PRODUCT INFORMATION & DISTRIBUTION GUIDE

ZYNYZ®
retifanlimab-dlwr
Injection 500 mg

ZYNYZ® (retifanlimab-dlwr) 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 (MCC).

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.

IMPORTANT SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

Important immune-mediated adverse reactions listed may not be inclusive of all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can occur at any time after starting or discontinuing treatment with a PD-1/PD-L1–blocking antibody, and can affect more than one body system simultaneously.

Monitor patients closely for symptoms and signs that may be clinical manifestations of such reactions. Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1–blocking antibodies. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. If suspected, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue ZYNYZ depending on severity. In general, if ZYNYZ requires interruption or discontinuation, administer systemic corticosteroid therapy (1-2 mg/kg/day prednisone or equivalent) until improvement to ≤ Grade 1. Then, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroids.

Manufactured By	Incyte Corporation - **1-855-463-3463**
Marketed By	Incyte Corporation - **www.Incyte.com**
Product Name	ZYNYZ
Generic Name	retifanlimab-dlwr
Product Website	**www.ZYNYZHCP.com/MCC**

NATIONAL DRUG CODE (NDC)

500 mg/20 mL (25 mg/mL)	10-Digit	11-Digit
	50881-006-03	50881-**0**006-03

HCPCS CODING

J9345 (Injection, retifanlimab-dlwr, 1 mg)
Effective October 1, 2023

WHOLESALE ACQUISITION COST (WAC)

$14,743 / Vial
WAC current as of April 2025

PRODUCT BARCODES

Use the barcodes shown here to facilitate the loading of ZYNYZ into your EHR platform.

Carton

N 3 50881-00603 6

Vial

N 3 5088-1006-03 6

HCPCS, Healthcare Common Procedure Coding System.

INDICATIONS AND USAGE

ZYNYZ® (retifanlimab-dlwr) 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 (MCC).

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IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-Mediated Pneumonitis

ZYNYZ can cause immune-mediated pneumonitis. Immune-mediated pneumonitis occurred in 3% (13/440) of patients, including fatal (0.2%), Grade 3 (0.9%), and Grade 2 (1.4%) reactions. Pneumonitis led to permanent discontinuation of ZYNYZ in 1 patient and withholding in 0.9%.

Systemic corticosteroids were required in 77% (10/13) of patients. Pneumonitis resolved in 10 of the 13 patients.

Immune-Mediated Colitis

ZYNYZ can cause immune-mediated colitis. Cytomegalovirus infections/reactivations have occurred in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 1.6% (7/440) of patients, including Grade 4 (0.2%), Grade 3 (0.2%), and Grade 2 (0.7%). Colitis led to permanent discontinuation of ZYNYZ in 1 patient and withholding in 0.9%.

Systemic corticosteroids were required in 71% (5/7) of patients. Colitis resolved in 4/7 patients.

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ORDERING & DISTRIBUTION

ZYNYZ® (retifanlimab-dlwr) is available through the following network of Specialty Distributors:

CardinalHealth™ | cencora | McKESSON

Prescribers who do not wish to use buy-and-bill should check with their preferred Specialty Pharmacy for availability. Specialty Pharmacies may obtain access to ZYNYZ through the Specialty Distributors above.

HOW SUPPLIED

Sales Unit	One single-dose vial: 500 mg/20 mL (25 mg/mL)		
Units Per Carton	One vial per carton		
Pack Dimensions (Approximate)	**Length**	**Width**	**Height**
	2.3622”	1.3779”	2.9531”
Global Trade Identification Numbers	00350881006036 (Sales Unit) 30350881006037 (Shipper)		
Product Expiration	Expiration date printed on both single-dose vial and carton		

DESCRIPTION

500 mg/20 mL (25 mg/mL), sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution, free from visible particles in a single-dose vial.

STORAGE & HANDLING

Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze or shake.

IMPORTANT SAFETY INFORMATION (CONT’D)

Immune-Mediated Hepatitis

ZYNYZ can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 3% (13/440) of patients, including Grade 4 (0.2%), Grade 3 (2.3%), and Grade 2 (0.5%). Hepatitis led to permanent discontinuation of ZYNYZ in 1.4% of patients and withholding in 0.9%.

Systemic corticosteroids were required in 85% (11/13) of patients. Hepatitis resolved in 6/13 patients.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

ZYNYZ can cause primary or secondary adrenal insufficiency. For ≥ Grade 2 adrenal insufficiency, initiate symptomatic treatment per institutional guidelines, including hormone replacement as clinically indicated. Withhold or permanently discontinue ZYNYZ depending on severity.

Adrenal insufficiency occurred in 0.7% (3/440) of patients, including Grade 3 (0.5%) and Grade 2 (0.2%). ZYNYZ was permanently discontinued in no patients and was withheld for 1 patient with adrenal insufficiency.

