

PHARMACY / MEDICAL POLICY – 5.01.532

Cutaneous T-Cell Lymphomas (CTCL): Systemic Therapies

Effective Date: Nov. 1, 2020

Last Revised: Oct. 22, 2020


Replaces: N/A

RELATED MEDICAL POLICIES:

8.01.36 Extracorporeal Photopheresis

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Introduction

The lymphatic system, which is part of the immune system, is composed of specialized cells. Most of these specialized cells are white blood cells known as lymphocytes. There are two main types of lymphocytes: B-cells and T-cells. Lymphoma is cancer that starts in lymphocytes.

Cutaneous T-cell lymphomas are cancers that start in the T-cell lymphocytes and affect the skin. Mycosis fungoides and Sézary syndrome are two examples of lymphomas of the skin.

T-cell lymphoma can arise in other parts of the body such as lymph nodes, lining of the intestines, or the spleen, liver, or colon.

Treating T-cell lymphomas depends on the specific type of cancer and how slow or fast it's growing. This policy describes when particular chemotherapy drugs may be considered medically necessary for T-cell lymphomas that did not respond to initial treatment.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
<p>Targretin® (bexarotene) oral, Bexarotene capsules oral, Zolinza® (vorinostat) oral, Istodax® (romidepsin) IV</p>	<p>Targretin® (bexarotene capsules), bexarotene capsules, Zolinza® (vorinostat), or Istodax® (romidepsin) may be considered medically necessary in patients who are refractory to at least one prior systemic therapy and have:</p> <ul style="list-style-type: none"> • Cutaneous or peripheral T-cell lymphoma <p>OR</p> <ul style="list-style-type: none"> • Mycosis fungoides/Sezary syndrome <p>AND</p> <p>Systemic therapies:</p> <ul style="list-style-type: none"> • For simple skin involvement: <ul style="list-style-type: none"> ○ Systemic retinoids (isotretinoin, acitretin, etc.) ○ Interferons (alpha, gamma) ○ Methotrexate ○ Campath® (alemtuzumab) <p>OR</p> <ul style="list-style-type: none"> • For late stage disease usually with solid organ involvement, more aggressive therapy is usually required, for example: <ul style="list-style-type: none"> ○ Gemcitabine ○ Liposomal doxorubicin
<p>Targretin® (bexarotene) topical gel</p>	<p>Targretin® (bexarotene) topical gel may be considered medically necessary for the topical treatment of cutaneous lesions in patients with cutaneous T-cell lymphoma (Stage IA and IB) when at least 3 of the following therapies have failed:</p> <ul style="list-style-type: none"> • Phototherapy (UVB, NB-UVB, PUVA) • Topical imiquimod • Topical corticosteroids • Topical mechlorethamine • Local radiation
<p>Beleodaq® (belinostat) IV</p>	<p>Beleodaq® (belinostat) may be considered medically necessary for the treatment of patients with relapsed or refractory angioimmunoblastic T-cell lymphoma, anaplastic large cell lymphoma, enteropathy-associated T-cell lymphoma or other peripheral T-cell lymphoma who have failed or are refractory to at least one prior systemic therapy.</p>



Drug	Medical Necessity
Valchlor® (mechlorethamine) topical gel	Valchlor® (mechlorethamine) may be considered medically necessary for topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have tried and failed at least 2 of the following therapies: <ul style="list-style-type: none"> • Topical corticosteroids (prednisone, triamcinolone, etc.) • Topical imiquimod • Phototherapy • Local radiation
Poteligeo® (mogamulizumab-kpkc) IV	Poteligeo® (mogamulizumab-kpkc) may be considered medically necessary in adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy.

Drug	Investigational
As listed	All other uses of the medications listed in this policy are considered investigational.

Length of Approval	
Approval	Criteria
Initial authorization	Oral and topical drugs listed in policy may be approved up to 3 months. Injectable drugs listed in policy may be approved up to 6 months.
Re-authorization criteria	Future re-authorization of oral, topical and injectable drugs may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the patient continues to show a positive clinical response to therapy.

Documentation Requirements
The patient's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:



Documentation Requirements

- Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	
J9032	Injection, belinostat (Beleodaq®), 10 mg
J9204	Injection, mogamulizumab-kpkc, (Poteligeo®) 1 mg
J9315	Injection, romidepsin (Istodax®), 1 mg

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Benefit Application

The drugs included in this policy may be managed under either the pharmacy or medical benefit.

