Clinical Policy: Retifanlimab-dlwr (Zynyz)

Reference Number: PA.CP.PHAR.629
Effective Date: 06/2023
Last Review Date: 04/2026

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 PA Health & Wellness® 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, recurrent locally advanced, or in-transit N+ 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;
   c. Other NCCN recommendations listed as category 1, 2A, or 2B;
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*).

Approval duration: 12 months

B. Anal Carcinoma (must meet all)**:**
1. Diagnosis of locally recurrent, progressive, or metastatic anal carcinoma;

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 one of the following (i or ii):
      i. 375 mg (1 vial) every three weeks;
      ii. 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*).

Approval duration: 12 months

C. NCCN Recommended Uses (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a - f):
   a. Appendiceal neoplasm or cancer;
   b. Endometrial carcinoma;
   c. Colon cancer;
   d. Rectal cancer;
   e. Small bowel adenocarcinoma;
   f. Other NCCN recommendations listed as category 1, 2A, or 2B;
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 one of the following (i or ii):
      i. 375 mg (1 vial) every three weeks;
      ii. 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*).

Approval duration: 12 months

D. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;

2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b or c):
   a. For MCC: New dose does not exceed 500 mg (1 vial) every four weeks;
   b. For all other indications: New dose does not exceed one of the following (i or ii):
      i. 375 mg (1 vial) every three weeks;
      ii. 500 mg (1 vial) every four weeks;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.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 policies – PA.CP.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/20mL (25 mg/mL)

VII. References

1. Zynyz Prescribing Information. Wilmington, DE: Incyte Corporation.; May 2026. Available at: https://www.zynyz.com/. Accessed June 17, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium. Accessed June 17, 2026.
3. National Comprehensive Cancer Network. Merkel Cell Carcinoma Version 2.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf. Accessed January 28, 2026.
4. National Comprehensive Cancer Network. Anal Carcinoma Version 2.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed June 17, 2026.
5. National Comprehensive Cancer Network. Uterine Neoplasms Version 3.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed June 17, 2026.

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
Policy created	05/2023
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.	04/2024
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.	04/2025
2Q 2026 annual review: RT4: added new FDA-approved indication for SCAC; RT4: updated FDA Approved Indication(s) section for MCC from accelerated approval to full approval per PI; extended 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; added off-label criteria for appendiceal neoplasms and cancers per NCCN; simplified NCCN off-label uses under section "NCCN Recommended Uses (off-label)"; references reviewed and updated.	04/2026