Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Mogamulizumab-kpkc (Poteligeo®)	MP-RX-FP-127-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Mogamulizumab-kpkc (Poteligeo®)* a CC chemokine receptor type 4 (CCR4)- directed monoclonal antibody approved by the Food and Drug Administration (FDA) for the treatment of of adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy.

Background Information

Mycosis fungoides (MF) is a rare type of non-Hodgkin lymphoma (NHL) originating from T cells and primarily affecting the skin. It represents approximately 4 percent of NHL cases and is more prevalent in individuals over 55 years old, with a higher incidence in males and Black patients. The exact cause of MF is uncertain, but various genetic abnormalities have been identified, affecting genes related to chromatin maintenance, immune surveillance, RNA splicing, and intracellular signaling. Patients with MF typically present with pruritic skin changes, which may precede diagnosis by months to years. Cutaneous manifestations vary and include patches, plaques, tumors, erythroderma, poikiloderma, and papules. Extracutaneous involvement is uncommon but may affect regional lymph nodes, lungs, spleen, liver, gastrointestinal tract, and bone marrow. Sézary syndrome, a related condition, is diagnosed when abnormal T cells (Sézary cells) are present in the blood at a certain concentration. The diagnosis of MF is based on clinical, histopathologic, molecular, and immunopathologic criteria established by the International Society for Cutaneous Lymphoma and the European Organization of Research and Treatment of Cancer (ISCL/EORTC) consensus scoring system. Staging follows ISCL/EORTC criteria and helps determine disease severity and prognosis.

Mogamulizumab is an innovative type of antibody that specifically targets a receptor called C-C chemokine receptor 4 (CCR4). This receptor plays a crucial role in directing lymphocytes to different tissues, including the skin and various organs. Importantly, CCR4 is consistently found on the surface of certain T-cell malignancies, such as mycosis fungoides, Sézary syndrome, adult T-cell leukemia/lymphoma, and peripheral T-cell lymphoma. When mogamulizumab binds to CCR4, it marks the cell for destruction through a process called antibody-dependent cellular cytotoxicity (ADCC), leading to the depletion of the target cell.

In the MAVORIC trial, mogamulizumab demonstrated superior efficacy compared to vorinostat in patients previously treated for mycosis fungoides (MF) and Sézary syndrome (SS), with higher overall response rates (ORR) and longer median progression-free survival (PFS). Specifically, mogamulizumab achieved an ORR of 28% and a median PFS of 8 months, compared to vorinostat's ORR of 5% and median PFS of 3 months. Additionally, patients with SS had a higher ORR (37%) than those with MF (21%). Notably, the number of prior therapies did not impact

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the efficacy of mogamulizumab. In a post hoc analysis, 31% of patients who crossed over from vorinostat to mogamulizumab experienced an ORR. Adverse events associated with mogamulizumab were primarily grade 1-2 infusion-related reactions, skin eruptions, and diarrhea, with grade 3 adverse events such as pyrexia and cellulitis being less common. Patients with significant symptom burden and functional impairment showed the most improvement in quality of life with mogamulizumab treatment.Mogamulizumab demonstrated greater clinical benefit in patients with advanced stage III or IV disease, as well as in those with B1 and B2 blood involvement. In a post-hoc subgroup analysis, higher overall response rates (ORRs) were observed with mogamulizumab compared to vorinostat across all disease compartments, including skin, blood involvement, and lymph nodes. Specifically, ORRs for mogamulizumab were 23% and 36% for patients with stage III or IV disease, and 26% and 37% for those with B1 and B2 blood involvement. Additionally, mogamulizumab was associated with sustained reductions in CD4+ CD26- cell counts and CD4:CD8 ratios across all classes of blood involvement. However, the trial was not designed to detect differences in overall survival between the treatment groups within the specified follow-up period.

Mogamulizumab can lead to a drug-induced skin eruption with diverse clinical and pathologic characteristics, sometimes resembling cutaneous T-cell lymphoma (CTCL). This adverse event was the most common reason for discontinuing treatment in the MAVORIC trial. Additionally, mogamulizumab-induced skin rash has been suggested as a potential indicator of tumor response. It is recommended to perform a skin biopsy, including appropriate immunohistochemical stains and clonality assessment, in patients experiencing drug eruptions or skin rash associated with mogamulizumab to exclude disease progression.

The NCCN Drug and Biologics Compendia offers a category 2A recommendation for the use of Mogamulizumab-kpkc in the following settings:

- In the treatment of Stage IB MF (Skin only disease with ≥10% BSA) – STAGE IIA MF - MFSS-7 (preferred regimen)
- In the treatment of Stage IIB MF (Tumor stage disease)- preferred regimen
- In the treatment of Stage III MF (Erythrodermic disease)- preferred regimen
- In SÉZARY SYNDROME (Stage IVA1 or IVA2) - MFSS-11- preferred agent as a single therapy, in patients with low-intermediate burden or High burden disease (NCCN2A).
- In Non-Sézary (stage IVA2) or Visceral/Solid Organ (stage IVB) Disease (MFSS-11)- Mogamulizumab is recommended as an alternate treatment.

