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Section:	Prescription Drugs	**Effective Date:**	July 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	April 14, 2023
Subject:	Zynyz	**Page:**	1 of 4

Last Review Date: June 12, 2025

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 indication: Zynyz is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (1).

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

Diagnosis

Patient must have the following:

1. Metastatic or recurrent locally advanced Merkel cell carcinoma

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

Diagnosis

Patient must have the following:

1. Metastatic or recurrent locally advanced Merkel cell carcinoma

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**

Rationale

Summary

Zynyz is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma. 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; April 2024.
2. NCCN Drugs & Biologics Compendium® Retifanlimab-dlwr 2025. National Comprehensive Cancer Network, Inc. Accessed on April 22, 2025.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 12, 2025 and is effective on July 1, 2025.