Clinical Policy: Retifanlimab-dlwr (Zynyz)

Reference Number: LA.PHAR.629
Effective Date:
Last Review Date: 07.11.25
Line of Business: Medicaid

Coding Implications
Revision Log

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

****Please note: This policy is for medical benefit****

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)*

**This indication is approved under accelerated approval based on tumor response and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.*

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 Louisiana Healthcare Connections 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, b, or c):
   a. Metastatic;
   b. Primary (*off-label*) or recurrent locally advanced;
   c. Recurrent regional disease (*off-label*);
5. Disease is not amenable to surgery or radiation therapy;
6. Prescribed as a single agent;
7. 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: 6 months

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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: 6 months

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: 6 months

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. The no coverage criteria policy LA.PMN.255

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 LA.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections, 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: 12 months

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 LA.PMN.255
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 LA.PMN.53.

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 policy LA.PMN.53.

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.; May 2025. Available at: https://www.zynyz.com/. Accessed May 21, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium. Accessed May 21, 2025.
3. National Comprehensive Cancer Network. Merkel Cell Carcinoma Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf. Accessed May 21, 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	LDH Approval Date
Converted to local policy	07.11.25	

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. Louisiana Healthcare Connections 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. 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.