PDL DRUG REVIEW

Proprietary Name: Valchlor®
Common Name: mechlorethamine gel
PDL Category: Antineoplastics

Comparable Products	Preferred Drug List Status
Targretin	Preferred

Summary

Pharmacology/Usage: Mechlorethamine, the active ingredient of Valchlor®, is also known as nitrogen mustard. It is an alkylating agent which inhibits rapidly proliferating cells.

Indication: For the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.

This is a pregnancy category D medication. Mechlorethamine can cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy or it the patient becomes pregnant while taking this drug, the patient should be educated of the potential hazard to the fetus. The safety and efficacy of use in the pediatric population have not been established.

Dosage Forms: Each tube contains 60g of 0.016% w/w mechlorethamine clear gel (equivalent to 0.02% mechlorethamine HCl)

Recommended Dosage: Apply thin film of gel once daily to affected areas of the skin. Stop treatment for any grade of skin ulceration, blistering, or moderately-severe or severe dermatitis (i.e. marked skin redness with edema). Upon improvement, treatment with Valchlor® can be restarted at a reduced frequency of once every 3 days. If reintroduction of treatment is tolerated for at least 1 week, the frequency of application can be increased to every other day for at least one week and then to once daily application if tolerated.

Apply gel immediately or within 30 minutes after removal from the refrigerator. Return Valchlor® to the refrigerator immediately after each use. Apply to completely dry skin at least 4 hours before or 30 minutes after showering or washing. Allow treated areas to dry 5 to 10 minutes after application before covering with clothing. Emollients may be applied to the treated areas 2 hours before or 2 hours after application. Do not use occlusive dressings on areas of the skin where Valchlor® was applied. Last, avoid fire, flame, and smoking until Valchlor® has dried.

Valchlor® is a cytotoxic drug, thus follow applicable special handling and disposal procedures. Caregivers must wear disposable nitrile gloves when applying Valchlor® to patients and wash hands thoroughly with soap and water after removal of gloves. If there is accidental skin exposure to Valchlor®, caregivers must immediately wash exposed areas thoroughly with soap and water for at least 15 minutes and remove contaminated clothing.

Drug Interactions: There have been no drug interaction studies performed; however, systemic exposure has not been observed with topical administration of Valchlor® and thus systemic drug interactions are not likely.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Valchlor®) minus reported % incidence for comparator for any grade. Please note that an incidence of 0% means the incidence was the same as or that the active drug was less than comparator.* The most frequently reported adverse events included dermatitis (0%), pruritus (4%), bacterial skin infection (2%), skin ulceration or blistering (1%), and skin hyperpigmentation (0%). Reductions in hemoglobin, neutrophil count, or platelet count occurred in 13% of patients treated with Valchlor® and 17% with comparator.

Exposure of the eyes to mechlorethamine causes pain, burns, inflammation, photophobia, and blurred vision. Blindness and severe irreversible anterior eye injury may occur. Advise patients that if eye exposure occurs, immediately irrigate for at least 15 minutes with copious amounts of water, normal saline, or a balanced salt ophthalmic irrigating solution, as well as obtain immediate medical care.

Avoid direct skin contact with Valchlor® in individuals other than patients. Risks of secondary exposure include dermatitis, mucosal injury, and secondary cancers.

Dermatitis was the most common adverse reaction, occurring in 56% of patients. Monitor patients for redness, swelling, inflammation, itchiness, blisters, ulceration, and secondary skin infections. The face, genitalia, anus, and intertriginous skin are at increased risk for dermatitis. Follow dose modifications for dermatitis.

Patients in clinical trials with Valchlor® (2%) developed a non-melanoma skin cancer during the trial or during one year of post-treatment follow-up, as well as 6% of patients receiving the mechlorethamine ointment comparator. Monitor patients for non-melanoma skin cancers during and after treatment with Valchlor®. Non-melanoma skin cancer may occur on any area of the skin, including untreated areas.

Alcohol-based products, including Valchlor®, are flammable.

Contraindications: In patients with known severe hypersensitivity to mechlorethamine

Manufacturer: Helsinn Therapeutics

Analysis: The safety and efficacy of Valchlor® were assessed in a randomized, multicenter, observer-blind, active-controlled, non-inferiority study that included patients (N=260) with Stage IA, IB, and IIA mycosis fungoides-type cutaneous T-cell lymphoma who had received at least 1 prior skin-directed therapy. Qualifying prior therapies included topical corticosteroids, phototherapy, Targretin® gel, and topical nitrogen mustard. Patients were stratified based on stage and then randomized to either Valchlor® or Aquaphor®-based mechlorethamine ointment (comparator), which were applied daily for 12 months. Concomitant use of topical corticosteroids was not permitted during the study. In this study, most patients were male (60% in Valchlor® arm and 59% in comparator) and white (75% in both treatment arms). The most common prior therapy was topical corticosteroids, and the median body surface area (BSA) involvement at baseline was 8.5% in the Valchlor® arm and 9% in the comparator arm.

Patients were assessed for a response on a monthly basis for the first 6 months and then every 2 months for the last 6 months using the Composite Assessment of Index Lesion Severity (CAILS) score. The CAILS score is obtained by adding the severity score of each of the following categories for up to 5 index lesions: erythema, scaling, plaque elevation, and surface area. Severity was graded from 0 (none) to 8 (severe) for erythema and scaling; 0 to 3 for plaque elevation; and 0 to 9 for surface area. A response was defined as ≥50% reduction in baseline CAILS score which was confirmed at the next visit at least 4 weeks later. A complete response was defined as a confirmed CAILS score of 0.

Patients were also assessed using the Severity Weighted Assessment Tool (SWAT). The SWAT score is derived by measuring each involved area as a percentage of total body surface area (%BSA) and multiplying it by a severity weighting factor (1=patch, 2=plaque, 3=tumor or ulcer). A response was defined as ≥50% reduction in baseline SWAT score which was confirmed at the next visit at least 4 weeks later.

Results suggested that 60% of the Valchlor® arm and 48% of the comparator arm achieved a response based on the CAILS score. Valchlor® was non-inferior to the comparator based on a CAILS overall response rate ratio of 1.24. Complete responses constituted a minority of the CAILS or SWAT overall responses. The onset of CAILS overall response for both treatment arms demonstrated a wide range from 1 to 11 months. Results can be seen in the table below, which was adapted from the prescribing information.

	Valchlor® (N=119)	Comparator (N=123)
CAILS Overall Response (CR+PR)	60%	48%
CAILS Complete Response (CR)	14%	11%
CAILS Partial Response (PR)	45%	37%
SWAT Overall Response (CR+PR)	50%	46%
SWAT CR	7%	3%
SWAT PR	43%	43%

Place in Therapy: Valchlor® is a topical cytotoxic drug indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy. It was found in clinical trials to be non-inferior to a comparator mechlorethamine ointment

There is no evidence at this time that Valchlor® is safer or more effective than the currently preferred, more cost-effective medications. It is therefore recommended that Valchlor® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

Reference

[1] Valchlor [package insert]. Iselin, NJ: Helsinn Therapeutics; 2018.