Evidence Review

Description

Cutaneous T-Cell Lymphoma

Cutaneous T-cell lymphoma (CTCL) is a rare type of cancer of unknown etiology. In the United States, the estimated annual incidence of CTCL is 0.4 to 1 case per 100,000 (or 1,000 to 3,000 new cases per year). Since most cases are not fatal and patients can live with CTCL for 10 or



more years, estimated U.S. prevalence is approximately 20,000. Approximately 25% of these cases (5,000) have advanced disease.

CTCL is characterized by abnormal malignant T-cells residing in the skin which cause skin lesions and pruritis. The disease often remains confined to the skin and has an indolent course. However, in more aggressive CTCL, the disease may progress to involve other areas of the body such as lymph nodes, blood, and organs. The most common indolent form is mycosis fungoides. This form usually manifests as flat red or pink scaly patches that first appear in sun-protected areas of the body (eg, buttocks or trunk). As the disease progresses, the patches evolve into a raised pruritic plaque phase. Plaques can also evolve into nodular skin tumors which may ulcerate.

The most common aggressive form of CTCL is Sézary syndrome. This syndrome accounts for about 5% of all CTCL cases and the prognosis is poor. Median survival is usually less than 3 years. It is characterized by widespread erythroderma and the presence of abnormal CD4+ T-cells (called Sézary cells) in both the skin and peripheral blood. This condition may also be accompanied by scaling pruritic plaques or tumors. In advanced stages, patients with Sézary syndrome may develop alopecia, leonine facies, hyperkeratosis of the palms and soles, nail dystrophy, and parasthesia.

Therapeutic management of CTCL is based largely on the stage of the disease. In early, mild, and slowly progressive stages of the disease, treatment is mainly targeted at reducing symptoms and lesions with topical therapies (topical corticosteroids, topical retinoids (bexarotene, tazarotene), topical chemotherapy (nitrogen mustard, carmustine), local radiation (for limited skin involvement) or electron beam therapy (for severe skin involvement), phototherapy (UVB, nbUVB or patch/thin plaques; PUVA for thicker plaques), topical imiquimod (for limited localized skin involvement). In patients with advanced stages of the disease, mycosis fungoides and Sezary syndrome, systemic therapies, such as retinoids (eg, bexarotene, acitretin), may be employed.

Targretin® (bexarotene) is a member of a subclass of retinoids that selectively activate retinoid X receptors (RXRs). These retinoid receptors have biologic activity distinct from that of retinoic acid receptors (RARs). Retinoids are associated with birth defects in humans. Targretin® (bexarotene) also caused birth defects when administered orally to pregnant rats. Therefore, it must not be administered during pregnancy.

Targretin® (bexarotene) selectively binds and activates retinoid X-receptor subtypes (RXR α , RXR β , RXR γ). RXRs can form heterodimers with various receptor partners such as retinoic acid receptors (RARs), vitamin D receptor, thyroid receptor, and peroxisome proliferator activator receptors (PPARs). Once activated, these receptors function as transcription factors that regulate



the expression of genes that control cellular differentiation and proliferation. Targretin® (bexarotene) inhibits the growth in vitro of some tumor cell lines of hematopoietic and squamous cell origin. It also induces tumor regression in vivo in some animal models. The exact mechanism of action of Targretin® (bexarotene) in the treatment of cutaneous T-cell lymphoma (CTCL) is unknown.

Bexarotene (Targretin) is indicated for the treatment of cutaneous manifestations of cutaneous T cell lymphoma in patients who are refractory to at least one prior systemic therapy.

Zolinza® (vorinostat) and Istodax® (romidepsin) are histone deacetylase (HDAC) inhibitors with enzymatic inhibitory activity at nanomolar concentrations for HDAC1, HDAC2, HDAC3 [class I], and HDAC6 [class II]. These enzymes catalyze the removal of acetyl groups from the lysine residues of proteins, including histones and transcription factors. In some cancer cells, HDACs are overexpressed or are aberrantly recruited for oncogenic transcription causing hypoacetylation of core nucleosomal histones. While the exact mechanism of action of these agents has not been fully characterized, in vitro, they cause accumulation of acetylated histones, induces cell cycle arrest, and/or apoptosis of some transformed cells.

Zolinza® (vorinostat) is indicated for treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma (CTCL) who have progressive, persistent or recurrent disease on or following two systemic therapies.

Istodax® (romidepsin) is indicated for treatment of cutaneous T-cell lymphoma (CTCL) or peripheral T-cell lymphoma in patients who have received at least one prior systemic therapy.

