The **first anti-PD-1 monoclonal antibody** indicated in Merkel cell carcinoma (MCC).[1-3*]

PrZYNYZ®

retifanlimab for injection

500 mg / 20 mL (25 mg / mL)

PrZYNYZ® (retifanlimab for injection), as monotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent locally advanced MCC not amenable to curative surgery or radiation therapy.[1]

RECOMMENDED DOSING AND ADMINISTRATION

* Comparative clinical significance is unknown.
PD-1: programmed death receptor 1.

ZYNYZ® PREPARATION AND RECONSTITUTION[1]

1 Parenteral medicinal products should be inspected visually for particulate matter and discoloration prior to administration.

Discard the vial if the solution is cloudy, discolored, or visible particles are observed.

2 Withdraw 20 mL (500 mg) of ZYNYZ® concentrate from the vial and discard vial with any unused portion.

3 Dilute ZYNYZ® with either sodium chloride 9 mg/mL (0.9%) solution for injection, USP or glucose 50 mg/mL (5%) solution for injection, USP to prepare a diluted solution with a final concentration between 1.4 mg/mL to 10 mg/mL.

4 Mix the diluted solution by gentle inversion. Do not shake the infusion bag.

Once prepared, administer the diluted solution immediately.
If not administered immediately, it may be stored temporarily.*

ZYNYZ® OFFERS THE CONVENIENCE OF A ONCE-EVERY-4-WEEK DOSING SCHEDULE[1]

Quick infusion delivers ZYNYZ® 500 mg over 30 minutes

- The recommended dose of ZYNYZ® is 500 mg every 4 weeks administered as an IV infusion after dilution over 30 minutes.
- Treatment should continue until disease progression, unacceptable toxicity, or up to 24 months.
- Routine prophylaxis for infusion reactions is not required.
  - For patients who have had previous clinically significant reactions to infusions of therapeutic proteins, premedication with an antipyretic and/or an antihistamine should be considered.
- No dose reductions are recommended.
- Dosing delay or discontinuation may be required based on individual safety and tolerability.
- After each dose, flush the infusion line.

Use a polyethylene, polyurethane, or PVC with DEHP IV 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 co-administer other drugs through the same infusion line.

*It may be stored temporarily either: (1) at room temperature up to 25°C for no more than 8 hours from the time of preparation to the end of the infusion or (2) under refrigeration at 2°C to 8°C 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.

IV: intravenous; PVC: polyvinylchloride; DEHP: di-2-ethylhexyl phthalate.

NO DOSE REDUCTIONS OF ZYNYZ® ARE RECOMMENDED

Recommended dosage modifications for adverse reactions[1]

ADVERSE REACTION	SEVERITY*	DOSAGE MODIFICATION
Pneumonitis	Grade 2	Withhold until ≤Grade 1.†
	Grade 3 or 4	Permanently discontinue.
Colitis	Grade 2 or 3	Withhold until ≤Grade 1.†
	Grade 4	Permanently discontinue.
Hepatitis with no tumor involvement of the liver **OR** Increased total bilirubin	ALT or AST greater than 3 but no more than 8 times the ULN **OR** Total bilirubin increases to more than 1.5 and up to 3 times ULN	Withhold until ≤Grade 1.†
	AST or ALT increases to more than 8 times ULN **OR** Total bilirubin greater than 3 times ULN	Permanently discontinue.
Hepatitis with tumor involvement of the liver **OR** Increased total bilirubin	AST or ALT more than 5 and up to 10 times ULN **OR** Total bilirubin greater than 1.5 but no more than 3 times ULN	Withhold until ≤Grade 1.†
	ALT or AST increase to more than 10 times ULN **OR** Total bilirubin greater than 3 times ULN	Permanently discontinue.
Endocrinopathies Adrenal insufficiency Hypothyroidism Hyperthyroidism Type 1 diabetes mellitus Hyperglycemia Hypophysitis	Grade 2 adrenal insufficiency	Withhold until ≤Grade 1 or otherwise clinically stable.
	Grade 3 or 4 adrenal insufficiency	Withhold until ≤Grade 1.† Permanently discontinue for worsening while on adequate hormonal therapy.
	Grade 3 or 4 hypothyroidism	Withhold until ≤Grade 1 or is otherwise clinically stable.
	Grade 3 or 4 hyperthyroidism	Withhold until ≤Grade 1 or is otherwise clinically stable.
	Grade 3 or 4 type 1 diabetes mellitus (or hyperglycemia)	Withhold until ≤Grade 1 or is otherwise clinically stable.
	Grade 2 hypophysitis (asymptomatic)	Withhold until ≤Grade 1. May restart after controlled by hormone replacement therapy.
	Grade 2 hypophysitis (symptomatic; e.g., headaches, visual disturbances)	Withhold until ≤Grade 1. May restart study drug after controlled with hormone replacement therapy, if indicated and steroid taper is complete.
	Grade 3 or 4 hypophysitis (symptomatic)	Withhold until ≤Grade 1.† Permanently discontinue for worsening while on adequate hormonal therapy.
Nephritis with renal dysfunction	Grade 2 increased blood creatinine	Withhold until ≤Grade 1.†
	Grade 3 or 4 increased blood creatinine	Permanently discontinue.‡
Skin Reactions	Grade 3 or suspected SJS or suspected TEN	Withhold until ≤Grade 1.
	Grade 4 or confirmed SJS or confirmed TEN	Permanently discontinue.
Myocarditis	Confirmed Grades 2, 3 or 4	Permanently discontinue.
Other immune-mediated adverse reactions (including myositis, encephalitis, demyelinating neuropathy, Guillain-Barré syndrome, sarcoidosis, autoimmune hemolytic anemia, pancreatitis, uveitis, diabetic ketoacidosis, arthralgia)	Grade 3 (symptomatic)	Withhold until ≤Grade 1.†
	Confirmed Grade 3 and Grade 4	Permanently discontinue.
Persistent Grade 2 or 3 adverse reactions (excluding endocrinopathies)	Grade 2 or 3 adverse reactions ≥12 weeks after last dose	Permanently discontinue.
Recurrent immune-mediated adverse reactions	Recurrent Grade 3 or 4	Permanently discontinue.
	Recurrent Grade 2 pneumonitis	
Infusion-related reactions	Grades 1 and 2	Interrupt or slow the rate of infusion.
	Grade 3§ or 4 or persistent Grade 2	Permanently discontinue.