All patients required systemic corticosteroids. Adrenal insufficiency resolved in 1 of the 3 patients.

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PRODUCT INFORMATION

For additional information on ZYNYZ, please contact:

Phone: 1-855-463-3463

Email: MedInfo@Incyte.com

US MEDICAL INFORMATION INQUIRIES

For all medical information requests, please contact Incyte Medical Information:

Phone: 1-855-463-3463

Email: MedInfo@Incyte.com

PRODUCT RETURNS

Credit for returns is subject to Incyte's current Specialty Return Goods Policy. Please request a Return Goods Authorization by calling:

1-855-751-7958

ADVERSE EVENT REPORTING

Contact Incyte or the FDA to report an adverse event.

Incyte:

Phone: 1-855-463-3463

Email: MedInfo@Incyte.com

FDA:

Phone: 1-800-FDA-1088

Web: www.fda.gov/medwatch

IMPORTANT SAFETY INFORMATION (CONT'D)

Hypophysitis

ZYNYZ can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts, and can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue ZYNYZ depending on severity.

Hypophysitis occurred in 0.5% (2/440, both Grade 2) of patients. No patients discontinued or withheld ZYNYZ due to hypophysitis.

All patients required systemic steroids. Hypophysitis resolved in 1 of the 2 patients.

Thyroid Disorders

ZYNYZ can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue ZYNYZ depending on severity.

Thyroiditis occurred in 0.7% (3/440, all Grade 1) of patients. No patients discontinued or withheld ZYNYZ due to thyroiditis. Thyroiditis resolved in 1 of the 3 patients.

Hypothyroidism

Hypothyroidism occurred in 10% (42/440) of patients receiving ZYNYZ, including Grade 2 (4.8%). No patients discontinued due to hypothyroidism. ZYNYZ was withheld in 0.5% of patients.

Systemic corticosteroids were required for 1 patient, and 79% (33/42) of patients received endocrine therapy.

Hyperthyroidism

Hyperthyroidism occurred in 6% (24/440) of patients receiving ZYNYZ® (retifanlimab-dlwr), including Grade 2 (2.5%). ZYNYZ was not discontinued in any patient and was withheld in 1 patient. Systemic corticosteroids were required for 13% (3/24) of patients, and 46% (11/24) of patients received endocrine therapy.

Type 1 Diabetes Mellitus, Which Can Present with Diabetic Ketoacidosis

Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold ZYNYZ depending on severity.

Type 1 diabetes mellitus occurred in 0.2% (1/440) of patients, including Grade 3 (0.2%) adverse reactions.

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DOSAGE & ADMINISTRATION HIGHLIGHTS

Recommended Dosage

The recommended dosage of ZYNYZ® (retifanlimab-dlwr) for adult patients with metastatic or recurrent locally advanced MCC is 500 mg administered as an intravenous infusion over 30 minutes every 4 weeks until disease progression, unacceptable toxicity, or up to 24 months.

Administer ZYNYZ as an intravenous infusion after dilution.

Please see the Full Prescribing Information for dosage modifications for adverse reactions.

Preparation and Administration

Do not administer ZYNYZ using a polyurethane infusion set.

Visually inspect the vial for particulate matter and discoloration prior to administration. ZYNYZ is a clear to slightly opalescent, colorless to pale yellow solution and is free of particles. Discard the vial if the solution is cloudy, discolored, or contains particulate matter.

Do not shake the vial.

Preparation

1. Withdraw 20 mL (500 mg) of ZYNYZ from one vial and discard vial with any unused portion.
2. Dilute ZYNYZ with either 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a final concentration between 1.4 mg/mL to 10 mg/mL. Use polyvinylchloride (PVC) and di-2-ethylhexyl phthalate (DEHP), polyolefin copolymer, polyolefin with polyamide, or ethylene vinyl acetate infusion bags.
3. Mix diluted solution by gentle inversion. Do not shake.
4. Visually inspect the infusion bag for particulate matter and discoloration prior to administration. Discard if the solution is discolored or contains particulate matter.

Storage of Diluted ZYNYZ Solution

Protect the diluted ZYNYZ solution from light during storage.

Store diluted ZYNYZ solution:

- At room temperature [up to 25°C (77°F)] for no more than 8 hours from the time of preparation to the end of the infusion.

  Or
- Under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 24 hours from the time of preparation to the end of the infusion. If refrigerated, allow the diluted solution to come to room temperature prior to administration. The diluted solution must be administered within 4 hours (including infusion time) once it is removed from the refrigerator.

Do not freeze or shake diluted solution.

