What is topical nitrogen mustard?

Topical nitrogen mustard (mechlorethamine), also called Mustargen™ or NM, is a commonly used topical chemotherapy agent that is prescribed to patients with mycosis fungoides (MF). It is efficient in treating patches or plaques. Since its discovery of use in 1959, NM has been the most widely used topical (applied to the skin) chemotherapy in treating MF. While NM is not FDA-approved for MF, clinical trials are currently being conducted in order to get FDA approval. Topical NM may be used as an aqueous (water)-based preparation, ointment-based preparation (mixed with Aquaphor), or as a propylene glycol gel-preparation.

How does nitrogen mustard work?

When nitrogen mustard is administered systemically, it acts as an alkylating agent with an anti-mitotic effect. The NM used in medicine includes mechlorethamine, cyclophosphamide, ifosfamide, melphalan, and chlorambucil. Mechlorethamine is the only NM used as a topical agent in the management of cutaneous lymphomas. The alkylating agents have a common property of becoming strong electrophiles which then result in formation of covalent linkages by alkylation of various nucleophilic moieties. The cytotoxic effects are directly related to the alkylation of DNA. Mechlorethamine is a bifunctional alkylating agent with two 2-chlorethyl side chains. The 7-nitrogen atom of guanine residues in DNA is highly susceptible to the formation of a covalent bond with bifunctional alkylating agents such as NM. The modified guanine leads to DNA damage and ultimately causes cell death. The mechanism of action of topical NM is still being studied. One theory suggests that NM has a unique effect on the immune mechanisms (e.g. immunostimulation) against MF.

Does topical nitrogen mustard have any risks?

Patients who use topical NM alone and not in combination with other therapies do not have an increased risk of developing melanoma or non-melanoma skin cancers. This risk has been primarily for patients who are receiving multiple skin treatments (such as phototherapy or radiation) in addition to topical NM. However, the risk is higher for those patients who use the aqueous preparation rather than the ointment. There is no systemic (internal) absorption of topical NM, thus no organs or bone marrow are at risk from using this medication. Patients should not apply topical NM to sensitive areas (such as the face and genitals). Patients should notify their doctor if they are pregnant or breast-feeding because of potential side effects. In studies of the use of topical nitrogen mustard amongst children, no increase in risk was found.

What are the side effects of using topical NM?

Patients should test for any allergies by applying NM to a small patch of skin and waiting to see if an allergic reaction occurs. The most common side effect found amongst patients who use topical nitrogen mustard is an irritant dermatitis, resulting in itching, rash, or redness—this is especially common in more sensitive areas such as skin folds. Acute allergic reactions can be treated with a topical steroid. Patients are typically advised to decrease the frequency of the NM application when there is a mild reaction or irritation to the medication. In most cases, patients are able to continue the medicine with a decrease in frequency or concentration, and eventually the irritant reactions improve and allow for the patient to increase the strength and frequency of the medication. Another potential side effect is hyperpigmentation (darkening of skin) in the area where NM was applied. However, this side effect is usually reversible over time once the medication is discontinued.

Instructions for Patient Use of Topical Nitrogen Mustard

For the best outcome, the following instructions apply to the nitrogen mustard (NM), which must be refrigerated.

In order to check for any allergic reactions, we start you off by applying the medicine to a test patch.

1. Apply a small amount of NM preparation to a small patch on the forearm, once a day, for 3 days. The test-patch can be a palm-sized patch on your arm, leg, or trunk.

2. If there is no significant irritation, new rash, increased redness or itching, apply the NM preparation to all the instructed areas. Patients who have specific patches or plaques should apply NM only to the affected skin area. Patients with patches or plaques spread all over the body should apply NM all over the skin. Usually, you apply the NM only once a day, in the morning or at night on completely dry skin (30 minutes after showering).

3. Please apply only a very thin film of NM on your skin with each application; there is no need to leave large amounts of residue on your skin. Topical NM is maximally absorbed within the first hour after application; thus, additional moisturizer may
be used two hours after. Since, NM is unsuitable in water and becomes rapidly inactive with contact; no water-based emollients should be used one hour before or after its application.

4. You can wear disposable gloves or simply wash your hands after applying the NM. The NM ointment does NOT get absorbed into your blood and it does NOT result in systemic toxicity. If someone else helps apply the NM, they should wear disposable gloves. If the medicine gets on the skin of other person, have them wash their hands with soap and water.

5. In the initial month of NM application, you may see new areas of mycosis fungoides patches, since NM can bring out faint, subtle lesions. Please continue the application to these ‘new’ areas until you are seen for a follow-up visit.

6. Please use additional moisturizing lotions or creams throughout the day as needed.

7. Always, feel free to call us if you have any questions.

How long does the treatment take?

Topical NM should be applied on a daily basis until your skin has completely cleared, which should then be followed by a time of maintenance therapy for about one to two months.