Draft Revision Policy: Do Not Implement

Retifanlimab-dlwr (Zynyz™)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

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

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 are considered experimental/investigational and not medically necessary.

Compendial Uses

Merkel cell carcinoma
~~Anal Carcinoma~~
Squamous cell carcinoma of the anal canal
Appendiceal neoplasms and cancers
Colorectal cancer
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.

EXCLUSIONS

Coverage will not be provided for members who have experienced disease progression while on PD-1 or PD-L1 inhibitor therapy.

COVERAGE CRITERIA

Merkel Cell Carcinoma (MCC)

Authorization of 6 months may be granted as a single agent for treatment of ~~metastatic, primary clinical~~ locally advanced, ~~recurrent locally advanced, or recurrent~~ regional, or metastatic MCC.

~~**Anal Carcinoma**~~

~~Authorization of 6 months may be granted as a single agent for subsequent treatment of metastatic anal carcinoma.~~

Squamous Cell Carcinoma of the Anal Canal (SCAC)

Authorization of 6 months may be granted for treatment of SCAC when either of the following criteria is met:

- The requested medication will be used in combination with carboplatin and paclitaxel for one 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

Authorization of 6 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 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

Authorization of 6 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).

Small Bowel Adenocarcinoma

Authorization of 6 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

Squamous Cell Carcinoma of the Anal Canal

Authorization of 6 months may be granted (up to 12 months total) for continued treatment in combination with carboplatin and paclitaxel in members requesting reauthorization for SCAC when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Authorization of 6 months may be granted (up to 24 months total) for continued treatment as a single agent in members requesting reauthorization for ~~an indication~~ SCAC ~~listed in the coverage criteria section~~ when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

All Other Indications

Authorization of 6 months may be granted (up to 24 months total) for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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.

EFFECTIVE DATE

ID_CHS_2026a