09-J3000-05

Original Effective Date: 12/15/18

Reviewed: 03/10/21

Revised: 04/15/21

Next Review: 03/09/22

Subject: Mogamulizumab-kpkc (Poteligeo®)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Cutaneous T-cell lymphomas (CTCLs) are a group of Non-Hodgkin's lymphomas of mature T cells that present in the skin and may involve lymph nodes and visceral organs. Mycosis Fungoides (MF) is the most common subtype with primary cutaneous involvement and accounts for 50 to 70% of CTCLs. In 2016, approximately 1620 people in the US were diagnosed with MF. Sézary Syndrome (SS) accounts for approximately 1 to 3% of CTCLs and involves blood and lymph nodes. Treatment varies by disease stage and blood involvement and may include topical therapy, phototherapy, radiation, or systemic therapy.

Mogamulizumab-kpkc (Poteligeo®) is a humanized monoclonal antibody that binds to CC chemokine receptor type 4 (CCR4). CCR4 is expressed on the surface of some T-cell malignancies, regulatory T-cells, and a subset of Th2 T-cells and is involved with transferring lymphocytes to organs. Mogamulizumab-kpkc was approved by the US Food and Drug Administration (FDA) in August 2018 for the treatment of adult patients with relapsed or refractory mycosis fungoides or Sezary syndrome after at least one prior systemic therapy.

In a multicenter, open-label trial, 372 patients with relapsed or refractory MF/SS were randomized to receive either mogamulizumab or vorinostat after at least one prior systemic therapy. Patients were excluded with histologic transformation, prior allogeneic HSCT, autologous HSCT within 90 days, active autoimmune disease, or active infection. Patients receiving topical corticosteroids or low dose systemic steroids were permitted to continue use if stable (at least 4 weeks of therapy) and had received a median of 3 prior systemic therapies. Patients were included regardless of tumor CCR4 expression and immunohistochemistry was available in 140 patients (75%) in the mogamulizumab treatment arm. Patients in the mogamulizumab treatment arm with an available skin biopsy had CCR4 detected on ≥1%

of lymphocytes and 96% had CCR4 detected on ≥ 10% of the lymphocytes. Efficacy was evaluated by investigator-assessed progression-free survival (PFS), defined as the time from randomization until disease progression or death. The overall response rate (ORR) was evaluated based on global composite response criteria that combined measures from each disease compartment (skin, blood, lymph nodes, and viscera). Mogamulizumab resulted in a superior median PFS (7.6 months vs 3.1 months; p<0.001) and significantly higher overall response rate (ORR 28% vs 5%; p<0.001) after a median of 17 months of follow-up as compared to vorinostat. The ORR was higher in SS than with MF (37% vs 21%), and for patients with stage III or IV disease as compared to stage IIB or stage IB/IIA disease (23% and 36% vs 16% and 19%). The most common grade 1-2 adverse events with mogamulizumab were infusion related reactions (37%), skin eruptions (25%), and diarrhea (14%). The most common grade 3 adverse events were pyrexia (4%) and cellulitis (3%).

National Comprehensive Cancer Network (NCCN) Guidelines for T-cell lymphomas include mogamulizumab as a systemic therapy option (Category A) for MF and SS. It is also recommended as a second-line therapy option for relapsed or refractory Adult T-cell leukemia/lymphoma.

POSITION STATEMENT:

Initiation of mogamulizumab-kpkc (Poteligeo®) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. The member's dosage of mogamulizumab-kpkc does not exceed 1 mg/kg administered intravenously on day 1,8, 15, and 22 of the first 28 day cycle, then 1 mg/kg on days 1 and 15 of each subsequent 28 day cycle
2. The member has an indication listed in Table 1 and **ALL** indication-specific criteria are met

Table 1

Disease	Criteria for Use
Adult T-cell Leukemia/Lymphoma	When used as a single agent for acute or lymphoma subtypes with an inadequate response to first-line therapy.
Mycosis fungoides (MF)/ Sézary syndrome (SS)	When used as a single systemic agent (may be used with or without skin-directed therapy or local radiation therapy) for disease classified as **ONE** of the following: 1. Stage IB-IIA disease with higher disease burden (e.g., predominately plaque disease) 2. Stage IIB disease with tumor lesions 3. Stage III disease 4. Stage IV disease 5. Disease refractory to prior systemic therapy
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	**ONE** of the following is met: 1. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member

	meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) 2. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

Approval duration: 6 months

Continuation of mogamulizumab-kpkc (Poteligeo®) **meets the definition of medical necessity** for the indications in Table 1 when **ALL** of the following criteria are met:

