



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/28/2014
LAST REVIEW DATE: 11/18/2021
LAST CRITERIA REVISION DATE: 11/18/2021
ARCHIVE DATE:

VALCHLOR™ (mechlorethamine)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**



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Criteria:

➤ **Criteria for initial therapy:** Valchlor (mechlorethamine) gel is considered *medically necessary* when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Dermatologist
2. Individuals 18 years of age or older
3. A confirmed diagnosis of **ONE** of the following:
 - a. Stage IA and IB mycosis fungoides-type cutaneous T-cell Lymphoma who have received prior skin-directed therapy
 - b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 or 2A
4. Individual has failure, contraindication or intolerance to at least **two** prior skin-directed therapy
 - a. Skin directed therapies include:
 - i. Topical corticosteroid
 - ii. Topical retinoid
 - iii. Topical imiquimod
 - iv. Topical carmustine
 - v. Local superficial radiation
 - vi. Phototherapy (such as PUVA for thicker plaques, UVB, and NB-UVB for patch/thin plaques)
 - vii. Total skin electron beam radiation (TSEBT)
5. There are **NO** FDA-label contraindications, such as:
 - a. Severe hypersensitivity to mechlorethamine

Initial approval duration: 6 months

➤ **Criteria for continuation of coverage (renewal request):** Valchlor (mechlorethamine) gel is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Dermatologist
2. Individual's condition has not worsened while on therapy
 - a. Worsening is defined as:
 - i. Progressive disease defined as worsening of index lesion(s) or development of new cutaneous tumor lesions or development of non-cutaneous manifestations of disease

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3. Individual has been adherent with the medication
4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
 - a. Skin ulceration, blistering, or moderately severe or severe dermatitis

Renewal duration: 6 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:
1. **Off-Label Use of a Non-cancer Medications**
 2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

Description:

Valchlor (mechlorethamine, also known as nitrogen mustard) is an alkylating agent that inhibits rapidly proliferating cells, is 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.

The efficacy of Valchlor (mechlorethamine) was assessed in a randomized, multicenter, observer-blind, active-controlled, non-inferiority clinical trial of 260 patients with Stage IA, IB, and IIA mycosis fungoides-type cutaneous T-cell lymphoma who had received at least one prior skin-directed therapy. Ninety-eight percent (256 study subjects) of enrolled patients were Stage IA and IB. There were too few Stage IIA patients to evaluate. Qualifying prior therapies included topical corticosteroids, phototherapy, bexarotene gel, and topical nitrogen mustard.

Mycosis fungoides (MF) and Sezary syndrome

- MF (also known as Alibert-Bazin syndrome or granuloma fungoides), is the most common form of cutaneous T-cell lymphoma (CTCL)
- It is a rare indolent form of non-Hodgkin's lymphoma that affects approximately 1,400 individuals yearly in the US and occurs more commonly in men than in women
- In MF, malignant T-cells migrate and accumulate in the skin, initially resulting in dry skin and red rash that may or may not itch; eventually other skin lesions form
 - The malignant T-cells may also involve lymph nodes and spread to other areas such as liver, spleen, and lungs
- Sezary syndrome is a more aggressive leukemic form of CTCL with widespread skin involvement, enlarged lymph nodes and malignant lymphocytes (Sezary cells) in the skin, lymph nodes, and blood

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- It is a leukemic form of CTCL in which there is significant blood involvement with sezary cells, lymphadenopathy, and erythrodermic skin
- It is an advanced variant form of MF
- MF may be classified into various stages depending upon skin (T), node (N), metastasis (M), and blood (B) involvement
- Stages IA, IB, and IIA are considered early stage MF
- Prognosis and survival depends on the stage at diagnosis
- In the management of early-stage MF, skin-directed therapies may be categorized in two ways: “skin-limited/local therapies” for limited or localized disease and “skin-generalized therapies” for generalized skin involvement
 - Skin-limited therapies include: topical corticosteroids, topical chemotherapy (such as nitrogen mustard), local superficial radiation (8-36 gray or Gy), topical retinoids (such as bexarotene and tazarotene), phototherapy (such as PUVA for thicker plaques, UVB, and NB-UVB for patch/thin plaques), and topical imiquimod
 - Skin-generalized therapies include: topical corticosteroids, topical chemotherapy (such as nitrogen mustard), phototherapy (such as PUVA for thicker plaques, UVB, and NB-UVB for patch/thin plaques), and total skin electron beam radiation (TSEBT [12-36 Gy])
- Systemic therapies include: oral retinoids (bexarotene and isotretinoin), alpha-interferon, Zolinza (vorinostat), Istodax (romidepsin), methotrexate, cyclophosphamide, chlorambucil, gemcitabine, liposomal doxorubicin, Nipent (pentostatin), and others

Definitions:

Staging of Mycosis fungoides:

In **Stage IA**, less than 10% of the skin is covered with patches, papules, and/or plaques, lymph nodes are not enlarged or abnormal, there is no visceral involvement, and the blood does not contain or has a low burden of circulating Sezary cells, defined as < 5% of peripheral blood. With **Stage IB**, 10% or more of the skin is covered with patches, papules, and/or plaques.