Rationale

Targretin® (bexarotene)

Efficacy

No randomized controlled trial for Targretin® (bexarotene) in CTCL was found on literature search. The efficacy of oral bexarotene was demonstrated in 2 pivotal multinational, open-label, phase II-III studies in 94 adults with advanced refractory CTCL and 58 with early stage refractory or persistent CTCL. At recommended dosing (300 mg/m²/day), overall response to monotherapy as measured by PGA and CAILDS was about 50%. Two supportive open-label studies show systemic combination therapy to be efficacious as measured by response rates.



The efficacy of topical bexarotene was demonstrated in 1 pivotal multinational, open-label, phase II-III study in 50 adults with treatment refractory early stage CTCL. Like systemic bexarotene, overall response was about 50%. Bexarotene gel is the only topical product treatment of CTCL which has received approval by the U.S. Food and Drug Administration (FDA).

Off-label studies for systemic bexarotene have been reported for prevention of breast cancer, head and neck cancer, psoriasis, non-small cell lung cancer, and acute myeloid leukemia. Off-label studies for topical bexarotene have been reported for alopecia areata, parapsoriasis, severe hand dermatitis, and psoriasis.

No comparative studies between bexarotene and therapeutic alternatives for CTCL have been published and no comparative trials are currently underway.

Safety

Targretin® (bexarotene) carries a boxed warning the drug should not be used in pregnant females because of its association with birth defects. Systemic bexarotene induces major lipid abnormalities in most patients, particularly hypertriglyceridemia. Lipids should be monitored at baseline, weekly for 2-4 weeks, then at 8 week intervals. Abnormalities are reversible with cessation of therapy and can be managed with dose reduction or concomitant antilipemic agents. Other serious adverse events reported following use of systemic bexarotene are pancreatitis, liver function test abnormalities and hepatotoxicities, hypothyroidism, leukopenia, and cataracts. Regular monitoring of related laboratory measures and ophthalmologic evaluations are recommended.

In oral CTCL trials, adverse events leading to dose reduction or study drug discontinuation in at least two patients were hyperlipemia, neutropenia/leukopenia, diarrhea, fatigue/lethargy, hypothyroidism, headache, liver function test abnormalities, rash, pancreatitis, nausea, anemia, allergic reaction, muscle spasm, pneumonia, and confusion. In topical CTCL trials, adverse events leading to dose reduction or study drug discontinuation in at least two patients were rash, contact dermatitis, and pruritus.

In 504 patients participating in oral CTCL and non-CTCL clinical trials, 3 patients experienced a severe adverse event that was fatal; one each from acute pancreatitis, a subdural hematoma, and liver failure. In topical CTCL trials, only one patient (2%) experienced a severe adverse event (rash).

The most common adverse events observed in patients with CTCL (n=86) receiving Zolinza® (vorinostat) 400 mg once-daily in uncontrolled clinical were diarrhea, fatigue, nausea,



thrombocytopenia, anorexia, and dysgeusia. The most commonly reported serious adverse events, regardless of causality, were pulmonary embolism and anemia. In addition, laboratory abnormalities (eg, increased serum glucose, increased serum creatinine, proteinuria) were observed in all patients. Approximately 9% of the 86 patients discontinued the drug due to adverse events.

Istodax® (romidepsin)

Efficacy

Istodax® (romidepsin) was evaluated in 2 multicenter, single-arm clinical studies in patients with CTCL. Overall, 167 patients with CTCL were treated in the US, Europe, and Australia. Study 1 included 96 patients with confirmed CTCL after failure of at least 1 prior systemic therapy. Study 2 included 71 patients with a primary diagnosis of CTCL who received at least 2 prior skin directed therapies or one or more systemic therapies. Patients were treated with romidepsin at a starting dose of 14 mg/m² infused over 4 hours on days 1, 8, and 15 every 28 days. In both studies, patients could be treated until disease progression at the discretion of the investigator and local regulators. Objective disease response was evaluated according to a composite endpoint that included assessments of skin involvement, lymph node and visceral involvement, and abnormal circulating T-cells ("Sézary cells"). The primary efficacy endpoint for both studies was overall objective disease response rate (ORR) based on the investigator assessments, and defined as the proportion of patients with confirmed complete response (CR) or partial response (PR). CR was defined as no evidence of disease and PR as $\geq 50\%$ improvement in disease. Secondary endpoints in both studies included duration of response and time to response. Median time to first response was 2 months (range 1 to 6) in both studies. Median time to CR was 4 months in Study 1 and 6 months in Study 2 (range 2 to 9).

