- *N,N*-Bis(2-chloroethyl)methylamine
- Bis(2-chloroethyl)methylamine
- Bis( $\beta$ -chloroethyl)methylamine
- Caryolysin
- Chloramine
- Chlormethine
- Cloramin
- $\beta,\beta'$ -Dichlorodiethyl-*N*-methylamine
- Di(2-chloroethyl)methylamine
- $\beta,\beta'$ -Dichloro-*N*-methyldiethylamine
- Embichin
- HN2
- MBA
- Mechlorethamine
- *N*-Methyl-bis(2-chloroethyl)amine
- *N*-Methyl-bis( $\beta$ -chloroethyl)amine
- Methylbis( $\beta$ -chloroethyl)amine
- Methylbis(chloroethyl)amine
- *N*-Methyl-2,2'-dichlorodiethylamine

- Methyl-di(2-chloroethyl)amine
- Mustargen
- Mustine
- Mutagen
- Nitrogen mustard

### **Synonyms for Nitrogen mustard hydrochloride**

- Azotoperite
- *N,N*-Bis(2-chloroethyl)methylamine hydrochloride
- Bis(2-chloroethyl)methylamine hydrochloride
- Caryolysine
- Chloramin
- Chloramine
- Chlorethamine
- Chlorethazine
- Dichloren
- $\beta_1$ -Dichlorodiethyl-*N*-methylamine hydrochloride
- Di(2-chloroethyl)methylamine hydrochloride
- Di(chloroethyl)methylamine chloride
- $\beta,\beta'$ -Dichloro-*N*-methyl-diethylamine hydrochloride
- Dimitan
- Embichin
- Embikhine
- Erasol
- HN2
- HN2 hydrochloride
- MBA hydrochloride
- Mebichloramine
- Mechlorethamine
- Mechlorethamine hydrochloride
- Metagen
- *N*-Methylbis(2-chloroethyl)amine hydrochloride
- Methylbis(2-chloroethyl)amine hydrochloride
- *N*-Methylbis( $\beta$ -chloroethyl)amine hydrochloride
- Methylbis( $\beta$ -chloroethyl)amine hydrochloride
- *N*-Methyl-2,2'-dichlorodiethylamin hydrochloride
- Methyl-di(2-chloroethyl)amine hydrochloride
- Methyl-di( $\beta$ -chloroethyl)amine hydrochloride
- Mitoxine
- Mustargen
- Mustargen hydrochloride
- Mustine
- Mustine Hydrochlor
- Mustine hydrochloride
- Nitrogen mustard
- Nitrogranulogen
- N-Lost
- NSC-762 hydrochloride

