Zynyz® (retifanlimab-dlwr)
(Intravenous)

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I. Length of Authorization Δ [1,13-15]

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter for up to a maximum of 24 months (26 total doses) of therapy, unless otherwise specified.
  - Squamous Cell Carcinoma of the Anal Canal in combination with chemotherapy: Prior authorization validity may be renewed for up to a maximum of 12 months (13 total doses).

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 500 billable units every 4 weeks

III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1,2]

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy, unless otherwise specified [Δ]; **AND**
- Used as single agent therapy, unless otherwise specified; **AND**

Squamous Cell Carcinoma of the Anal Canal (SCAC) † ‡ Φ [1-2,9-10,16]

- Used in combination with carboplatin and paclitaxel for first-line treatment of inoperable locally recurrent or metastatic disease †; **OR**
- Used for locally recurrent disease with progression on or intolerance to platinum-based chemotherapy; **OR**
- Used as subsequent therapy for metastatic disease

Merkel Cell Carcinoma (MCC) † ‡ Φ [1-4]

- Patient has metastatic or recurrent locally advanced disease †; **OR**
- Patient has primary locally advanced disease ‡; **AND**

- Both curative surgery and curative radiation therapy are not feasible; **OR**

- Patient has primary or recurrent regional disease ‡; **AND**
  - Both curative surgery and curative radiation therapy are not feasible; **OR**

- Patient has in-transit regional disease ‡

Small Bowel Adenocarcinoma (SBA) ‡ [2,13]

- Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease OR polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype [e.g., tumor mutational burden (TMB) >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Patient has advanced or metastatic disease; **OR**
  - Patient has locally unresectable or medically inoperable disease; **AND**
    - Used as primary treatment

Colon Cancer ‡ [2,14]

- Patient has MSI-H/dMMR disease OR POLE/POLD1 mutation with ultra-hypermutated phenotype (e.g., TMB >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used for locally unresectable, medically inoperable, advanced, or metastatic disease

Appendiceal Adenocarcinoma – Colon Cancer ‡ [2,14]

- Patient has MSI-H/dMMR disease OR POLE/POLD1 mutation with ultra-hypermutated phenotype (e.g., TMB >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used for advanced or metastatic disease

Rectal Cancer ‡ [2,15]

- Patient has MSI-H/dMMR disease OR POLE/POLD1 mutation with ultra-hypermutated phenotype (e.g., TMB >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖**; AND**
- Used for advanced or metastatic disease

❖ *If confirmed using an FDA approved assay – http://www.fda.gov/CompanionDiagnostic*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria Δ [1,2]

Prior authorization validity may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**

- Duration of authorization has not been exceeded *(refer to Section I)*; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions, severe immune-mediated adverse reactions (e.g., pneumonitis, hepatitis, colitis, endocrinopathies, nephritis with renal dysfunction, dermatologic adverse reactions/rash, etc.), complications of allogeneic hematopoietic stem cell transplantation (HSCT), solid organ transplant rejection, etc.

Δ Notes:

- Patients responding to therapy who relapse ≥ 6 months after discontinuation due to duration (i.e., receipt of 24 months of therapy) are eligible to re-initiate PD-directed therapy.
- Patients previously presenting with aggressive disease who are exhibiting stable disease on treatment as their best response (or if therapy improved performance status) may be eligible for continued therapy beyond the 24-month limit without interruption or discontinuation.
- Patients whose tumors, upon re-biopsy, demonstrate a change in actionable mutation (e.g., MSS initial biopsy; MSI-H subsequent biopsy) may be eligible to re-initiate PD-directed therapy and will be evaluated on a case-by-case basis

V. Dosage/Administration Δ [1,9-15]

Indication	Dose
Squamous Cell Carcinoma of the Anal Canal	Combination Therapy: Administer 500 mg intravenously every four weeks until disease progression or unacceptable toxicity, or up to 12 months. Monotherapy: Administer 500 mg intravenously every four weeks until disease progression or unacceptable toxicity, or up to 24 months.
All other indications	Administer 500 mg intravenously every four weeks until disease progression or unacceptable toxicity, or up to 24 months.

VI. Billing Code/Availability Information

HCPCS Code:

- J9345 – Injection, retifanlimab-dlwr, 1 mg; 1 billable unit = 1 mg

NDC:

- Zynyz 500 mg/20 mL solution in a single-dose vial: 50881-0006-xx

VII. References

1. Zynyz [package insert]. Wilmington, DE; Incyte Corporation; May 2025. Accessed September 2025.

2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) retifanlimab-dlwr. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2025.
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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority

Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C4A.0	Merkel cell carcinoma of lip
C4A.10	Merkel cell carcinoma of unspecified eyelid, including canthus
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus
C4A.20	Merkel cell carcinoma of unspecified ear and external auricular canal
C4A.21	Merkel cell carcinoma of right ear and external auricular canal
C4A.22	Merkel cell carcinoma of left ear and external auricular canal
C4A.30	Merkel cell carcinoma of unspecified part of face

ICD-10	ICD-10 Description
C4A.31	Merkel cell carcinoma of nose
C4A.39	Merkel cell carcinoma of other parts of face
C4A.4	Merkel cell carcinoma of scalp and neck
C4A.51	Merkel cell carcinoma of anal skin
C4A.52	Merkel cell carcinoma of skin of breast
C4A.59	Merkel cell carcinoma of other part of trunk
C4A.60	Merkel cell carcinoma of unspecified upper limb, including shoulder
C4A.61	Merkel cell carcinoma of right upper limb, including shoulder
C4A.62	Merkel cell carcinoma of left upper limb, including shoulder
C4A.70	Merkel cell carcinoma of unspecified lower limb, including hip
C4A.71	Merkel cell carcinoma of right lower limb, including hip
C4A.72	Merkel cell carcinoma of left lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C4A.9	Merkel cell carcinoma, unspecified
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C7B.1	Secondary Merkel cell carcinoma
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.821	Personal history of Merkel cell carcinoma

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC