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MEDICAL EXCEPTIONS AND PATIENT SUPPORT SERVICES GUIDE

- What is a Medical Exception?
- Information / Document Checklist
- Template Reimbursement Letters
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  - Medical Exception Letter
  - Letter of Appeal - Prior Authorization and Claim Denial
- IncyteCARES - Program Overview

Please note this information is provided for your background education and is not intended to serve as guidance for specific coding, billing, and claims submissions. Decisions on which codes best describe the services provided must be made by individual providers based on specific payer guidance and requirements.

Incyte cannot guarantee payment of any claim and providers should contact third-party payers for specific information on their coding, coverage, and payment policies as needed.

For questions regarding IncyteCARES reimbursement and access, please call IncyteCARES at 1-855-452-5234 Monday through Friday, 8 am–8 pm ET.

What is a Medical Exception?

When a product is not covered by an insurance plan, it is sometimes referred to as non-formulary or requiring a medical exception. A medical exception describes the process whereby a healthcare professional can request that a payer consider covering a product not approved or covered for a specific patient due to medical necessity.

A medical exception is commonly used when new drugs become available and the payer has not yet determined coverage or established a medical policy. When a healthcare professional has determined that a drug is medically necessary, he or she can demonstrate that necessity by providing appropriate documentation and requesting that the payer approve the treatment.

Prior authorizations are standard for many oncology therapies and require accompanying documentation. If a prior authorization is denied, the medical exception request process can be used as a prior authorization appeal, and the same forms and processes can typically be used.

Similar to a traditional prior authorization process, the medical exception request process varies by payer. Therefore, it is important to follow the steps required, submit all requested documentation, and use the correct forms.

SOURCES OF PAYER REQUIREMENT INFORMATION

Commercial Payers

The medical exception request process specific to a given payer may be obtained by contacting the payer's provider relations department, and may also be available online.

Additionally, IncyteCARES may be able to provider payer-specific details as needed.

Medicare

- Medicare Part B does not require prior authorization
- Medicare Advantage plans may utilize a prior authorization or a medical exception process
- Specific requirements related to a given Medicare Advantage plan may be obtained by contacting the payer's provider relations department, and/or may also be available online

IncyteCARES

Contact IncyteCARES at 1-855-452-5234 for Assistance in Obtaining Payer-Specific Details and Forms

INDICATION

ZYNYZ™ (retifanlimab-dlwr) is 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.

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Information / Document Checklist

Patients' health plans may request additional information before approving coverage for treatment. In your efforts to secure ZYNYZ™ (retifanlimab-dlwr) coverage for individual patients, you may need to provide one or more supporting letters. For your reference, we've provided template reimbursement letters as well as the following checklist to help you generate accurate payer correspondence to support your ZYNYZ patients.

CHECKLIST

✔ Patient Information

- ☐ Patient Name
- ☐ Date of Birth
- ☐ Insurance Carrier
- ☐ Insurance ID
- ☐ Insurance Group Number
- ☐ Case ID Number (if applicable)

✔ Clinical Rationale

- ☐ Patient's diagnosis for a condition ZYNYZ is FDA-approved to treat
- ☐ Severity of patient's condition, patient's performance status
- ☐ Summary of patient's previous treatments, including the duration of each treatment, response to past treatments, the rationale for discontinuation, and recent symptoms / condition. Include coding information for prior treatments / services if available
- ☐ Patient's disease progression and scan history
- ☐ Clinical rationale for ZYNYZ treatment, including clinical trial data supporting FDA approval, administration, and dosage information

✔ Additional Enclosures

- ☐ ZYNYZ Full Prescribing Information (**www.ZYNYZHCP.com**)
- ☐ Clinical Notes / Medical Records
- ☐ FDA Approval Information (**www.fda.gov/drugsatfda**)
- ☐ Relevant Peer-reviewed Articles

If you have questions about appeals or medical exceptions, IncyteCARES may be able to help. Call **1-855-452-5234**

Access more information online at **HCP.IncyteCARES.com/ZYNYZ**

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. Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PD-L1–blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1–blocking antibodies, they can also manifest after discontinuation of PD-1/PD-L1–blocking antibodies. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously.

