

DRUG NAME: Chlormethine

SYNONYM(S)¹: chlormethine hydrochloride; mechlorethamine, nitrogen mustard; HN2

COMMON TRADE NAME(S): LEDAGA®, LEDAGA® (Europe); VALCHLOR® (USA)

CLASSIFICATION: alkylating agent

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Chlormethine is a bifunctional alkylating agent which forms inter- and intra-strand DNA cross-links that cause the inhibition of DNA synthesis in rapidly proliferating cells. It possesses weak immunosuppressant properties.¹⁻³

USES:

Primary uses:

Other uses:

Mycosis fungoides (topical)^{2,4,5}

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Contraindications:

- history of hypersensitivity reaction to chlormethine (mechlorethamine) by any route²

Caution:

- topical chlormethine is an alcohol based gel and is **flammable**; smoking and/or proximity to fire or flames must be avoided until product has dried on the skin²
- caregivers and others in close contact with the patient must take care to avoid **accidental exposure** (increased risk of skin reactions, mucosal injury, and development of secondary skin cancers following exposure)²
- not recommended for use in **pregnant** patients²
- possible increased risk of systemic exposure in **newborns/infants** through any contact with treated skin (i.e., via close contact with the mother or other treated patient)²

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment **with topical chlormethine** but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in bold, italics	
immune system	cutaneous hypersensitivity, including anaphylaxis (2%)
infections and infestations	skin infections (12%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in bold, italics	
neoplasms	secondary skin cancer; see paragraph following Side Effects table
skin and subcutaneous tissue (see paragraph following Side Effects table)	dermatitis (55%)
	hyperpigmentation (6%)
	pruritus (20%)
	skin ulceration and blistering (6%)

Adapted from standard reference² unless specified otherwise.

Contact with **mucous membranes**, especially the eyes, must be avoided because topical chlormethine can cause burns, ulceration, severe pain, inflammation, photophobia, and blurred vision. Blindness and severe irreversible eye injury can occur. Immediately irrigate unintentionally exposed areas with water and continue for at least 15 minutes. Seek emergency help if appropriate.²

Like other skin-directed therapies for Mycosis fungoides, chlormethine has been associated with an increased risk of **secondary skin cancers**, although the exact relationship with its use is unknown. Monitor all patients for development of skin cancer during and after discontinuation of treatment with chlormethine.²

Topical chlormethine causes **skin reactions** such as dermatitis (e.g., redness, swelling, inflammation), pruritus, blisters, ulceration, and skin infections. The face, genitalia, anus, and intertriginous skin are at increased risk of skin reactions. Treatment should be stopped for any grade skin ulceration or blistering or moderately severe to severe dermatitis with marked skin redness and edema. Upon improvement, treatment may be restarted at a reduced frequency of once every three days. If reintroduction is tolerated for at least one week, the frequency of application can be increased to every other day. If tolerated at the higher frequency of application for at least another week, once-daily application can be resumed.²

INTERACTIONS: no known interactions²

SUPPLY AND STORAGE:

Topical: Recordati Rare Diseases Canada Inc. supplies chlormethine as a clear gel containing 160 mcg per gram (equivalent to 0.02% chlormethine hydrochloride). Store in the freezer until dispensed. Once defrosted, store in the fridge. Discard 60 days after defrosting.⁶

Additional information:

- gel should be applied to the skin within 30 minutes of removal from the fridge and the tube returned to the fridge immediately after each use.²
- formulation contains propylene glycol and butylhydroxytoluene as excipients and these ingredients can cause skin irritation and contact dermatitis; butylhydroxytoluene may also cause irritation of the eyes and mucous membranes.²

TOPICAL ADMINISTRATION²:

- chlormethine gel should be applied to completely dry skin (i.e., 30 minutes *after* showering/washing OR at least four hours *before* showering/washing)
- apply chlormethine gel in a thin film to affected areas of the skin; after application, treated areas should be allowed to dry for 5-10 minutes before covering with clothing
- smoking or exposure to fire or flame should be avoided until the treated areas are dry
- occlusive dressings should NOT be used over the treated areas; non-occlusive dressings may be used if needed to reduce contact or chafing of the affected areas

- emollients or other topical products may only be applied to the treated areas 2 hours or more after application of chlormethine or 2 hours or more before the next application of chlormethine
- all secondary exposure or any direct skin contact in individuals other than the patient should be avoided due to risk of skin reactions, mucosal injury, and development of secondary skin cancers

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated.

Adults:

		BC Cancer usual dose noted in <i>bold, italics</i>
Topical ^{1/2} :	Cycle Length: n/a:	Apply in a thin film once daily to affected areas of skin.

REFERENCES:

1. MARTINDALE - The Complete Drug Reference (database on the Internet). Chlormethine hydrochloride. Thomson MICROMEDEX®, 2019. Available at: <https://online.lexi.com/lco/action/home>. Accessed 15 February, 2019
2. Recordati Rare Diseases Inc for Actelion Registration Ltd. LEDAGA® summary of product characteristics. London, United Kingdom; 3 March 2017
3. Lexi-Drugs® (database on the Internet). Mechlorethamine (topical). Lexi-Comp Inc., 2019. Available at: <http://online.lexi.com>. Accessed 27 February, 2019
4. Lessin SR, Duvic M, Guitart J, et al. Topical chemotherapy in cutaneous T-cell lymphoma. JAMA Dermatol 2013;149(1):25-32
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