Zynyz (retifanlimab-dlwr)
PAM – 069

Iowa Medicaid Program	Prior Authorization	**Effective Date**	10/01/2023
Revision Number	3	**Last Reviewed**	10/16/2026
Reviewed By	Medicaid Medical Director	**Next Review**	01/15/2027
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	04/19/2024

Overview

Medication: [1]	retifanlimab-dlwr
Brand Name:	Zynyz®
Pharmacologic Category:	Antineoplastics; Immune Checkpoint Inhibitor; Programmed death receptor-1 (PD-1)–blocking antibody
FDA-Approved Indication(s):	1. In combination with carboplatin and paclitaxel: indicated for the first-line treatment of adult patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC). ➢ **NEW** indication: FDA-approved 5/15/2025 2. As a single agent: indicated for the treatment of adult patients with locally recurrent or metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy. ➢ **NEW** indication: FDA-approved 5/15/2025 3. Treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma. ➢ **CONVERTED** from accelerated to traditional approval, effective 12/17/2025 (via FDA).
How Supplied:	Single-dose vial, 500 mg/20 mL (25 mg/mL)
Dosage and Administration:	See table on next page
Benefit Category:	Medical

Dosage and Administration

Indication	Zynyz Dose	Duration of Treatment
Combination Therapy		
Adult patients with inoperable locally recurrent or metastatic **SCAC** in combination with carboplatin and paclitaxel	500 mg every 4 weeks or 375 mg every 3 weeks	Until disease progression, unacceptable toxicity, or up to 12 months
Monotherapy		
Adult patients with locally recurrent or metastatic **SCAC** with disease progression on or intolerance to platinum-based chemotherapy	500 mg every 4 weeks or 375 mg every 3 weeks	Until disease progression, unacceptable toxicity, or up to 24 months
Adult patients with metastatic or recurrent locally advanced **MCC**	500 mg every 4 weeks	Until disease progression, unacceptable toxicity, or up to 24 months

MCC – Merkel cell carcinoma **SCAC –** squamous cell carcinoma of the anal canal

Descriptive Narrative

Merkel cell carcinoma (MCC)

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]

Squamous cell carcinoma of the anal canal (SCAC)

Anal cancer is uncommon, with approximately 11,000 new cases diagnosed annually in the U.S. and over 50,000 cases diagnosed annually worldwide. However, the incidence of anal cancer is increasing globally. The histologic types of malignancies that arise within the anus include anal squamous cell carcinomas (SCCs), adenocarcinomas, and neuroendocrine tumors.

An anal cancer is clinically defined as a tumor that develops from any of the three types of mucosae located in the anal region. Anal squamous cell carcinomas (SCCs) are the most common histologic type of anal carcinoma. Anal SCCs, regardless of whether they arise within transitional or squamous mucosa, appear to behave similarly, despite their sometimes variable morphologic appearance. By convention, most studies that report outcomes of "anal cancer" refer exclusively to SCCs arising within the mucosa of the anus.[3]

Among all patients diagnosed with anal SCC, less than 15 percent will initially present with metastatic disease. For patients with metastatic anal SCC, the goals of treatment include treating cancer-related symptoms, controlling disease burden, and prolonging overall survival (OS). The estimated five-year OS for metastatic anal SCC is approximately 36 percent.[4]

Guidelines

The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology document evidence-based, consensus-driven management to ensure that all patients receive preventive, diagnostic, treatment, and supportive services that are most likely to lead to optimal outcomes. The guidelines are developed and updated by 63 individual panels, comprising over 1,900 clinicians and oncology researchers from the 33 NCCN Member Institutions. The categories for recommendations are based on both the level of clinical evidence available and the degree of consensus within the NCCN Guidelines Panel.

The library of NCCN Guidelines® currently apply to more than 97 percent of people living with cancer or anyone at risk for a diagnosis of cancer in the United States. The guidelines incorporate real-time updates in keeping with the rapid advancements in the field of cancer research and management and are intended to assist all individuals who impact decision-making in cancer

care, including physicians, nurses, pharmacists, payers, patients and their families, and others.

The NCCN Guidelines® provide recommendations based on the best evidence available at the time they are derived. Because new data are published continuously, it is essential that the NCCN Guidelines also be continuously updated and revised* to reflect new data and clinical information that may add to or alter current clinical practice standards.[5,6]

The information referenced at the time of this policy writing/revision (note version number and effective date) is from the NCCN Guidelines® for:[7]

- Anal Carcinoma (v.2.2026 – April 7, 2026)
- Merkel Cell Carcinoma (v.2.2026 – October 24, 2025)

* 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.