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Template Reimbursement Letters

The following template letters are included to help support the development of payer-specific communications in the event of medical policy restrictions, prior authorizations, and/or denials.

Please note, the example letters included here are for reference and should be used for guidance only.

1. **Letter of Medical Necessity**
   - If the payer's medical policy includes a prior authorization for the patient to be treated with ZYNYZ™ (retifanlimab-dlwr), you can submit a Letter of Medical Necessity
2. **Medical Exception Request**
   - If ZYNYZ is not available on the payer's medical policy, you may want to submit a Medical Exception Request
3. **Prior Authorization and Claim Denial**
   - If you have experienced a health plan's denial of ZYNYZ and would like to appeal the denial, you can submit a Letter of Appeal - Prior Authorization and Claim Denial

Example Reimbursement Letters Can Also Be Obtained by Calling IncyteCARES at **1-855-452-5234** or Visiting **HCP.IncyteCARES.com/ZYNYZ**

Some health plans will require supporting documentation with your outreach. This documentation could include:

- Chart documentation
- Data from clinical trials (included in the Prescribing Information) supporting use of ZYNYZ
- Patient treatment plan
- Relevant peer-reviewed articles

To avoid delays in a coverage decision, it is recommended that you provide as much documentation as possible when submitting your requests. It is important to note that supplying information in your request does not guarantee coverage for ZYNYZ and this information is not intended to substitute or influence a physician's independent medical judgment.

The IncyteCARES Team Can Assist in Obtaining Payer-Specific Forms and Further Describe Payer Processes

IMPORTANT SAFETY INFORMATION (CONT'D)

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1–blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, 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. Upon improvement to ≤ Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed subsequently.

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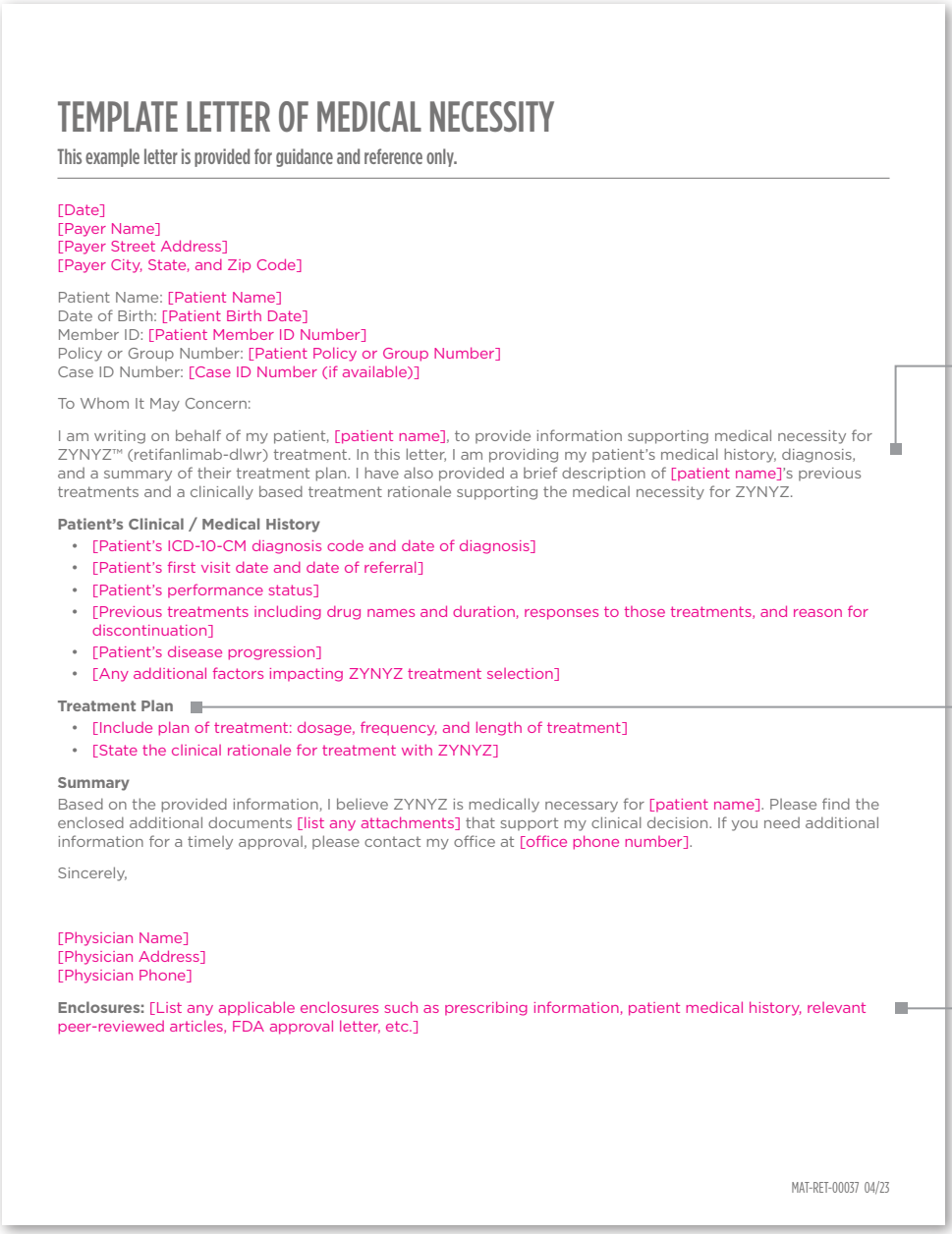
MEDICAL NECESSITY

