CONDUENT

Drug Monograph

Drug/Drug Class:	**Poteligeo® (mogamulizumab-kpkc) injection / Antineoplastic Agent, Monoclonal Antibody**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Poteligeo® is available as a 20 mg/5mL (4 mg/mL) intravenous solution in a single-dose vial. Distributed by: Kyowa Kirin Inc., Bedminster, NJ 07921.
Summary of Findings:	Poteligeo® is a first-in-class monoclonal antibody indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy. The safety and efficacy of Poteligeo® was assessed in an open-label, multi-center, randomized study comparing Poteligeo® versus Zolinza® in patients with mycosis fungoides and Sézary syndrome. In the MAVORIC Study, treatment with Poteligeo® resulted in a median progression-free survival of 6.7 months versus 3.8 months with Zolinza®. Poteligeo® also significantly improved response rates overall (28% versus 5%; P < .0001), and the median duration of response was 13.9 versus 9 months, respectively.
Status Recommendation:	☐ Prior Authorization (PA) Required ☒ Open Access ☐ Clinical Edit ☐ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Non-Preferred Agent ☐ Appropriate Indications ☒ No PA Required

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [2]

Mycosis fungoides and Sézary syndrome are the two most common types of cutaneous T-cell lymphoma. These are rare, hard-to-treat forms of non-Hodgkin's Lymphoma. In mycosis fungoides, T-cell lymphocytes become cancerous and affect the skin. In Sézary syndrome, cancerous T-cell lymphocytes affect the skin and are in the blood. Treatment is usually palliative, to relieve symptoms and improve the quality of life.

Dosage Form [1,3]

Poteligeo® is available as a sterile, preservative-free 20 mg/5mL (4 mg/mL) intravenous solution in a single-dose vial.

Manufacturer [1]

Distributed by: Kyowa Kirin Inc., Bedminster, NJ 07921.

Indication(s) [1,3]

Poteligeo® is indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy.

Clinical Efficacy [1,3,4] (mechanism of action/pharmacology, comparative efficacy)

Poteligeo® is a first-in-class defucosylated, humanized IgG1 kappa monoclonal antibody which selectively binds to C-C chemokine receptor 4 (CCR4). CCR4 mediates cell trafficking of lymphocytes to skin and various organs and is consistently expressed on the surface of T-cell malignancies. Poteligeo® binding to CCR4 targets a cell for antibody-dependent cellular cytotoxicity, resulting in target cell depletion.

Pharmacokinetics:

	Poteligeo®
Volume of Distribution	3.6 L
Excretion	Clearance: 12 mL/hr
Half-life	17 days

MAVORIC (Mogamulizumab anti-CCR4 Antibody versus Comparator In CTCL) Study

STUDY DESIGN	An open-label, multi-center, randomized, phase 3 clinical trial (MAVORIC, N=372).
INCLUSION CRITERIA	Male and female subjects ≥ 18 years of age at the time of enrollment (except in Japan where subjects must be ≥ 20 years of age at the time of enrollment). Histologically confirmed diagnosis of MF or SS (Stage IB, II-A, II-B, III and IV). Subjects who have failed at least one prior course of systemic therapy. Resolution of all clinically significant toxic effects of prior cancer therapy to grade ≤1. Adequate hematological, renal and hepatic function. Women of childbearing potential (WOCBP) must have a negative pregnancy test within 7 days of receiving study medication. WOCBP and male subjects as well as their female partners of childbearing potential must agree to use effective contraception throughout the study and for 6 months after the last dose of Poteligeo®
EXCLUSION CRITERIA	Prior treatment with Poteligeo® or Zolinza®. Diagnosed with a malignancy in the past two years. Clinical evidence of central nervous system (CNS) metastasis. Psychiatric illness, disability or social situation that would compromise the subject's safety or ability to provide consent, or limit compliance with study requirements. Known or tests positive for human immunodeficiency virus (HIV), human T-cell leukemia virus (HTLV-1), hepatitis B or hepatitis C. Active herpes simplex or herpes zoster. Experienced allergic reactions to monoclonal antibodies or other therapeutic proteins. Known active autoimmune disease (ex: Grave's disease, systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, psoriasis). Pregnant or lactating women.

TREATMENT REGIMEN	Patients were randomized to receive Poteligeo® 1 mg/kg administered intravenously 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 or Zolinza® 400 mg orally once daily, continuously for 28-day cycles. Treatment continued until disease progression or unacceptable toxicity. Zolinza® -treated patients with disease progression or unacceptable toxicities were permitted to cross over to Poteligeo®.
RESULTS	The primary endpoint was investigator-assessed progression-free survival. The results showed that Poteligeo® demonstrated significantly superior progression-free survival at a median of 6.7 months compared to 3.8 months with Zolinza® (hazard ratio = 0.64; P = .0007). Poteligeo® also significantly improved response rates overall (28% vs 5%; P < .0001). The median duration of response was 13.9 vs 9 months, respectively.
SAFETY	Not specified.

Contraindications [1]

- There are no contraindications listed per the manufacturer labeling.

