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5.21.203

Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Antineoplastic Agents	**Original Policy Date:**	April 14, 2023
Subject:	Zynyz	**Page:**	1 of 5

Last Review Date: March 6, 2026

Zynyz

Description

Zynyz (retifanlimab-dlwr)

Background
Zynyz (retifanlimab-dlwr) is a programmed death receptor-1 (PD-1) blocking antibody. Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells, inhibits T-cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. Zynyz binds to the PD-1 receptor, blocks interaction with its ligands PD-L1 and PD-L2, and potentiates T-cell activity (1).

Regulatory Status
FDA-approved indications: Zynyz is a programmed death receptor-1 (PD-1) blocking antibody indicated: (1)

- Squamous Cell Carcinoma of the Anal Canal (SCAC)
  - in combination with carboplatin and paclitaxel for the first-line treatment of adult patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal.
  - as a single agent 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 (MCC)
  - for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma.

Zynyz contains warnings for the following: immune-mediated adverse reactions, infusion-related reactions, and complications of allogenic hematopoietic stem cell transplantation (HSCT) (1).

Zynyz can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to use effective contraception during treatment with Zynyz and for 4 months after the last dose (1).

The safety and effectiveness of Zynyz have not been established in pediatric patients less than 18 years of age (1).

Related Policies
Keytruda, Loqtorzi, Opdivo

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zynyz may be considered **medically necessary** if the conditions indicated below are met.

Zynyz may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC)
    a. Used in combination with carboplatin and paclitaxel for first-line treatment
2. Locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC)
    a. Used as a single agent
    b. Disease progression on or intolerance to platinum-based chemotherapy

3. Metastatic or recurrent locally advanced Merkel cell carcinoma (MCC)

AND ALL of the following:

a. Prescriber agrees to discontinue treatment for any immune-mediated adverse reaction (e.g., encephalitis, nephritis, rash, decreased renal function, and endocrinopathies) or disease progression
b. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zynyz and for 4 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC)
2. Metastatic or recurrent locally advanced Merkel cell carcinoma (MCC)

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to discontinue treatment for any immune-mediated adverse reaction (e.g., encephalitis, nephritis, rash, decreased renal function, and endocrinopathies) or disease progression
c. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zynyz and for 4 months after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 3 vials every 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity 3 vials every 84 days

Duration 12 months*
*One renewal **ONLY**
****NO** renewal for inoperable locally recurrent or metastatic SCAC

Rationale

Summary
Zynyz is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of adult patients with squamous cell carcinoma of the anal canal (SCAC) or Merkel cell carcinoma (MCC). Patients taking Zynyz should be monitored for immune-mediated adverse reactions. The safety and effectiveness of Zynyz have not been established in pediatric patients less than 18 years of age (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Zynyz while maintaining optimal therapeutic outcomes.

References
1. Zynyz [package insert]. Wilmington, DE: Incyte Corporation; December 2025.
2. NCCN Drugs & Biologics Compendium® Retifanlimab-dlwr 2026. National Comprehensive Cancer Network, Inc. Accessed on January 15, 2026.

Policy History

Date	Action
April 2023	Addition to PA
September 2023	Annual review and reference update
March 2024	Annual review and reference update
September 2024	Annual review and reference update
December 2024	Annual review and reference update
March 2025	Annual review and reference update
June 2025	Annual review and reference update
July 2025	Per PI update, added indications of squamous cell carcinoma of the anal canal (SCAC)

September 2025	Annual review and reference update
March 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.