Reference number(s)
5851-A

Standard Medicare Part B Management Zynyz

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Zynyz	retifanlimab-dlwr

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1]

Squamous Cell Carcinoma of the Anal Canal

Zynyz, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of adult patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC).

Zynyz, as a single agent, is indicated for the treatment of adult patients with locally recurrent or metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy.

Merkel Cell Carcinoma

Zynyz is indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC).

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

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Compendial Uses[2]

Merkel cell carcinoma
Squamous cell carcinoma of the anal canal
Appendiceal neoplasms and cancers
Colorectal cancer
Endometrial carcinoma
Small bowel adenocarcinoma

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- Documentation of laboratory report confirming microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or polymerase epsilon/delta (POLE/POLD1) tumor status with ultra-hypermutated tumor mutational burden [TMB] (greater than 50 mutations/megabase [mut/Mb]), where applicable.

Coverage Criteria

Merkel Cell Carcinoma (MCC)[1,2]

Authorization of 12 months may be granted as a single agent for treatment of locally advanced, regional, or metastatic MCC.

Squamous Cell Carcinoma of the Anal Canal (SCAC)[1,2]

Authorization of 12 months may be granted for treatment of SCAC when any of the following criteria are met:

- The requested medication will be used in combination with carboplatin and paclitaxel for one of the following:
  - Primary treatment of metastatic disease.
  - Treatment of recurrent disease.
- The requested medication will be used as a single agent for subsequent therapy for locally recurrent or metastatic disease if the member has progressed on or is intolerant to platinum-based chemotherapy.

Appendiceal Neoplasms and Cancers[2]

Authorization of 12 months may be granted as a single agent for treatment of recurrent, progressive, or metastatic deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase

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epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype (e.g., tumor mutational burden [TMB] greater than 50 mut/Mb) appendiceal neoplasms and cancers.

Colorectal Cancer[2]

Authorization of 12 months may be granted as a single agent for treatment of locally unresectable, medically inoperable, advanced, recurrent, or metastatic deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype (e.g., tumor mutational burden [TMB] greater than 50 mut/Mb) colorectal cancer (including appendiceal adenocarcinoma).

Endometrial Carcinoma[2]

Authorization of 12 months may be granted as a single agent for subsequent treatment of recurrent microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) endometrial carcinoma.

Small Bowel Adenocarcinoma[2]

Authorization of 12 months may be granted as a single agent for treatment of deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermutated phenotype (e.g., tumor mutational burden [TMB] greater than 50 mut/Mb) small bowel adenocarcinoma when either of the following criteria is met:

- The requested medication will be used as primary treatment for locally unresectable or medically inoperable disease.
- The requested medication will be used for advanced or metastatic disease.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested medication.

Authorization for 12 months may be granted (up to 24 months total) when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat an indication in the coverage criteria section.
- For members requesting reauthorization for SCAC in combination with carboplatin and paclitaxel, the maximum treatment duration is 12 months.
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen AND
    - No evidence of disease progression while on the current regimen.

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Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Zynyz
- The available compendium
  - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
  - Micromedex DrugDex
  - American Hospital Formulary Service- Drug Information (AHFS-DI)
  - Lexi-Drugs
  - Clinical Pharmacology
- NCCN Guidelines: Merkel Cell Carcinoma
- NCCN Guidelines: Anal Carcinoma
- NCCN Guidelines: Colon Cancer
- NCCN Guidelines: Rectal Cancer
- NCCN Guidelines: Small Bowel Adenocarcinoma
- NCCN Guidelines: Uterine Neoplasms
- NCCN Guidelines: Appendiceal Neoplasms and Cancers

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Zynyz are covered in addition to the following:

- Colorectal cancer, including appendiceal adenocarcinoma
- Endometrial carcinoma
- Small bowel adenocarcinoma
- Appendiceal neoplasms and cancers

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Zynyz to treat Merkel cell carcinoma, anal carcinoma, colorectal cancer (including appendiceal adenocarcinoma), endometrial carcinoma, small bowel adenocarcinoma, and appendiceal neoplasms and cancers can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

References

1. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; May 2025.
2. The NCCN Drugs & Biologics Compendium® © 2026 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 3, 2026.

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