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale [8]

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 themselves, 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 to 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 housework, 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.

Merkel cell carcinoma (MCC)

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.

Squamous cell carcinoma of the anal canal (SCAC)

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

1. Diagnosis of squamous cell carcinoma of the anal canal (SCAC); **AND**
2. Disease is locally recurrent or metastatic; **AND**
3. Member is 18 years of age or older; **AND**
4. Member has not been previously treated with anti-PD-1, anti-PD-L1, or anti-CTLA-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. Zynyz® is prescribed in one of 2 ways (a or b):
    a. In combination with carboplatin and paclitaxel for the first-line treatment of inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC); or,
    b. As monotherapy for the treatment of locally recurrent or metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy; **AND**

8. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 500 mg every 4 weeks or 375 mg every 3 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.

Continuation criteria (all above indications)

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, b, c, or d):
    a. Zynyz® is prescribed in combination with carboplatin and paclitaxel for the treatment of locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC). Dose does not exceed 500 mg every 4 weeks or 375 mg every 3 weeks until disease progression, unacceptable toxicity, or up to a total of 12 months of treatment; **OR**
    b. Zynyz® is prescribed as monotherapy for the treatment of locally recurrent or metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy. Dose does not exceed 500 mg every 4 weeks or 375 mg every 3 weeks until disease progression, unacceptable toxicity, or up to a total of 24 months of treatment; **OR**
    c. Zynyz® is prescribed as monotherapy for the treatment of metastatic or recurrent locally advanced Merkel cell carcinoma. Dose does not exceed 500 mg every 4 weeks until disease progression, unacceptable toxicity, or up to a total of 24 months of treatment; **OR**
    d. 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

MCC	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

SCAC	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months • not to exceed total of 12 months of treatment when used as combination therapy • not to exceed total of 24 months of treatment when used as monotherapy
Quantity Limits	500 mg every 4 weeks or 375 mg every 3 weeks	500 mg every 4 weeks or 375 mg every 3 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
C21.0 – C21.8	Squamous cell carcinoma of the anal canal

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units /Pkg
50881-0006-03 (500 mg/20 mL)	Incyte Corporation (50881)	1 mg	1	EA	500

Compliance

1. Should conflict exist between the 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 (05/2026). Incyte Corporation: Wilmington, DE. Available online: www.zynyzhcp.com. Accessed August 5, 2026.

[2] Tai P, Nghiem PT, Park SY. Pathogenesis, clinical features, and diagnosis of Merkel cell (neuroendocrine) carcinoma. Corona R, Yushak M, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed August 5, 2026.

[3] Willett CG, Eng C. Treatment of metastatic anal squamous cell carcinoma. Shah SM, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed August 5, 2026.

[4] Willett CG, Eng C. Anatomy, pathology, epidemiology, and risk factors of anal cancer. Shah SM, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed August 5, 2026.

[5] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed October 20, 2025.

[6] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 20, 2025.

[7] NCCN Clinical Practice Guidelines in Oncology. The NCCN Guidelines® are continuously updated and revised to reflect new data and clinical information that may add to or alter current clinical practice standards. To view the most recent and complete version, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- Anal Carcinoma (v.2.2026 – April 7, 2026)
- Merkel Cell Carcinoma (v.2.2026 – October 24, 2025)

[8] 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.

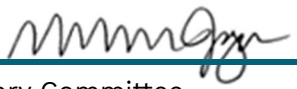
Criteria Change History

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

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

Change Date	Changed By	Description of Change	Version
10/16/2026	CAC	Annual review. Updated references. 5/15/2025: FDA approved new indication for squamous cell carcinoma of the anal canal (SCAC). Added information to policy (e.g., Overview table, Criteria, etc.). 12/17/2025: Indication for Merkel cell carcinoma (MCC) converted from accelerated to traditional approval per FDA. 3/30/2026: FDA approved new dosing regimen for SCAC (option to continue dose of 500 mg every 4 weeks or may dose at 375 mg every 3 weeks). No change for dosing of MCC (still 500 mg every 4 weeks). Policy format update: Removed current NCCN Guidelines recommendations, as guidelines may change more frequently than the review cadence of this document. Will continue to reference NCCN when writing criteria, and include the specific version referenced at the time of the policy writing/revision.	3
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
01/17/2025	CAC	Annual review. Reviewed NCCN Guidelines, no changes.	2
Signature William (Bill) Jagiello, DO			

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

CAC = Medicaid Clinical Advisory Committee