MEDICAL MUTUAL®

Drug Policy

Policy:	**201833-CC**	**Initial Effective Date: 10/20/2018**
Code(s):	**HCPCS C9038**	**Annual Review Date:**
SUBJECT:	**Poteligeo® (mogamulizumab-kpkc)**	**Last Revised Date: 12/26/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Overview

Poteligeo 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] Poteligeo is a recombinant humanized monoclonal antibody that targets CC chemokine receptor 4 (CCR4)-expressing cells. CCR4 is highly expressed on malignant T cells in mycosis fungoides skin lesions and on circulating malignant T cells in patients with Sézary syndrome.[2] Non-clinical *in vitro* studies show that Poteligeo-CCR4 cell binding targets a cell for antibody-dependent cellular cytotoxicity (ADCC), which results in depletion of the target cells.[1]

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on T-cell lymphomas (version 4.2018) provide treatment recommendations for the different types of T-cell lymphomas (Note: NCCN mentions that mogamulizmab is being studied for adult T-cell leukemia/lymphoma [ATLL] in the US).[3] Initial treatment options for patients with mycosis fungoides or Sézary syndrome consist of skin-directed therapies, alone or in combination with other skin-directed therapies, including local radiation. Multiple systemic therapies are recommended for treatment of patients with mycosis fungoides or Sézary syndrome refractory or unresponsive to skin-directed therapies and for patients with more aggressive or advanced disease. NCCN categorizes systemic therapies as Category A, B, or C. Examples of drugs in each category are as follows: Category A: electrocorporeal photopheresis (ECP), interferons (Intron-A®/Pegasys® [interferon-alpha injection], Actimmune® [interferon-gamma injection], systemic retinoids (bexarotene capsules [Targretin®, generics], tretinoin capsules, isotretinoin [Absorica®, Amnesteem®, Claravis™, Myorisan™, Zenatane™, generics], acitretin capsules [Soriatane®, generics]), HDAC inhibitors (Zolinza® [vorinostat capsules], Istodax® [romidepsin injection]), low-dose methotrexate (≤ 100 mg once a week), or Adcetris® (brentuximab vedotin injection); Category B or C: gemcitabine injection [Gemzar®, generics], liposomal doxorubicin injection [Doxil®, generics], Leukeran® [chlorambucil tablets], cyclophosphamide tablets or injection, and Velcade® [bortezomib injection]). NCCN also recommends use of combination therapies (most commonly, phototherapy plus either interferon or systemic retinoid or ECP plus either interferon or system retinoid or both). Participation in a clinical trial is recommended for all patients with refractory or progressive disease.

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Policy Statement
This policy involves the use of Poteligeo. Prior authorization is recommended for medical benefit coverage of Poteligeo. Coverage is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section.

Due to the specialized skills required for evaluation and diagnosis of patients treated with Poteligeo, as well as the monitoring required for adverse events and long-term efficacy, approval requires Poteligeo to be prescribed by, or in consultation with, a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is required, a response to therapy is required for continuation of therapy.

Recommended Authorization Criteria
Coverage of Poteligeo is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Mycosis Fungoides.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** The patient has relapsed or refractory mycosis fungoides; AND
   - **B)** The patient has received at least one prior systemic therapy (e.g., extracorporeal photopheresis, oral retinoid [bexarotene capsules {Targretin®, generics}, tretinoin capsules, isotretinoin capsules {Amnesteem®, Claravis™, generics}, acitretin capsules {Soriatane®, generics}], interferons [Intron-A®/Pegasys® {interferon-alpha injection}, Actimmune® {interferon-gamma injection}], HDAC inhibitors [Zolinza® {vorinostat capsules}, Istodax® {romidepsin injection}], methotrexate, or Adcetris® [brentuximab vedotin injection], cyclophosphamide tablets or injection, or Folotyn® [pralatrexate injection]); AND
   - **C)** The medication is prescribed by, or in consultation with, an oncologist or a dermatologist.

   Poteligeo is indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides after at least one prior systemic therapy.[1]

   Dosing in the Treatment of Mycosis Fungoides. The recommended dose of Poteligeo is 1 mg/kg administered as an intravenous (IV) infusion on Days 1, 8, 15, and 22 of the first 28-day cycle; and then on Days 1 and 15 of each subsequent 28-day cycle.[1]

   Initial Approval/Extended Approval.
   - **A)** *Initial Approval*. Approve for 1 year.
   - **B)** *Extended Approval*. Approve at 1 year intervals.

   Duration of Therapy in the Treatment of Mycosis Fungoides. Indefinite.

   Labs/Diagnostics. There are no required labs/diagnostics for Poteligeo therapy.