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Approved Indications

A. Treatment of adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy.

Other Uses

i. Relapsed or refractory adult T-cell leukemia/lymphoma (ATLL)

Mogamulizumab has shown efficacy in relapsed or refractory CCR4-positive adult T-cell leukemia/lymphoma (ATLL) and is approved for this indication in Japan. Studies outside Japan also demonstrate its safety and efficacy in this patient population. In a prospective randomized study involving 71 patients with relapsed or refractory ATLL, mogamulizumab resulted in higher overall response rates (ORRs) compared to an investigator choice (IC) regimen. The confirmed ORRs were 15% and 11% for mogamulizumab versus 0% for IC regimen, as assessed by the investigator and independent review. Additionally, the best ORR was 28% for mogamulizumab compared to 8% for IC regimen, as assessed by independent review, and 34% versus 0%, respectively, as assessed by investigator review. Responses to mogamulizumab were observed across all ATLL subtypes, with varying best response rates. The most common adverse events associated with mogamulizumab included infusion reactions, drug eruption, thrombocytopenia, and anemia.

Mogamulizumab is not FDA-approved for relapsed or refractory adult T-cell leukemia/lymphoma (ATLL) in the United States. However, based on findings from a prospective randomized study conducted outside of Japan, NCCN recommends mogamulizumab (off-label use) as a preferred single-agent second-line therapy option for relapsed or refractory ATLL (NCCN 2A).

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9204	Inj mogamulizumab-kpkc, 1 mg

ICD-10	Description
C84.00-C84.09	Mycosis fungoides
C84.10-C84.19	Sézary disease
Z85.72	Personal history of non-Hodgkin lymphomas
C91.50	Adult T-cell lymphoma/leukemia (HTLV-1-associated) not having achieved remission
C91.52	Adult T-cell lymphoma/leukemia (HTLV-1-associated), in relapse

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Mogamulizumab-kpkc (Poteligeo®)

A. **Criteria For Initial Approval** (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of Mycosis fungoides (MF) or Sézary syndrome (SS) (Label; NCCN 2A); **AND**
   A. Individual has tried and failed ≥ 1 systemic therapy; **AND**
   B. Poteligeo will be used as a single agent therapy.

OR

ii. Individual has a diagnosis of Adult T-Cell Leukemia/Lymphoma (NCCN 2A)
   A. Patient has chronic high risk, acute, or lymphoma subtypes, **AND**
   B. Individual is using as a second-line or subsequent therapy; **AND**
   C. Poteligeo will be used as a single agent therapy.

B. **Criteria For Continuation of Therapy**

i. MMM considers continuation of Mogamulizumab-kpkc (Poteligeo®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:
   A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
   B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. **Authorization Duration**

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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i. Mogamulizumab-kpkc (Poteligeo®) may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Mogamulizumab-kpkc (Poteligeo®) 20mg/5ml (4 mg/mL) SDV	1 mg/kg IV on days 1, 8, 15, and 22 of the first 28-day cycle, then on days 1 and 15 of each subsequent 28-day cycle until disease progression or unacceptable toxicity.
Exceptions	
None	

Reference Information

1. Hoppe RT, Kim YH, Horwitz S. Clinical manifestations, pathologic features, and diagnosis of mycosis fungoides. UpToDate [online serial). Waltham, MA: UpToDate; reviewed September 2022
2. Hoppe RT, Kim YH, Horwitz S. Treatment of advanced stage (IIB to IV) mycosis fungoides. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2023.
3. Kim YH, Bagot M, Pinter-Brown L, et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): An international, open-label, randomised, controlled phase 3 trial. Lancet Oncol 2018;19:1192-1204.
4. National Comprehensive Cancer Network (NCCN). Mogamulizumab-kpkc. NCCN Drugs and Biologics Compendium. Plymouth Meeting, PA: NCCN; January 2024.
5. National Comprehensive Cancer Network Guidelines
   - T-Cell Lymphomas Version 1.2024 — Accessed January 24, 2024
   - Primary Cutaneous Lymphomas Version 1.2024 — Accessed January 24, 2024

6. Poteligeo Prescribing Information. Bedminster, NJ: Kyowa Kirin, Inc.; March 2022. Accessed January 24, 2024. Available at: https://www.poteligeohcp.com/assets/files/full-prescribing-information.pdf. Accessed January 24, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 12/18/2024	Updated dosage table: added dosage form and strength and specified IV administration. Added federal statement. Minor formatting changes. Coding reviewed: No changes.	3/20/2025	4/2/2025
Policy Inception 01/24/2024	New Medical Policy creation	4/18/2024	6/28/2024