Istodax® (romidepsin) was evaluated in a multicenter, single-arm, international clinical study in patients with PTCL who had failed at least 1 prior systemic therapy (Study 3). Patients in US, Europe and Australia were treated with romidepsin at a dose of 14 mg/m² infused over 4 hours on days 1, 8, and 15 every 28 days. Of the 131 patients treated, 130 patients had histological confirmation by independent central review and were evaluable for efficacy (HC Population). Six cycles of treatment were planned; patients who developed progressive disease (PD), significant toxicity, or who met another criterion for study termination were to discontinue treatment. Responding patients had the option of continuing treatment beyond 6 cycles at the discretion of the patient and Investigator until study withdrawal criteria were met. Primary assessment of efficacy was based on rate of complete response (CR + CRu) as determined by an Independent Review Committee (IRC) using the International Workshop Response Criteria (IWC). Secondary



measures of efficacy included IRC assessment of duration of response and objective disease response (ORR, CR + CRu + PR). The complete response rate was 15% and overall response rate was 25%. Similar complete response rates were observed by the IRC across the 3 major PTCL subtypes (NOS, AITL, and ALK-1 negative ALCL). Median time to objective response was 1.8 months (~2 cycles) for the 33 patients who achieved CR, CRu or PR and was 3.7 months (~4 cycles) for the 19 patients with complete response. The responses in 11 of the 19 patients achieving CR and CRu were known to exceed 9.2 months; the follow-up on the remaining 8 patients was discontinued prior to 9.2 months.

Safety

The safety of Istodax® (romidepsin) was evaluated in 185 patients with CTCL in 2 single arm clinical studies in which patients received a starting dose of 14 mg/m². The mean duration of treatment in these studies was 5.6 months (range: <1 to 83.4 months). Infections were the most common type of serious adverse event reported in both studies with 8 patients (8%) in Study 1 and 26 patients (31%) in Study 2 experiencing a serious infection. Serious adverse reactions reported in > 2% of patients in Study 1 were sepsis and pyrexia (3%). In Study 2, serious adverse reactions in > 2% of patients were fatigue (7%), supraventricular arrhythmia, central line infection, neutropenia (6%), hypotension, hyperuricemia, edema (5%), ventricular arrhythmia, thrombocytopenia, nausea, leukopenia, dehydration, pyrexia, aspartate aminotransferase increased, sepsis, catheter related infection, hypophosphatemia and dyspnea (4%). Most deaths were due to disease progression. In Study 1, there were two deaths due to cardiopulmonary failure and acute renal failure. In Study 2, there were six deaths due to infection (4), myocardial ischemia, and acute respiratory distress syndrome. Discontinuations Discontinuation due to an adverse event occurred in 21% of patients in Study 1 and 11% in Study 2. Discontinuations occurring in at least 2% of patients in either study included infection, fatigue, dyspnea, QT prolongation, and hypomagnesemia.

Zolinza® (vorinostat)

The efficacy and safety of Zolinza® (vorinostat) was established in two nonrandomized, uncontrolled, open-label studies in adult patients with treatment refractory CTCL. A response rate (defined as at least 50% improvement in cutaneous manifestations) of approximately 30% was observed in patients receiving the approved dosing regimen of 400 mg once daily. Median time to response was <3 months, median response duration was approximately 3-4 months, and median time to progression was approximately 6-7 months.



Beleodaq® (belinostat)

Efficacy

Beleodaq® (belinostat) is a histone deacetylase (DHAC) inhibitor indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL). It received accelerated approval based on the results of 1 single-arm, phase 2 study using tumor response rate as the primary outcome measure. An improvement in survival or disease-related symptoms has not been established. The pivotal trial has not been published.

In all evaluable patients (n=120) treated with belinostat, the overall response rate per independent central review using the International Workshop Group (IWG) criteria was 25.8% (n=31), with rates of 23% for PTCL not otherwise specified (NOS) and 46% for angioimmunoblastic T-cell lymphoma (AITL), the 2 largest subtypes enrolled. Further, the response rate was higher (28%) in patients with baseline platelet counts at or above 100,000/ μ L and lower (15%) in those with baseline platelet counts below 100,000/ μ L. The median duration of response based on the first date of response to disease progression or death was 8.4 months (95% confidence interval [CI], 4.5 to 29.4). Of the responders, the median time to response was 5.6 weeks (range, 4.3-50.4 weeks).

