CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – Programmed Death Receptor-1) – Zynyz Utilization Management Medical Policy
- Zynyz™ (retifanlimab-dlwr intravenous infusion – Incyte)

REVIEW DATE: 03/18/2026

OVERVIEW

Zynyz, a programmed death receptor-1 (PD-1) blocking antibody, is indicated for the following in adults:[1]

- **Anal Carcinoma,** in adults:
  - 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).
  - As a single agent for the treatment of locally recurrent or metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy.
- **Merkel Cell Carcinoma**, metastatic or recurrent locally advanced disease in adults.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Zynyz. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Zynyz as well as the monitoring required for adverse events and long-term efficacy, approval requires Zynyz to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zynyz is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Anal Carcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has locally recurrent, progressive, or metastatic disease; AND
   - **C)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** The medication is used in combination with chemotherapy; OR
       Note: Examples of chemotherapy include carboplatin and paclitaxel.
     - **ii.** The medication is administered before proceeding to abdominoperineal resection; OR
     - **iii.** The medication is used as subsequent therapy; AND
   - **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 500 mg administered by intravenous infusion no more frequently than once every 4 weeks.

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2. Merkel Cell Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i, ii, iii, or iv):
  - **i.** Patient has primary or recurrent locally advanced disease, if according to the prescriber curative surgery and curative radiation therapy are not feasible; OR
  - **ii.** Patient has primary or recurrent regional disease, if according to the prescriber curative surgery and curative radiation therapy are not feasible; OR
  - **iii.** Patient has metastatic disease; OR
  - **iv.** Patient has in-transit disease; AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 500 mg administered by intravenous infusion no more frequently than once every 4 weeks.

Other Uses with Supportive Evidence

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3. Colon, Rectal, or Appendiceal Cancer. Approve for the duration noted if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i or ii):
  - **i.** Patient has a deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H); OR
  - **ii.** Patient has polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype; AND
    Note: Ultra-hypermutated phenotype is defined as tumor mutational burden > 50 mutations/megabase.
- **C)** Patient meets ONE of the following (i or ii):
  - **i.** Approve for 1 year if the patient has locally unresectable, advanced, recurrent, metastatic, or medically inoperable disease; OR
  - **ii.** Approve for 6 months if the medication is used for neoadjuvant therapy; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 500 mg administered by intravenous infusion no more frequently than once every 4 weeks.

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4. Endometrial Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has recurrent or metastatic disease; AND
- **C)** Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 500 mg administered by intravenous infusion no more frequently than once every 4 weeks.

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5. **Small Bowel Adenocarcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has locally unresectable, medically inoperable, advanced, or metastatic disease; OR
     - **ii.** The medication is used as neoadjuvant therapy; AND
   - **C)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has a deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H); OR
     - **ii.** Patient has polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype; AND
       Note: Ultra-hypermutated phenotype is defined as tumor mutational burden > 50 mutations/megabase.
   - **D)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve 500 mg administered by intravenous infusion no more frequently than once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zynyz is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Zynyz™ intravenous infusion [prescribing information]. Wilmington, DE: Incyte; December 2025.
2. The NCCN Drugs & Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 16, 2026. Search term: retifanlimab.
3. The NCCN Merkel Cell Carcinoma Clinical Practice Guidelines in Oncology (version 2.2026 – October 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 16, 2026.
4. The NCCN Anal Carcinoma Clinical Practice Guidelines in Oncology (version 1.2026 – January 22, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 16, 2026.
5. The NCCN Small Bowel Adenocarcinoma Clinical Practice Guidelines in Oncology (version 1.2026 – January 22, 2026) © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 16, 2026.
6. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 1.2026 – March 5, 2026) © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 16, 2026.
7. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 1.2026 – March 5, 2026) © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 16, 2026.
8. The NCCN Appendiceal Neoplasms and Cancers Clinical Practice Guidelines in Oncology (version 1.2026 – October 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 16, 2026.
9. Berton D, Pautier P, Lorusso D, et al. Antitumor activity and safety of the PD-1 inhibitor retifanlimab in patients with recurrent microsatellite instability-high or deficient mismatch repair endometrial cancer: Final safety and efficacy results from cohort H of the POD1UM-101 phase I study. *Gynecol Oncol*. 2024;186:191-198.
10. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 2.2026 – November 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 18, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Merkel Cell Carcinoma.** Removed "recurrent" from criterion "Patient has locally advanced disease". **Anal Carcinoma.** Added condition of approval.	03/27/2024
Annual Revision	**Merkel Cell Carcinoma.** Removed "patient has not received prior systemic therapy" as a requirement. Added "primary or recurrent" and "if according to the prescriber curative surgery and curative radiation therapy are not feasible" to patient has locally advanced disease. Added "primary" and "if according to the prescriber curative surgery and curative radiation therapy are not feasible" to patient has recurrent regional disease. **Anal Carcinoma**. Removed "persistent" and added "progressive" to patient has locally recurrent, progressive disease. Removed "medication is used as subsequent therapy". Added "medication is administered before proceeding to abdominoperineal resection" as new option of approval. **Small Bowel Adenocarcinoma**. Added new condition of approval. **Colon, Rectal or Appendiceal Cancer**. Added new condition of approval.	03/19/2025
Selected Revision	**Anal Carcinoma:** This condition was moved from "Other Uses with Supportive Evidence" to "FDA-Approved Indication". The qualifier of "metastatic" was moved from a separate approval option to the patient has locally recurrent, progressive, or metastatic disease. The medication is used as first-line therapy in combination with chemotherapy was added as an option of approval. The medication is used as second agent if patient progressed on or was intolerant to platinum-based chemotherapy was added as an option of approval condition. The requirement was revised that medication is administered before proceeding to abdominoperineal resection to include medication is used as single agent.	05/21/2025
Early Annual Revision	**Anal Carcinoma:** The medication used as single-agent was removed as an option for approval when the patient had progression or was intolerant to platinum-based chemotherapy and when the medication is administered before proceeding to abdominoperineal resection.	9/24/2025
Early Annual Revision	**Anal Carcinoma:** The option of approval for use as first-line therapy was removed when used in combination with chemotherapy. The option for approval that the patient has progressed on or was intolerant to platinum-based chemotherapy and the corresponding Note was removed. The medication is used as subsequent therapy was added as an option for approval. **Merkel Cell Carcinoma:** The patient has in-transit disease was added as an option for approval. **Colon, Rectal, or Appendiceal Cancer:** The approval duration was modified from 1 year to the duration noted. The option of approval that the patient has locally unresectable, advanced, metastatic, or medically inoperable disease was modified to approve for 1 year if the patient has locally unresectable, advanced, recurrent, metastatic, or medically inoperable disease. The approval option that the medication is used for neoadjuvant therapy was modified to approve for 6 months if the medication is used for neoadjuvant therapy. **Endometrial Carcinoma:** This new condition of approval was added. **Small Bowel Adenocarcinoma:** The medication is used as neoadjuvant therapy was added as an approval option.	03/18/2026