Warnings and Precautions [1,3]

- Dermatologic Toxicity: Fatal and life-threatening skin adverse reactions, including Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis have occurred. Onset, affected areas and appearance were variable. Monitor patients for rash throughout the treatment course. Interruption or permanent therapy discontinuation may be necessary.
- Infusion Reactions: Fatal and life-threatening infusion reactions have been reported. The majority of reactions occur during or shortly after the first infusion, but may also occur with subsequent infusions. Consider premedication (diphenhydramine and acetaminophen) prior to the first infusion in all patients, as well as in patients who experience any previous infusion reaction. Monitoring recommended and infusion rate reduction, therapy interruption or discontinuation may be necessary.
- Infections: Fatal and life-threatening infections have occurred, including sepsis, pneumonia and skin infections. Monitoring recommended.
- Autoimmune Complications: Fatal and life-threatening immune-mediated adverse reactions, including myositis, myocarditis, polymyositis, hepatitis, pneumonitis, and a variant of Guillain-Barré syndrome, have been reported. Therapy interruption or discontinuation may be necessary. Consider risk/benefit in patients with a history of autoimmune disease.
- Transplant Complications: Increased risk of transplant complications, including severe, acute and steroid-refractory graft-versus-host-disease with fatalities, has been reported when therapy was followed by allogenic hematopoietic stem cell transplantation. Higher risk when given within a shorter time frame (approximately 50 days). Monitoring recommended.
- Pregnancy: Poteligeo® is not recommended during pregnancy or in women of

childbearing potential not using contraception. Evaluate pregnancy status prior to use. Effective contraception should be used in females of reproductive potential during treatment and for at least 3 months after therapy is complete.

Adverse Effects [1]

Most Common, ≥10%	Poteligeo® (N=184)	Zolinza® (N=186)
Rash, Including Drug Eruption	35%	11%
Infusion Related Reaction	33%	0%
Upper Respiratory Tract Infection	22%	16%
Skin Infection	19%	13%
Musculoskeletal Pain	22%	17%
Pyrexia	17%	7%
Mucositis	12%	6%

Other Common Adverse Reactions in ≥10% of the Poteligeo® Arm:

- General disorders: fatigue (31%), edema (16%)
- Gastrointestinal disorders: diarrhea (28%), nausea (16%), constipation (13%)
- Blood and lymphatic system disorders: thrombocytopenia (14%), anemia (12%)
- Nervous system disorders: headache (14%)
- Vascular disorders: hypertension (10%)
- Respiratory disorders: cough (11%)

Drug Interactions [1]

- Immunosuppressive or immune-modulating agents.

Dosage and Administration [1,3]

Recommended Dosage

The recommended dose of Poteligeo® is 1 mg/kg administered as an intravenous infusion over at least 60 minutes. Do not administer Poteligeo® subcutaneously or by rapid intravenous administration. Administer 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. Administer Poteligeo® within 2 days of the scheduled dose.

Recommended Premedications

Administer premedication with diphenhydramine and acetaminophen for the first Poteligeo® infusion. If an infusion reaction occurs, give premedication for subsequent infusions.

Cost

Generic Name	Brand Name	Manufacturer	How Supplied	Dose	Cost**
mogamulizumab-kpkc	Poteligeo®	Kyowa Kirin	20 mg/5 mL single dose vial	1 mg/kg IV infusion on days 1,8,15,22 of 1st cycle and on days 1 and 15 of next cycles	$3,790.00/vial
vorinostat	Zolinza®	Merck	Bottle of 120 - 100 mg capsules	400 mg orally once daily	$15,009.60/bottle

** Wholesale Acquisition Cost

Conclusion

Poteligeo® is a monoclonal antibody indicated for the treatment of adult patients with relapsed or refractory MF or SS after at least one prior systemic therapy. In the open-label, multi-center, randomized, phase 3 MAVORIC Study, treatment with Poteligeo® resulted in superior progression-free survival, improved overall response rates and longer duration of response compared with Zolinza®. The most common side effects of Poteligeo® include rash, infusion-related reactions, fatigue, diarrhea, musculoskeletal pain and upper respiratory tract infection. Serious warnings of Poteligeo® treatment include risk of dermatologic toxicity, infusion reactions, infections, autoimmune complications and stem cell transplant complications.

Recommendation

MO HealthNet Division recommends Open Access status for this product.

References

1) Product Information: Poteligeo® (mogamulizumab-kpkc) Kyowa Kirin Inc., Bedminster, NJ 07921.
2) National Cancer Institute. Mycosis Fungoides (Including Sézary Syndrome). https://www.cancer.gov/types/lymphoma/patient/mycosis-fungoides-treatment-pdq#section/all. Accessed November 5, 2018.
3) Mogamulizumab-kpkc: Drug Information (Lexicomp) Wolters Kluwer Health.
4) 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 Sep;19(9):1192-1204. doi: 10.1016/S1470-2045(18)30379-6. Epub 2018 Aug 9.

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Date: November 6, 2018