STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Zynyz (retifanlimab-dlwr)
PAM–069

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	10/01/2023
Revision Number:	1	**Last Rev Date:**	04/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	04/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	04/19/2024

Overview

Medication:[1]	retifanlimab-dlwr
Brand Name:	Zynyz®
Pharmacologic Category:	Programmed death receptor-1 (PD-1)–blocking antibody
FDA-Approved Indication(s):	Treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma. ➢ This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
How Supplied:	Single-dose vial, 500 mg/20 mL (25 mg/mL)
Dosage and Administration:	500 mg administered as an intravenous infusion over 30 minutes every 4 weeks until disease progression, unacceptable toxicity, or up to 24 months
Benefit Category:	Medical

Descriptive Narrative

Merkel cell carcinoma (MCC) is a rare, aggressive, cutaneous malignancy has a high propensity for recurrence and metastases. Patients typically present with a rapidly growing, painless, firm, nontender, shiny, flesh-colored or bluish-red, intracutaneous nodule commonly located in the head and neck region. MCC is often clinically misdiagnosed as a benign lesion (e.g., cyst, lipoma, pyogenic granuloma). Recognized risk factors for MCC include light skin color, increasing age, male sex, immunosuppression, and other malignancies.

Data from the Surveillance, Epidemiology, and End Results (SEER) Program database indicate that in the United States, the estimated annual incidence rate rose from 0.5 cases per 100,000 persons in 2000 to 0.7 cases per 100,000 persons in 2013. MCC incidence increases exponentially with advancing age, from 0.1 to 1 to 9.8 (per 100,000 person-years) among age groups 40 to 44, 60 to 64, and > 85 years, respectively. Due to aging of the population, the United States' MCC incidence is predicted to climb to more than 3200 cases in 2025.[2]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[3]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Merkel Cell Carcinoma (Version 1.2024 – November 22, 2023)[4]

NCCN Guidelines® Recommendation(s) for retifanlimab-dlwr (Zynyz®) in Merkel Cell Carcinoma [a, b]
(1) Local Disease N0 [c] A. Primary locally advanced (if curative surgery and curative radiation therapy [RT] not feasible) i. Retifanlimab-dlwr (Zynyz®): Category 2A, other recommended regimen B. Recurrent locally advanced (if curative surgery and curative RT not feasible) i. Retifanlimab-dlwr (Zynyz®): Category 2A, preferred regimen (2) Regional Disease N+ [d] A. Recurrent regional disease (if curative surgery and curative RT not feasible) i. Retifanlimab-dlwr (Zynyz®): Category 2A, preferred regimen (3) Disseminated Disease M1 A. Retifanlimab-dlwr (Zynyz®): Category 2A, preferred regimen
[a] When available and clinically appropriate, enrollment in a clinical trial is recommended. [b] Data from non-randomized trials in patients with MCC demonstrate that rates of durable response are improved with PD-1/PD-L1 blockade compared with cytotoxic therapy. The safety profiles for checkpoint immunotherapies are significantly different from cytotoxic therapies. Consult prescribing information for recommendations on detection and management of immune-related adverse events associated with checkpoint immunotherapies. Clinician and patient education is critical for safe administration of checkpoint immunotherapies. [c] For primary disease, adjuvant systemic therapy is not recommended outside of a clinical trial. [d] For regional disease, adjuvant chemotherapy is not routinely recommended as survival benefit has not been demonstrated in available retrospective studies but could be used on a case-by-case basis if clinical judgement dictates. No data are available to support the adjuvant use of immunotherapy outside of a clinical trial.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale[5]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Prior authorization is required.

Zynyz® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of Merkel cell carcinoma (MCC); **AND**
2. Disease is metastatic or recurrent, locally advanced, and is not amenable to surgery or radiation therapy; **AND**
3. Member is 18 years of age or older; **AND**
4. Member has not been previously treated with anti-PD-1 (programmed death receptor-1), anti-PD-L1 (programmed death ligand-1), or anti-CTLA-4 (cytotoxic T-lymphocyte antigen 4) antibodies; **AND**
5. Member has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; **AND**
6. Prescribed by, or in consultation with, an oncologist; **AND**
7. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 500 mg every 4 weeks; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Zynyz® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 500 mg every 4 weeks until disease progression, unacceptable toxicity, or up to a total of 24 months of treatment; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months **(not to exceed total of 24 months of treatment)**
Quantity Limits	500 mg every 4 weeks	500 mg every 4 weeks

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9345	Injection, retifanlimab-dlwr, 1 mg

ICD-10	Description
C4A.0 – C4A.9	Merkel cell carcinoma

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
50881-0006-03	Incyte Corporation (50881)	1 mg	1	EA	500

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions

are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Zynyz® prescribing information (11/2023). Incyte Corporation: Wilmington, DE. Available online at: www.zynyzhcp.com. Accessed December 8, 2023.

[2] Tai P, Nghiem PT, Park SY. Pathogenesis, clinical features, and diagnosis of Merkel cell (neuroendocrine) carcinoma. Corona R, Shah SM, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed October 8, 2023.

[3] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[4] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Merkel Cell Carcinoma (v.1.2024 – November 22, 2023). Accessed December 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[5] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
04/19/2024	CAC	Criteria implementation (policy originally presented at January 2024 meeting; tabled for further review until April 2024).	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee