Utilization Review Policy 307

POLICY: Oncology (Injectable – Programmed Death Receptor-1) – Zynyz Utilization Management Medical Policy

- Zynyz™ (retifanlimab-dlwr intravenous infusion – Incyte)

EFFECTIVE DATE: 06/15/2023
LAST REVISION DATE: 09/24/2025

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

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

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

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.** Patients meets BOTH of the following (a and b):

a) The medication is used as first-line; AND
b) The medication is used in combination with chemotherapy; OR
Note: Examples of chemotherapy include carboplatin and paclitaxel.

ii. Patient has progressed on or was intolerant to platinum-based chemotherapy; OR
Note: Examples of platinum-based chemotherapy include carboplatin and paclitaxel.

iii. The medication is administered before proceeding to abdominoperineal resection; AND

D) 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.

---

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, or iii):

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; 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

---

3. Colon, Rectal, or Appendiceal Cancer. 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, ii, or iii):

i. Patient has locally unresectable or medically inoperable disease; OR

ii. Patient has advanced or metastatic disease; OR

iii. 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.

4. **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 or medically inoperable disease; OR
     - **ii.** Patient has advanced or metastatic disease; 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; May 2025.
2. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 12, 2025. Search term: retifanlimab.
3. The NCCN Merkel Cell Carcinoma Clinical Practice Guidelines in Oncology (version 1.2026 – September 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 12, 2025.
4. The NCCN Anal Carcinoma Clinical Practice Guidelines in Oncology (version 4.2025 – May 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 12, 2025.
5. The NCCN Small Bowel Adenocarcinoma Clinical Practice Guidelines in Oncology (version 3.2025 – March 31, 2025 © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 12, 2025.
6. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – June 27, 2025 © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 12, 2025.
7. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – August 26, 2025 © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 12, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	03/29/2023
Selected Revision	**Merkel Cell Carcinoma.** Patient has recurrent regional disease added as new option of approval.	04/19/2023
Annual Revision	**Merkel Cell Carcinoma.** Removed "recurrent" from criterion "Patient has locally advanced disease". **Anal Carcinoma.** Added condition of approval.	03/27/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
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	03/19/2025

	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.	
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
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025
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