Safety

Sixty-one patients (47.3%) in the pivotal study experienced serious adverse reactions (grade 3 or higher) while taking belinostat or within 30 days after their last dose. The most common serious adverse reactions (>2%) were pneumonia, pyrexia, infection, anemia, increased creatinine, thrombocytopenia, and multiorgan failure. One treatment-related death associated with hepatic failure was reported in the study. Twenty-five patients (19.4%) in the pivotal study discontinued treatment with belinostat due to adverse reactions. Dose adjustments were made in 12%.

Valchlor® (mechlorethamine)

Efficacy

Valchlor® (mechlorethamine) is an alkylating agent 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 (MF-CTCL) who had received at least one prior skin-directed therapy. Qualifying prior therapies included topical corticosteroids, phototherapy, TargretinR[®] gel, and topical nitrogen mustard. Patients were not required to be refractory to or intolerant of prior therapies. Study drug was to be applied topically on a daily basis for 12 months. Concomitant use of topical corticosteroids was not permitted during the study. Dosing could be suspended or continued with reduced frequency for dermatitis. The mean daily usage of Valchlor[®] gel was 2.8 g (1 to 2 tubes per month). The maximum daily usage was 10.5 g (5 to 6 tubes per month). Patients were evaluated 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 greater than or equal to 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. Non-inferiority was considered to have been demonstrated if the lower bound of the 95% confidence interval (CI) around the ratio of response rates (Valchlor[®]/Comparator) was greater than or equal to 0.75. Patients were also evaluated 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 greater than or equal to 50% reduction in baseline SWAT score which was confirmed at the next visit at least 4 weeks later. Sixty percent (60%) of the patients on the Valchlor[®] arm and 48% of patients on the comparator arm achieved a response based on the CAILS score. Valchlor[®] was noninferior to the comparator based on a CAILS overall response rate ratio of 1.24 (95% CI: 0.98, 1.58). Complete responses constituted a minority of the CAILS or SWAT overall responses. The onset of CAILS overall response for both treatment arms showed a wide range from 1 to 11 months.

Safety

In the clinical trial, moderately-severe to severe skin-related adverse events were managed with treatment reduction, suspension, or discontinuation. Discontinuations due to adverse reactions occurred in 22% of patients treated with Valchlor[®] and 18% of patients treated with the comparator. Sixty-seven percent (67%) of the discontinuations for adverse reactions occurred within the first 90 days of treatment. Temporary treatment suspension occurred in 34% of patients treated with Valchlor[®] and 20% of patients treated with the comparator. Reductions in



dosing frequency occurred in 23% of patients treated with Valchlor® and 12% of patients treated with the comparator. Reductions in hemoglobin, neutrophil count, or platelet count occurred in 13% of patients treated with Valchlor® and 17% treated with Comparator. Systemic exposure was undetectable after topical administration of Valchlor® to patients. Blood samples were analyzed from 16 and 15 patients following treatment with Valchlor® (mechlorethamine gel 0.016%) and an identical formulation consisting of mechlorethamine 0.032% w/w, respectively. For patients who received mechlorethamine 0.016%, samples were collected to measure mechlorethamine concentrations prior to dosing, on day 1, and at the first month visit. Following the topical administration of mechlorethamine 0.016%, there were no detectable plasma mechlorethamine concentrations observed in any of the patients. Patients who received mechlorethamine 0.032% had no measurable concentrations of mechlorethamine or half-mustard after 2, 4, or 6 months of treatment.

For more details, please see package insert for mechlorethamine.

2013 Update

A literature search for new publications from 01/01/2012 to 04/30/2013 did not reveal new evidence that would require changes to this policy. The policy was compared with current NCCN guideline recommendations and found to be consistent. An updated systematic review of treatment for mycosis fungoides/Sezary syndrome was published by the Cochrane Skin Group in September 2012.

2014 Update

A literature search for new publications from 01/01/2013 to 10/31/2014 did not reveal new evidence that would require changes to the drugs previously in this policy. Added Beleodaq® (belinostat), recently approved by FDA with medically necessary indications consistent with current NCCN guideline recommendations.

2015 Update

Valchlor® (mechlorethamine) was added to the policy on 07/27/2015, per the NCCN guideline recommendations.



2016 Update

Safety and efficacy reorganized to be under each relevant drug. No major NCCN guideline changes at this time.

2018 Update

A primary literature search from 04/11/2017 to 03/13/2018 did not reveal new evidence that would require change in this policy. No major NCCN guideline changes at this time.