This template letter is not meant to be used as a form letter. You should customize this letter to reflect the unique background and diagnosis of a particular patient, as well as the special requirements of the particular payer involved. The provider is responsible for ensuring the medical necessity of the procedure.



TEMPLATE LETTER OF MEDICAL NECESSITY

This example letter is provided for guidance and reference only.

[Date]
[Payer Name]
[Payer Street Address]
[Payer City, State, and Zip Code]

Patient Name: [Patient Name]
Date of Birth: [Patient Birth Date]
Member ID: [Patient Member ID Number]
Policy or Group Number: [Patient Policy or Group Number]
Case ID Number: [Case ID Number (if available)]

To Whom It May Concern:

I am writing on behalf of my patient, [patient name], to provide information supporting medical necessity for ZYNYZ™ (retifanlimab-dlwr) treatment. In this letter, I am providing my patient's medical history, diagnosis, and a summary of their treatment plan. I have also provided a brief description of [patient name]'s previous treatments and a clinically based treatment rationale supporting the medical necessity for ZYNYZ.

Patient's Clinical / Medical History

- [Patient's ICD-10-CM diagnosis code and date of diagnosis]
- [Patient's first visit date and date of referral]
- [Patient's performance status]
- [Previous treatments including drug names and duration, responses to those treatments, and reason for discontinuation]
- [Patient's disease progression]
- [Any additional factors impacting ZYNYZ treatment selection]

Treatment Plan

- [Include plan of treatment: dosage, frequency, and length of treatment]
- [State the clinical rationale for treatment with ZYNYZ]

Summary

Based on the provided information, I believe ZYNYZ is medically necessary for [patient name]. Please find the enclosed additional documents [list any attachments] that support my clinical decision. If you need additional information for a timely approval, please contact my office at [office phone number].

Sincerely,

[Physician Name]
[Physician Address]
[Physician Phone]

Enclosures: [List any applicable enclosures such as prescribing information, patient medical history, relevant peer-reviewed articles, FDA approval letter, etc.]

MAT-RET-00037 04/23

IMPORTANT! You must include your patient's medical history, diagnosis, and treatment plan or the health plan cannot make a coverage determination

In order to substantiate your request for ZYNYZ coverage, you should include any supporting documents that will assist the health plan in making a decision

It is highly recommended you include the FDA approval letter to support your clinical decision

This template letter is also available on **HCP.IncyteCARES.com/ZYNYZ**

IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-Mediated Pneumonitis

ZYNYZ can cause immune-mediated pneumonitis. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

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

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MEDICAL EXCEPTION

This template letter is not meant to be used as a form letter. You should customize this letter to reflect the unique background and diagnosis of a particular patient, as well as the special requirements of the particular payer involved. The provider is responsible for ensuring the medical necessity of the procedure.