2. Sézary Syndrome. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** The patient has relapsed or refractory Sézary syndrome; AND
- **B)** The patient has received at least one prior systemic therapy (e.g., extracorporeal photopheresis, oral retinoid [bexarotene capsules {Targretin®, generics}, tretinoin capsules, isotretinoin capsules {Amnesteem®, Claravis™, generics}, acitretin capsules {Soriatane®, generics}], interferons [Intron-A®/Pegasys® {interferon-alpha injection}, Actimmune® {interferon-gamma injection}], HDAC inhibitors [Zolinza® {vorinostat capsules}, Istodax® {romidepsin injection}], methotrexate, or Adcetris® [brentuximab vedotin injection], cyclophosphamide tablets or injection, or Folotyn® [pralatrexate injection]); AND
- **C)** The medication is prescribed by, or in consultation with, an oncologist or a dermatologist.

Poteligeo is indicated for the treatment of adult patients with relapsed or refractory Sézary Syndrome after at least one prior systemic therapy.[1]

Dosing in the Treatment of Sézary Syndrome. The recommended dose of Poteligeo is 1 mg/kg administered as an intravenous (IV) infusion on Days 1, 8, 15, and 22 of the first 28-day cycle; and then on Days 1 and 15 of each subsequent 28-day cycle.[1]

Initial Approval/Extended Approval.
- **A)** *Initial Approval*. Approve for 1 year.
- **B)** *Extended Approval*. Approve at 1 year intervals.

Duration of Therapy in the Treatment of Sézary Syndrome. Indefinite.

Labs/Diagnostics. There are no required labs/diagnostics for Poteligeo therapy.

Uses With Supportive Evidence

3. Adult T-cell Leukemia/Lymphoma (ATLL). Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** The patient has relapsed or refractory CCR4-positive ATLL; AND
- **B)** The patient has received at least one course of chemotherapy; AND
- **C)** Poteligeo is prescribed by, or in consultation with, an oncologist or a dermatologist.

The NCCN guidelines (version 5.2018) note chemotherapy as initial therapy for ATLL: CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone), dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), and hyperCVAD (cyclophosphamide vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine. Second-line therapies include single agents (Adcetris® [brentuximab vedotin for

injection] for CD30-expressing cases, Revlimid® [lenalidomide capsules], and Poteligeo [category 2A designation; off-label use]) and combination agents (e.g., interferon and zidovudine, DHAP [dexamethasone, cisplatin, cytarabine], ESHAP [etoposide, methylprednisolone, cytarabine, cisplatin], GemOx [gemcitabine, oxaliplatin]). The NCCN notes that with Poteligeo, there is a high risk of developing graft-versus-host disease (GVHD), nonrelapse mortality, and overall mortality in patients proceeding to allogenic hematopoietic cell transplant (HCT) within 50 days of Poteligeo therapy. Therefore, Poteligeo should be used with caution in patients with ATLL who are eligible for or proceeding directly to allogeneic HCT.

The efficacy of Poteligeo was evaluated in two studies involving patients with relapsed or refractory CCR4-positive ATLL (in Japan and outside of Japan).[3-6] Twenty-eight patients were in the multicenter phase II study in Japan and the overall response rate was 50%; median progression-free survival was 5 months and overall survival was 14 months.[3-5] Seventy-one patients were in the prospective randomized study conducted outside of Japan. Patients were randomized to receive either Poteligeo or an investigator choice regimen (GemOx [gemcitabine, oxaliplatin], DHAP, or Folotyn® [pralatrexate injection]).[3,6] The overall response rates as assessed by the investigator and independent review were higher for patients treated with Poteligeo (34% and 23%, respectively) compared with those treated with the investigator choice regimen (0% and 8%, respectively).

Dosing in the Treatment of Adult T-cell Leukemia/Lymphoma (ATLL). The dose of Poteligeo used in the studies involving patients with ATLL is 1 mg/kg administered as an intravenous (IV) infusion once a week.[1]

Initial Approval/Extended Approval.
C) *Initial Approval*. Approve for 1 year.
D) *Extended Approval*. Approve at 1 year intervals.

Duration of Therapy in the Adult T-cell Leukemia/Lymphoma (ATLL). Indefinite.

Labs/Diagnostics. There are no required labs/diagnostics for Poteligeo therapy

4. Other Cancer Indications. Forward to the Medical Director for review on a case-by-case basis.

Waste Management for All Indications.
Poteligeo injection is supplied as a 20 mg/5 mL (4 mg/mL) solution in a single-dose vial.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Poteligeo has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Poteligeo® injection [prescribing information]. Bedminster, NJ: Kyowa Kirin, Inc.; August 2018.
2. Ni X, Jorgensen JL, Goswami M, et al. Reduction of regulatory T cells by mogamulizumab, a defucosylated anti-CC chemokine receptor 4 antibody, in patients with aggressive/refractory mycosis fungoides and Sézary syndrome. *Clin Cancer Res*. 2015;21:274-285.
3. NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 4.2018 – May 14, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 2, 2018.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Code C9038

HCPCS Code(s):	
C9038	injection, mogamulizumab-kpkc, 1 mg (effective 1/1/2019)