2019 Update

Reviewed prescribing information for all drugs and conducted a primary literature search from 01/01/2018 to 03/31/2019. No new evidence was identified that would require changes to this policy.

2020 Update

Reviewed prescribing information for all drugs and conducted a primary literature search from 01/01/2019 to 08/31/2020. No new evidence was identified that would require changes to this policy.

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32. Valchlor® (mechlorethamine) prescribing information. Helsinn Therapeutics; Iselin, NJ. January 2020
33. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: T-Cell Lymphomas. Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx Accessed October 2020.

History

Date	Comments
05/10/11	Add to Prescription Drug Section - New Policy.
04/10/12	Replace policy. Policy updated with romidepsin (Istodax®) and a new medically necessary policy statement for the treatment of mycosis fungoides/Sezary syndrome for patients refractory to at least one prior systemic therapy. Description, Policy Guidelines and Rationale also updated.
05/28/13	Replace policy. Policy reviewed with literature search/ reference added. No change in policy statement.
12/08/14	Annual review. Medically necessary policy statement added for belinostat, recently approved by the FDA, per NCCN guideline recommendations; approved by P&T December 2014. Literature review performed.
06/18/15	Update Related Policies. Change title to 8.01.36
08/11/15	Annual Review. Added a new agent Valchlor® to the existing policy. Updated Policy Guidelines and Rationale sections accordingly.
01/19/16	Coding update. New HCPCS code J9032, effective 1/1/16, added to policy. Minor edit to correct spelling and punctuation.
02/23/16	Coding update. Add J9315.
01/01/17	Annual Review, changes approved December 13, 2016. Safety and efficacy reorganized. Grammar edits.
05/01/17	Annual Review, changes approved April 11, 2017. Criteria for topical bexarotene gel have been added. Also, statement outlining the length of therapy for initial and subsequent approval has been added to the policy.
10/24/17	Policy moved to new format; no change to policy statements.



Date	Comments
07/01/18	Annual Review, approved June 5, 2018. Literature review from 04/11/2017 to 03/13/2018. Revised wording on medical necessity.
02/01/19	Interim Review, approved January 8, 2019. Added Poteligeo (mogamulizumab-kpkc) criteria to policy.
05/01/19	Annual Review, approved April 18, 2019. Added bexarotene capsules to policy. No changes to policy statements. Added HCPCS code J3490.
08/01/19	Interim Review, approved July 9, 2019. Updated criteria for Targretin (bexarotene) topical gel. Removed HCPCS code J3490, added HCPCS code J3590.
10/01/19	Coding update, added HCPCS code J9204 (new code effective 10/1/19). Removed HCPCS code J3590.
11/01/20	Annual Review, approved October 22, 2020. No changes to policy statements.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2020 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.



Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:

- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
 - Qualified sign language interpreters
 - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
 - Qualified interpreters
 - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-722-1471 (TTY: 800-842-5357).

አማርኛ (Amharic):

ይህ ማስታወቂያ አስፈላጊ መረጃ ይዟል። ይህ ማስታወቂያ ስለ ማመልከቻዎ ወይም የ Premera Blue Cross ሽፋን አስፈላጊ መረጃ ሊኖረው ይችላል። በዚህ ማስታወቂያ ውስጥ ቁልፍ ቀናት ሊኖሩ ይችላሉ። የጤና ሽፋንዎን ለመጠበቅና በአስፈላጊ እርዳታ ለማግኘት በተውሰኑ የጊዜ ገደቦች እርምጃ መውሰድ ይገባዎት ይሆናል። ይህን መረጃ እንዲያገኙ እና የለምንም ክፍያ በቋንቋዎ እርዳታ እንዲያገኙ መሰታወቅ አለዎት። በስልክ ቁጥር 800-722-1471 (TTY: 800-842-5357) ይደውሉ።

العربية (Arabic):

يحتوي هذا الإشعار على معلومات هامة. قد يحوي هذا الإشعار معلومات مهمة بخصوص طلبك أو التخطيط التي تزيد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك تواريخ مهمة في هذا الإشعار. وقد تحتاج لاتخاذ إجراء في تاريخ معينة للحفاظ على تغطيتك الصحية أو للمساعدة في دفع التكاليف. يحق لك الحصول على هذه المعلومات والمساعدة بلغتك دون تكبد أية تكلفة. اتصل بـ 800-722-1471 (TTY: 800-842-5357)

中文 (Chinese):

本通知有重要的訊息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知內可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或者費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357)。

Oromoo (Cushite):