Adapted from the ZYNYZ® Product Monograph.[1]

Please refer to the Product Monograph for complete dosing and administration information.

* Toxicity graded per NCI CTCAE v5.
† Permanently discontinue once diagnosis is confirmed, or if symptoms have no resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg/day (or equivalent) within 12 weeks of initiating steroids.
‡ Permanently discontinue only if retifanlimab is directly implicated in renal toxicity.
§ Grade 3 infusion-related reactions: if rapidly responsive to symptomatic medication and/or to brief interruption of infusion, retifanlimab does not need to be permanently discontinued.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; ULN: upper limit of normal; SJS: Stevens-Johnson syndrome, TEN: toxic epidermal necrolysis; NCI: National Cancer Institute; CTCAE: Common Terminology Criteria for Adverse Events.

Visit our resource hub
for additional resources:
www.IncyteOnco.ca

Consult Product Monograph at pdf.hres.ca/dpd_pm/00078531.PDF for important information on:

- Contraindications in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.
- Relevant warnings and precautions, including exercise caution when driving or operating a vehicle or potentially dangerous machinery; immune-mediated adverse reactions (which may be severe or fatal) can occur in patients treated with antibodies blocking the PD-1/PD-L1 pathway, including ZYNYZ®, and these reactions usually occur during treatment with PD-1/PD-L1 blocking antibodies, but symptoms can also manifest after treatment discontinuation; immune-mediated adverse reactions: pneumonitis, immune-mediated colitis, immune-mediated nephritis, immune-mediated hepatitis, immune-mediated skin reactions (including toxic epidermal necrolysis), immune-mediated endocrinopathies, immune-mediated hypothyroidism and hyperthyroidism (including thyroiditis), immune-mediated hypophysitis, immune-mediated adrenal insufficiency, immune-mediated type 1 diabetes mellitus, have been reported in patients receiving ZYNYZ®; treatment with ZYNYZ® may increase the risk of rejection in solid organ transplant recipients; fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1-blocking antibody; transplant-related complications include hyperacute GvHD, acute GvHD, chronic GvHD, hepatic veno-occlusive disease after reduced intensity conditioning and steroid-requiring febrile syndrome (without an identified infectious cause); as with any therapeutic protein, ZYNYZ® can cause infusion-related reactions, some of which may be severe; ZYNYZ® can cause fetal harm when administered to a pregnant woman and is not recommended during pregnancy and in women of childbearing potential not using effective contraception unless the clinical benefit outweighs the potential risk; women of childbearing potential should use effective contraception during treatment with ZYNYZ® and for at least 4 months after the last dose; women should be advised not to breastfeed during treatment and for at least 4 months after the last dose.
- Conditions of clinical use, adverse reactions, drug interactions and dosing instructions.

The Product Monograph is also available by calling us at 1-833-309-2759 or contacting medinfocanada@incyte.com.

PD-1: programmed death receptor 1; PD-L1: programmed death ligand 1; HSCT: hematopoietic stem cell transplantation; GvHD: graft-versus-host disease.

References: 1. ZYNYZ® Product Monograph. Incyte Corporation. February 6, 2025. **2.** Incyte Biosciences Canada Corporation. Letter of attestation for ZYNYZ®. March 31, 2025. **3.** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Merkel Cell Carcinoma. Version 1.2024. November 22, 2023.

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REVIEWED BY PAAB

MEMBER OF INNOVATIVE MEDICINES CANADA

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