TEMPLATE LETTER OF MEDICAL EXCEPTION

This example letter is provided for guidance and reference only.

[Date]
[Payer Name]
[Payer Street Address]
[Payer City, State, and Zip Code]

Patient Name: [Patient Name]
Date of Birth: [Patient Birth Date]
Member ID: [Patient Member ID Number]
Policy or Group Number: [Patient Policy or Group Number]
Case ID Number: [Case ID Number (if available)]

To Whom It May Concern:

I understand that the [plan name] policy for [patient name] requires [restriction description] prior to approving ZYNYZ™ (retifanlimab-dlwr) treatment. However, I believe that [patient name] requires ZYNYZ without [restriction description] due to clinical and medical circumstances. Please see below for details about symptoms, previous treatments, medical history, and treatment rationale that supports the claim for medical exception for [patient name].

Patient's Clinical / Medical History

- [Patient's ICD-10-CM diagnosis code and date of diagnosis]
- [Patient's first visit date and date of referral]
- [Patient's performance status]
- [Prior treatments – drug names and duration, responses to those treatments, and reason for discontinuation]
- [Patient's disease progression]
- [Any additional factors impacting ZYNYZ treatment selection]

Justification for Medical Exception

- [State the clinical rationale for treatment with ZYNYZ]
- [Describe why the plan requirement is not appropriate for your patient]
- [List concerns (e.g., experience on similar therapies, drug side effects, other patient-specific considerations)]

Treatment Plan

- [Include plan of treatment: dosage, frequency, and length of treatment]
- [State the clinical rationale for treatment with ZYNYZ]

Summary

Based on the above, I hope you agree ZYNYZ is an appropriate treatment for [patient name]. A timely approval of ZYNYZ by [plan name] without [restriction description] would be greatly appreciated by myself and my patient. Please contact me at [phone number] if you need more information to approve this medical exception.

Sincerely,

[Physician Name]
[Physician Address]
[Physician Phone]

Enclosures: [List any applicable enclosures such as prescribing information, patient medical history, relevant peer-reviewed articles, FDA approval letter, etc.]

MAT-RET-00038 04/23

Be sure to describe the coverage restriction in detail

In this section, include any previous treatment the patient has received so the insurance company does not request a treatment that may not be appropriate for your patient

Be specific in this section so the health plan can make informed and timely decisions

This template letter is also available on **HCP.IncyteCARES.com/ZYNYZ**

IMPORTANT SAFETY INFORMATION (CONT'D)

Systemic corticosteroids were required in 77% (10/13) of patients with pneumonitis. Pneumonitis resolved in 10 of the 13 patients. Of the 4 patients in whom ZYNYZ was withheld for pneumonitis, 3 reinitiated ZYNYZ after symptom improvement; of these, 1 had recurrence of pneumonitis.

Immune-Mediated Colitis

ZYNYZ can cause immune-mediated colitis. Cytomegalovirus infection/reactivation 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.

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PRIOR AUTHORIZATION AND CLAIM DENIAL

This template letter is not meant to be used as a form letter. You should customize this letter to reflect the unique background and diagnosis of a particular patient, as well as the special requirements of the particular payer involved. The provider is responsible for ensuring the medical necessity of the procedure.

TEMPLATE LETTER OF PRIOR AUTHORIZATION AND CLAIM DENIAL

This example letter is provided for guidance and reference only.