Beeksisni kun odeeffannoo barbaachisaa qaba. Beeksisti kun sagantaa yookan karaa Premera Blue Cross tiin tajaajila keessan ilaalchisee odeeffannoo barbaachisaa qabaachuu danda'a. Guyyaawwan murteessaa ta'an beeksisa kana keessatti ilaalaa. Tarii kaffaltiidhaan deeggaramuuf yookan tajaajila fayyaa keessaniif guyyaa dhumaa irratti wanti raawwattan jiraachuu danda'a. Kaffaltii irraa bilisa haala ta'een afaan keessaniin odeeffannoo argachuu fi deeggarsa argachuuf mirga ni qabaattu. Lakkoofsa bilbilaa 800-722-1471 (TTY: 800-842-5357) tii bilbilaa.

Français (French):

Cet avis a d'importantes informations. Cet avis peut avoir d'importantes informations sur votre demande ou la couverture par l'intermédiaire de Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous devez peut-être prendre des mesures par certains délais pour maintenir votre couverture de santé ou d'aide avec les coûts. Vous avez le droit d'obtenir cette information et de l'aide dans votre langue à aucun coût. Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):

Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konsènan kouvèti asirans lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kèk aksyon avan sèten dat limit pou ka kenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resewva enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rele nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Diese Benachrichtigung enthält wichtige Informationen. Diese Benachrichtigung enthält unter Umständen wichtige Informationen bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Rufen Sie an unter 800-722-1471 (TTY: 800-842-5357).

Hmoob (Hmong):

Tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb txog koj daim ntawv thov kev pab los yog koj qhov kev pab cuam hnu ntawm Premera Blue Cross. Tej zaum muaj cov hnu tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau ua qee yam uas peb kom koj ua tsis pub dhau cov caij nyuog uas teev tseg rau hauv daim ntawv no mas koj thiaj yuav tau txais kev pab cuam kho mob los yog kev pab them tej nqi kho mob ntawd. Koj muaj cai kom lawv muab cov ntshiab lus no uas tau muab sau ua koj hom lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Iloko (Ilocano):

Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaon iti napateg nga impormasion maipanggep iti aplikasyonyo wenna coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petsa iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding nga aldaw tapno mapagtalinaedyo ti coverage ti salun-ayto wenna tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagsasao nga awan ti bayadanyo. Tumawag iti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente. Chiama 800-722-1471 (TTY: 800-842-5357).

日本語 (Japanese):

この通知には重要な情報が含まれています。この通知には、Premera Blue Cross の申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている可能性がある重要な日付をご確認ください。健康保険や有料サポートを維持するには、特定の期日までに行動を取らなければならない場合があります。ご希望の言語による情報とサポートが無料で提供されます。800-722-1471 (TTY: 800-842-5357)までお電話ください。

한국어 (Korean):

본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관하여 그리고 Premera Blue Cross 를 통한 커버리지에 관한 정보를 포함하고 있을 수 있습니다. 본 통지서에는 핵심이 되는 날짜들이 있을 수 있습니다. 귀하의 건강 커버리지를 계속 유지하거나 비용을 절감하기 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하의 이러한 정보와 도움을 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357) 로 전화하십시오.

ລາວ (Lao):

ແຈ້ງການນີ້ມີຂໍ້ມູນສໍາຄັນ. ແຈ້ງການນີ້ອາດຈະມີຂໍ້ມູນສໍາຄັນກ່ຽວກັບຄໍາຮ້ອງສະໝັກ ຫຼື ຄວາມຄົມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີ່ສໍາຄັນໃນແຈ້ງການນີ້. ທ່ານອາດຈະຈໍາເປັນຕ້ອງດໍາເນີນການຕາມກຳນົດ ເວລາສະເພາະເພື່ອຮັກສາຄວາມຄົມຄອງປະກັນສະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເວັ້ນເວີ້ ຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄດ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໃບທາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):

សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរៀបចំរបស់អ្នកកាមរយ: Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ជាក់សមត្ថភាព ដល់កិច្ចការផ្ទៃក្នុងរបស់នានា ដើម្បីនឹងរក្សាទុកការធានារ៉ាប់រងអនាគតរបស់អ្នក ឬប្រាក់ដុល្លារចេញផ្លូវ។ អ្នកមានសិទ្ធិទទួលបានព័ត៌មាននេះ និងដុល្លារនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ សូមទូរស័ព្ទ 800-722-1471 (TTY: 800-842-5357)។

ਪੰਜਾਬੀ (Punjabi):

