Clinical Policy: Retifanlimab-dlwr (Zynyz)

Reference Number: CP.PHAR.629
Effective Date: 06.01.23
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Retifanlimab-dlwr (Zynyz®) is a programmed death receptor-1 (PD-1)–blocking antibody.

FDA Approved Indication(s)

Zynyz is indicated:

- In combination with carboplatin and paclitaxel for the first-line treatment of adult patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC)
- As a single agent for the treatment of adult patients with locally recurrent or metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy
- For the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Zynyz is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Merkel Cell Carcinoma (must meet all)**:**

1. Diagnosis of MCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease meets one of the following (a or b):
   a. Metastatic, recurrent locally advanced, or in-transit regional disease;
   b. Both of the following (i and ii):
      i. Primary locally advanced, primary regional disease, or recurrent regional disease;
      ii. Disease is not amenable to surgery or radiation therapy;
5. Prescribed as a single agent;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg (1 vial) every four weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Anal Carcinoma (must meet all)**:**
1. Diagnosis of locally recurrent, progressive, or metastatic SCAC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as one of the following (a or b):
   a. A single agent;
   b. In combination with carboplatin and paclitaxel;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg (1 vial) every four weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Small Bowel Adenocarcinoma, Colon Cancer, Rectal Cancer (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. Small bowel adenocarcinoma;
   b. Colon cancer;
   c. Rectal cancer;
2. Disease is one of the following mutations (a, b, or c):
   a. Microsatellite instability-high (MSI-H);
   b. Deficient mismatch repair (dMMR);
   c. Polymerase epsilon/delta (POLE/POLD1) with ultra-hypermutated phenotype (e.g., tumor mutation burden [TMB] > 50 mut/Mb);
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Prescribed as a single agent;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg (1 vial) every four weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Zynyz for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 500 mg (1 vial) every four weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MCC: Merkel cell carcinoma
NCCN: National Comprehensive Cancer Network
SCAC: squamous cell carcinoma of the anal canal

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MCC, SCAC	500 mg IV infusion every 4 weeks	500 mg IV infusion every 4 weeks

VI. Product Availability

Single-dose vial: 500 mg/20 mL (25 mg/mL)

VII. References

1. Zynyz Prescribing Information. Wilmington, DE: Incyte Corporation.; December 2025. Available at: https://www.zynyz.com/. Accessed December 26, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium. Accessed December 26, 2025.
3. National Comprehensive Cancer Network. Merkel Cell Carcinoma Version 2.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf. Accessed December 26, 2025.
4. National Comprehensive Cancer Network. Anal Carcinoma Version 3.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed May 21, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9345	Injection, retifalimab-dlwr, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.13.23	05.23
2Q 2024 annual review: for MCC, added pathways for primary locally advanced disease and recurrent regional disease per NCCN 2A recommendation and added requirement that Zynyz be prescribed as a single agent; added criteria for anal carcinoma per NCCN 2A recommendation; added Zynyz HCPCS code and removed inactive codes; references reviewed and updated.	02.13.24	05.24
2Q 2025 annual review: added criteria for small bowel adenocarcinoma, colon cancer, and rectal cancer per NCCN 2A recommendation; for anal carcinoma, added option to be prescribed in combination with carboplatin and paclitaxel; references reviewed and updated.	03.06.25	05.25
RT4: added new FDA-approved indication for SCAC.	05.21.25	
RT4: updated FDA Approved Indication(s) section for MCC from accelerated approval to full approval per PI; extended Medicaid and HIM initial approval durations from 6 months to 12 months for this maintenance medication for a chronic condition; for MCC, added pathway for in-transit regional disease and primary regional disease per NCCN compendium and removed requirement of "Disease is not amenable to surgery or radiation therapy" for metastatic or recurrent locally advanced disease per PI.	12.26.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.