In **Stage IIA**, any amount of skin may be covered with patches, papules and/or plaques, lymph nodes are enlarged and may or may not have abnormal cells, there is still no visceral involvement, and the blood does not contain or has a low burden of circulating Sezary cells. **Stage IIB** has the same characteristics except now there are one or more tumorous skin lesions.

With **Stage III**, there is erythrodermic skin (greater than 80% of body surface with red patches, papules, or plaques), the lymph nodes may or may not be enlarged, when enlarged the nodes may or may not contain abnormal cells, and there is no visceral involvement. With **Stage IIIA** there are no circulating Sezary cells in the blood, with **Stage IIIB** there is a low burden of circulating Sezary cells.

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In **Stages IVA and IVB**, patches, papules, plaques or tumors involve any amount of the skin surface. The lymph nodes tend to be enlarged and contain atypical cells and there is a significant level of Sezary cells in the blood. Patients with visceral involvement are classified as Stage IVB.

Clinical staging system for mycosis fungoides and Sezary syndrome:

| Clinical stage | TNMB classification | | | |
|-------------------------------|--|----------------------------------|----------------|----------------------------------|
| | Skin | Node | Visceral | Blood |
| IA – limited skin involvement | T ₁ (patches, papules, &/or plaques covering < 10% BSA) | N ₀ | M ₀ | B ₀ or B ₁ |
| IB – skin only disease | T ₂ (patches, papules, &/or plaques covering ≥ 10% BSA) | N ₀ | M ₀ | B ₀ or B ₁ |
| IIA | T ₁ or T ₂ | N ₁ or N ₂ | M ₀ | B ₀ or B ₁ |
| IIB – tumor stage disease | T ₃ (one or more tumors: ≥ 1 cm in diameter) | N ₀ to N ₂ | M ₀ | B ₀ or B ₁ |
| IIIA – erythrodermic disease | T ₄ (confluence of erythema ≥ 80% BSA) | N ₀ to N ₂ | M ₀ | B ₀ |
| IIIB – erythrodermic disease | T ₄ (confluence of erythema ≥ 80% BSA) | N ₀ to N ₂ | M ₀ | B ₁ |
| IVA1 | T ₁ to T ₄ | N ₀ to N ₂ | M ₀ | B ₂ |
| IVA2 | T ₁ to T ₄ | N ₃ | M ₀ | B ₀ to B ₂ |
| IVB | T ₁ to T ₄ | N ₀ to N ₃ | M ₁ | B ₀ to B ₂ |
| | Large-cell transformation (LCT) | | | |

To be used in conjunction with the TNMB classification system for mycosis fungoides
 Skin (T), node (N), metastasis (M), and blood (B) involvement

Resources:

Valchlor (mechlorethamine) product information, revised by Helsinn Therapeutics, Inc. 01-2020. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed August 25, 2021.

Hoppe RT, Kim YH. Clinical manifestations, pathologic features, and diagnosis of mycosis fungoides. In: UpToDate, Kuzel TM, Zic JA, Rosmarin AG, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed August 25, 2021.

Hoppe RT, Kim YH, Horwitz S. Treatment of early stage (IA to IIA) mycosis fungoides. In: UpToDate, Kuzel TM, Zic JA, Rosmarin AG, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed August 25, 2021.

Hoppe RT, Kim YH, Horwitz S. Treatment of advanced stage (IIB to IV) mycosis fungoides. In: UpToDate, Kuzel TM, Zic JA, Rosmarin AG, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed August 25, 2021.



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Rook AH, Olen EA. Clinical manifestations, pathologic features, and diagnosis of Sezary syndrome. In: UpToDate, Kuzel TM, Zic JA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed August 25, 2021.

Hoppe RT, Kim YH. Staging and prognosis of mycosis fungoides and Sezary syndrome. In: UpToDate, Kuzel TM, Zic JA, Rosmarin AG, Corona R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed August 25, 2021.

Kim EJ, Rook AH. Treatment of Sezary syndrome. In: UpToDate, Kuzel TM, Zic JA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Accessed August 25, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Primary Cutaneous Lymphomas Version 2.2021 – March 04, 2021. Available at <https://www.nccn.org>. Accessed August 25, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): T-cell Lymphomas Version 1.2021 – October 05, 2020. Available at <https://www.nccn.org>. Accessed August 25, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Histiocytic Neoplasms Version 1.2021 – Updated March 01, 2021 . Available at <https://www.nccn.org>. Accessed August 25, 2021.