ਇਸ ਨੋਟਿਸ ਵਿਚ ਖਾਸ ਜਾਣਕਾਰੀ ਹੈ. ਇਸ ਨੋਟਿਸ ਵਿਚ Premera Blue Cross ਵਲੋਂ ਤੁਹਾਡੀ ਕਵਰੇਜ ਅਤੇ ਅਰਜੀ ਬਾਰੇ ਮਹੱਤਵਪੂਰਨ ਜਾਣਕਾਰੀ ਹੋ ਸਕਦੀ ਹੈ . ਇਸ ਨੋਟਿਸ ਨਵ ਖਾਸ ਤਾਰੀਖਾਂ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀਂ ਜਸਰਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾਂ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਛੁੱਕ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ ਤੋਂ ਪਹਿਲਾਂ ਢੁੱਝ ਖਾਸ ਕਦਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫਤ ਵਿੱਚ ਤੋਂ ਅਪਣੀ ਭਾਸ਼ਾ ਵਿੱਚ ਜਾਣਕਾਰੀ ਅਤੇ ਮਦਦ ਪ੍ਰਾਪਤ ਕਰਨ ਦਾ ਅਧਿਕਾਰ ਹੈ ,ਕਾਲ 800-722-1471 (TTY: 800-842-5357).

فارسی (Farsi):

این اعلامیه حاوی اطلاعات مهم میباشد. این اعلامیه ممکن است حاوی اطلاعات مهم درباره فرم تقاضا و یا پوشش بیمه ای شما از طریق Premera Blue Cross باشد. به تاریخ های مهم در این اعلامیه توجه نمایید. شما ممکن است برای حفظ پوشش بیمه تان یا کمک در پرداخت هزینه های درمانی تان، به تاریخ های مشخصی برای انجام کارهای خاصی احتیاج داشته باشید. شما حق این را دارید که این اطلاعات و کمک را به زبان خود به طور رایگان دریافت نمایید. برای کسب اطلاعات با شماره 800-722-1471 (کلیر بران TTY تماس باشماره 800-842-5357) تماس برقرار نمایید.

Polskie (Polish):

To ogłoszenie może zawierać ważne informacje. To ogłoszenie może zawierać ważne informacje odnośnie Państwa wniosku lub zakresu świadczeń poprzez Premera Blue Cross. Prosimy zwrócić uwagę na kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej informacji we własnym języku. Zadzwońcie pod 800-722-1471 (TTY: 800-842-5357).

Português (Portuguese):

Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir datas importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Română (Romanian):

Prezenta notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării dumneavoastră de sănătate prin Premera Blue Cross. Pot exista date cheie în această notificare. Este posibil să fie nevoie să acționați până la anumite termene limită pentru a vă menține acoperirea asigurării de sănătate sau asistența provizorie la costuri. Aveți dreptul de a obține gratuit aceste informații și ajutor în limba dumneavoastră. Sunați la 800-722-1471 (TTY: 800-842-5357).

Русский (Russian):

Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Fa'asamoa (Samoan):

Atonu ua iai i lenei fa'asilasilaga ni fa'amatalaga e sili ona taua e tatau ona e malamalama i ai. O lenei fa'asilasilaga o se fesoasoani e fa'amatala atili i ai i le tulaga o le polokalame, Premera Blue Cross, ua e tau fia maua atu i ai. Fa'amolemole, ia e iloilo fa'alelei i aso fa'apitoa olo'o iai i lenei fa'asilasilaga taua. Masalo o le'a iai ni feau e tatau ona e faia ao le'i aulia le aso ua ta'ua i lenei fa'asilasilaga ina ia e iai pea ma maua fesoasoani mai ai i le polokalame a le Malo olo'o e iai i ai. Olo'o iai iate oe le aia tatau e maua atu i lenei fa'asilasilaga ma lenei fa'matalaga i legagana e te malamalama i ai aunoa ma se togiga tupe. Vili atu i le telefoni 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):

Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Tagalog (Tagalog):

Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itinakdang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na walang gastos. May karapatan ka na makakuha ng ganiitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):

ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับกาการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือนี้ในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471 (TTY: 800-842-5357)

Український (Ukrainian):

Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страховального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретні кінцеві строки для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дзвоніть за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):

Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hợp đồng bảo hiểm của quý vị qua chương trình Premera Blue Cross. Xin xem ngày quan trọng trong thông báo này. Quý vị có thể phải thực hiện theo thông báo đúng trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357).