[Date]
[Payer Name]
[Payer Street Address]
[Payer City, State, and Zip Code]

Patient Name: [Patient Name]
Date of Birth: [Patient Birth Date]
Member ID: [Patient Member ID Number]
Policy or Group Number: [Patient Policy or Group Number]
Case ID Number: [Case ID Number (if available)]

To Whom It May Concern:

I am writing on behalf of my patient, [patient name], to request reconsideration for the coverage of ZYNYZ™ (retifanlimab-dlwr) treatment which was denied on [date] for the following reason: [describe reason given in denial letter]. For your convenience, I have attached documentation supporting my request for reversal of coverage denial:

- The Prior Authorization request for [patient name] which was denied on [date]
- [Patient name]'s relevant medical history, diagnosis, and treatment plan
- Clinical rationale supporting ZYNYZ treatment for [patient name]

Patient's Clinical / Medical History

- [Patient's ICD-10-CM diagnosis code and date of diagnosis]
- [Patient's first visit date and date of referral]
- [Patient's performance status]
- [Previous treatments including drug names and duration, responses to those treatments, and reason for discontinuation]
- [Patient's disease progression]
- [Any additional factors impacting ZYNYZ treatment selection]

Treatment Plan

- [Include plan of treatment: dosage, frequency, and length of treatment]
- [State the clinical rationale for treatment with ZYNYZ]

Summary

Based on the provided evidence, I hope you agree treatment with ZYNYZ is medically necessary. It is important that [plan name] allow the use of ZYNYZ and provide coverage so that [patient name] receives the care they may need. We appreciate your prompt review and reconsideration of this case. If you need additional information for a timely approval, please contact my office at [office phone number].

Sincerely,

[Physician Name]
[Physician Address]
[Physician Phone]

Enclosures: [List any applicable enclosures such as prescribing information, patient medical history, relevant peer-reviewed articles, FDA approval letter, etc.]

MAT-RET-00036 04/23

It is important to include a detailed description of the denial as including specific information may reduce the appeal process timeline and mitigate additional requests for information

A detailed patient history can support the rationale for the insurance plan to cover ZYNYZ. The patient history should describe information such as the severity of your patient's condition, previous treatments, and the patient's failure on prior treatments

This template letter is also available on **HCP.IncyteCARES.com/ZYNYZ**

IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-mediated colitis occurred in 1.6% (7/440) of patients receiving ZYNYZ, 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 of ZYNYZ in 0.9% of patients.

Systemic corticosteroids were required in 71% (5/7) of patients. Colitis resolved in 4 of the 7 patients. Of the 4 patients in whom ZYNYZ was withheld for colitis, 1 reinitiated ZYNYZ after symptom improvement; this patient did not have recurrence of colitis.

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IncyteCARES – Program Overview

We're Here to Support Your Eligible Patients During Treatment

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

When You Enroll a Patient, an IncyteCARES Representative Will:

- Call your patient to welcome them and explain their insurance coverage for ZYNYZ™ (retifanlimab-dlwr)
- Assess patient's eligibility for financial assistance programs,* and help them enroll
- Explain the additional support and resources available to them during treatment

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

For Eligible Patients With Commercial Health Insurance

IncyteCARES for ZYNYZ Savings Program

Eligible patients can receive ZYNYZ for as little as $15, subject to certain limits†

To qualify, patients must:

- Have commercial healthcare coverage. Patients insured under federal or state government healthcare programs—including Medicare Part B, Medicare Advantage, Medicaid, TRICARE or any state or medical or pharmaceutical assistance program—are not eligible. Patients without healthcare coverage are also not eligible
- Be a resident of the United States or Puerto Rico
- Have a valid prescription for ZYNYZ for an FDA-approved use

† Maximum benefits per claim and per calendar year apply. Program benefit applies to medication cost only and does not cover any costs to administer the medication. Uninsured, cash-paying patients are not eligible. Not valid for patients insured through Medicare Part B, Medicare Advantage, Medicaid, and TRICARE or any state medical or pharmaceutical assistance program. Offer valid only for an FDA-approved indication or recognized compendia use for ZYNYZ™ (retifanlimab-dlwr). Please see full criteria for eligibility at www.IncyteCARES.com or call IncyteCARES for ZYNYZ. Update effective as of January 1, 2023.

IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-Mediated Hepatitis

ZYNYZ can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 3% (13/440) of patients receiving ZYNYZ, 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 of ZYNYZ in 0.9% of patients.

Systemic corticosteroids were required in 85% (11/13) of patients. Hepatitis resolved in 6 of the 13 patients. Of the 4 patients in whom ZYNYZ was withheld for hepatitis, 2 reinitiated ZYNYZ after symptom improvement; of these, 1 had recurrence of hepatitis.