Administration

- Administer diluted ZYNYZ solution by intravenous infusion over 30 minutes through a polyethylene or PVC with DEHP intravenous line containing a sterile, non-pyrogenic, low-protein binding polyethersulfone, polyvinylidene fluoride, or cellulose acetate 0.2 micron to 5 micron in-line or add-on filter or 15 micron mesh in-line or add-on filter. DO NOT administer ZYNYZ as an intravenous push or bolus injection.
- Do not co-administer other drugs through the same infusion line.

IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-Mediated Nephritis with Renal Dysfunction

ZYNYZ can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 1.6% (7/440) of patients receiving ZYNYZ, including Grade 4 (0.5%), Grade 3 (0.7%), and Grade 2 (0.5%). Nephritis led to permanent discontinuation of ZYNYZ in 0.9% of patients and withholding in 1 patient.

Systemic corticosteroids were required in 57% (4/7) of patients. Nephritis resolved in 3/7 patients.

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PATIENT SUPPORT PROGRAM

IncyteCARES for ZYNYZ® (retifanlimab-dlwr) Supports Eligible Patients During Treatment

The IncyteCARES mission is to help patients start and stay on therapy by assisting with access and as-needed support.

IncyteCARES can help patients understand their health insurance coverage, can provide reimbursement support, and offers savings, financial assistance, and support options for eligible patients,* including:

IncyteCARES for ZYNYZ Savings Program
For Eligible Patients With Commercial Health Insurance

IncyteCARES for ZYNYZ Patient Assistance Program
For Eligible Patients Who Are Uninsured or Underinsured for ZYNYZ

Information About Nonprofit or Other Support Organizations
For All Patients

IncyteCARES

The IncyteCARES Team Is Available by Phone Every Weekday
Call **1-855-452-5234**, Monday to Friday 8 AM - 8 PM ET
Visit **HCP.IncyteCARES.com/ZYNYZ** to learn more

*Terms and conditions apply. Program terms may change at any time.

IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-Mediated Dermatologic Adverse Reactions

ZYNYZ can cause immune-mediated rash or dermatitis. Bullous and exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has occurred with PD-1/PD-L1–blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue ZYNYZ depending on severity.

Immune-mediated skin reactions occurred in 8% (36/440) of patients, including Grade 3 (1.1%) and Grade 2 (7%). Immune-mediated dermatologic adverse reactions led to permanent discontinuation of ZYNYZ in 1 patient and withholding in 2.3% of patients.

Systemic corticosteroids were required in 25% (9/36) of patients. Immune-mediated dermatologic adverse reactions resolved in 75% (27/36) of patients.

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of < 1% in 440 patients who received ZYNYZ or were reported with the use of other PD-1/PD-L1–blocking antibodies, including severe or fatal cases.

Cardiac/vascular: myocarditis, pericarditis, vasculitis

Gastrointestinal: pancreatitis, to include increases in serum amylase and lipase levels, gastritis, duodenitis

Musculoskeletal: myositis/polymyositis, rhabdomyolysis (and associated sequelae, including renal failure), arthritis, polymyalgia rheumatica

Neurological: meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy

Ocular: uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

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IMPORTANT SAFETY INFORMATION (CONT'D)

Endocrine: hypoparathyroidism

Other (Hematologic/Immune): hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection, other transplant (including corneal graft) rejection.

Infusion-Related Reactions

A severe infusion-related reaction (Grade 3) occurred in 1 (0.2%) of 440 patients. Monitor patients for signs and symptoms; interrupt or slow the rate of infusion or permanently discontinue ZYNYZ based on severity of reaction. Consider premedication with an antipyretic and/or an antihistamine for patients who have had previous systemic reactions to infusions of therapeutic proteins.

Complications of Allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause), which may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

ZYNYZ® (retifanlimab-dlwr) can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus, resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 4 months after the last dose.

Lactation

Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the last dose.

Adverse Reactions

The safety of ZYNYZ was evaluated in 105 patients with metastatic or recurrent locally advanced MCC.

Serious adverse reactions occurred in 22% of patients receiving ZYNYZ. The most frequent serious adverse reactions (≥ 2% of patients) were fatigue, arrhythmia, and pneumonitis.

Permanent discontinuation of ZYNYZ due to an adverse reaction occurred in 11% of patients. These included asthenia, atrial fibrillation, concomitant disease progression of chronic lymphocytic leukemia, demyelinating polyneuropathy, eosinophilic fasciitis, increased transaminases, infusion-related reaction, lung disorder, pancreatitis, polyarthritis, and radiculopathy (1 patient each).

Dosage interruptions due to an adverse reaction occurred in 25% of patients. Adverse reactions or laboratory abnormalities that required dosage interruption in ≥ 2% of patients were increased transaminases, increased lipase, increased amylase, pneumonitis, and pyrexia.

The most common (≥ 10%) adverse reactions were fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia, and nausea.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Incyte Corporation at 1-855-463-3463.

Please see the Full Prescribing Information.

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