1. An authorization or reauthorization for mogamulizumab-kpkc (Poteligeo®) has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of indications in Table 1, **OR** the member has previously met **ALL** indication-specific criteria.
2. The member's disease has not progressed during treatment with mogamulizumab-kpkc
3. The dose does not exceed 1 mg/kg on days 1 and 15 of each subsequent 28 day cycle

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

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FDA-approved

- Mogamulizumab-kpkc is indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy.
- 1 mg/kg is provided as an intravenous infusion over at least 60 minutes on days 1, 8, 15, and 22 of the first 28 day cycle and on days 1 and 15 of each subsequent cycle
- Administer within 2 days of the scheduled dose
- Administer premedication with diphenhydramine and acetaminophen for the first infusion.

Dose Adjustments

- Dermatologic Toxicity: Permanently discontinue for life-threatening (grade 4) rash or for any Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). Do not resume unless SJS or TEN has been excluded and the cutaneous reaction has resolved to Grade 1 or less. If moderate or severe (grades 2 or 3) rash occurs, interrupt treatment and administer at least 2 weeks of topical corticosteroids. If rash improves to grade 1 or less, treatment may be resumed. If mild rash (grade 1) occurs, consider topical corticosteroids.
- Infusion reactions: Permanently discontinue for life-threatening (grade 4) infusion reaction. Temporarily interrupt treatment for mild to severe (grade 1 to 3) infusion reaction and treat symptoms. Reduce the infusion rate by at least 50% when restarting after symptoms resolve. If reaction recurs and is unmanageable, discontinue. Administer premedication for subsequent infusions.

Drug Availability

- 20 mg/5 mL (4 mg/mL) solution in a single-dose vial

PRECAUTIONS:

Contraindications

- None

Precautions/Warnings

- Dermatologic Toxicity: Temporarily interrupt treatment for moderate or severe skin rashes. Permanently discontinue for life-threatening rash (grade 4). Rash occurred in 80/319 (25%) of patients treated: 82% were grade 1/2 and 18% were severe (grade 3). Manage with topical corticosteroids and interruption of treatment. Consider skin biopsy to distinguish drug eruption from disease progression.
- Infusion reactions: Temporarily interrupt treatment for any infusion reaction. Permanently discontinue for life-threatening infusion reaction. Infusion reactions occurred in 112/319 (35%) of patients with 8% of these being severe (grade 3). Most common signs include chills, nausea, fever, tachycardia, rigors, headache, and vomiting. Premedication with diphenhydramine and acetaminophen should be used although it is unknown if this reduces the risk or severity of reaction.
- Infections: Monitor and treat promptly. Grade 3 or higher infection or infection-related serious adverse reaction occurred in 34/184 (18%) of patients receiving mogamulizumab-kpkc.
- Autoimmune Complications: Interrupt or permanently discontinue. Grade 3 or higher immune-mediated reactions have included myositis, myocarditis, polymyositis, hepatitis, pneumonitis, and a variant of Guillain-Barre syndrome. Consider benefit/risk in patients with a history of autoimmune disease.
- Complications of Allogeneic HSCT after treatment with mogamulizumab-kpkc: Monitor for severe acute graft-versus-host disease (GVHD) and steroid-refractory GVHD. Transplant related mortality has occurred.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9204	Injection, mogamulizumab-kpkc, 1 mg

ICD-10 Diagnoses Codes That Support Medical Necessity

C84.00 – C84.19	Mycosis fungoides, Sézary disease
C91.50 – C91.52	Adult T-cell lymphoma/leukemia

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage:

- No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

Brentuximab (Adcetris) Injection, 09-J1000-53

OTHER:

Table 2: Common Terminology Criteria for Adverse Events v4.0 (CTCAE)

Grade	Description
1	Mild; asymptomatic or mild symptoms; clinical diagnostic observations only; intervention not indicated
2	Moderate; minimal, local or noninvasive intervention indicated; limited age-appropriate instrumental activities of daily living
3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living
4	Life-threatening consequences; urgent intervention indicated
5	Death related to adverse event

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 03/10/21.

GUIDELINE UPDATE INFORMATION:

12/15/18	New Medical Coverage Guideline.
01/01/19	Revision: HCPCS code updates. Added C9038.
01/15/19	Revision to position statement and references.
10/01/19	Revision: Added HCPCS J9204 and removed C9038 and J9999.
02/15/20	Review and revision to policy; consisting of updating the position statement and references.
04/15/21	Review and revision to guideline; consisting of updating references.