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.

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IncyteCARES – Program Overview

Enroll Your Eligible Patients in IncyteCARES for ZYNYZ™ (retifanlimab-dlwr)

Completing the enrollment form takes about 15 minutes. Simply download, complete, and fax it. Visit HCP.IncyteCARES.com/ZYNYZ for more information.

Other Financial Assistance and Support Options

When you enroll your patient in IncyteCARES for ZYNYZ, we will also review their eligibility for the following programs.

For Eligible Patients Who Are Uninsured or Underinsured for ZYNYZ

IncyteCARES for ZYNYZ Patient Assistance Program

For All Patients

Information About Nonprofit or Other Support Organizations

Questions?

Call IncyteCARES for ZYNYZ at 1-855-452-5234, Monday through Friday, 8 AM - 8 PM ET

Please see HCP.IncyteCARES.com/ZYNYZ for full program terms and conditions.

IMPORTANT SAFETY INFORMATION (CONT'D)

Adrenal insufficiency occurred in 0.7% (3/440) of patients receiving ZYNYZ, including Grade 3 (0.5%) and Grade 2 (0.2%). Adrenal insufficiency did not lead to permanent discontinuation of ZYNYZ. ZYNYZ was withheld for 1 patient with adrenal insufficiency. All patients required systemic corticosteroids. Adrenal insufficiency resolved in 1 of the 3 patients.

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. Hypophysitis 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 receiving ZYNYZ. 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 receiving ZYNYZ. No patients discontinued or withheld ZYNYZ due to thyroiditis. Thyroiditis resolved in 1 of the 3 patients.

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IMPORTANT SAFETY INFORMATION (CONT'D)

Hypothyroidism

Hypothyroidism occurred in 10% (42/440) of patients receiving ZYNYZ™ (retifanlimab-dlwr), including Grade 2 (4.8%). No patients discontinued ZYNYZ due to hypothyroidism. Hypothyroidism led to withholding of ZYNYZ 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, including Grade 2 (2.5%). No patients discontinued ZYNYZ due to hyperthyroidism. Hyperthyroidism led to withholding of ZYNYZ 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 receiving ZYNYZ, including Grade 3 (0.2%) adverse reactions. Type 1 diabetes mellitus led to withholding of ZYNYZ in 1 patient. This event led to ZYNYZ being withheld and did not lead to permanent discontinuation of ZYNYZ. The patient received insulin.

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 of ZYNYZ in 1 patient.

Systemic corticosteroids were required in 57% (4/7) of patients. Nephritis resolved in 3 of the 7 patients. The 1 patient in whom ZYNYZ was withheld for immune-mediated nephritis had ZYNYZ reinitiated after symptom improvement and did not have recurrence of immune-mediated nephritis.

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 receiving ZYNYZ, 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 of ZYNYZ 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. Of the 10 patients in whom ZYNYZ was withheld for immune-mediated dermatologic adverse reactions, 7 reinitiated ZYNYZ after symptom improvement; of these, 1 had recurrence of immune-mediated dermatologic adverse reactions.

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.

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.

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IMPORTANT SAFETY INFORMATION (CONT'D)

Infusion-Related Reactions

A severe infusion-related reaction (Grade 3) occurred in 1 (0.2%) of 440 patients receiving ZYNYZ™ (retifanlimab-dlwr). Monitor patients for signs and symptoms of infusion-related reactions. 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). These complications 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

Based on its mechanism of action, ZYNYZ 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 with ZYNYZ and for 4 months after the last dose.

Adverse Reactions

The safety of ZYNYZ was evaluated in 105 patients enrolled in the POD1UM-201 trial 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 who received ZYNYZ. Adverse reactions or laboratory abnormalities that required dosage interruption in ≥ 2% of patients who received ZYNYZ were increased transaminases, increased lipase, increased amylase, pneumonitis, and pyrexia.

The most common (≥ 10%) adverse reactions that occurred in patients receiving ZYNYZ were fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia, and nausea.

Specific Populations

Based on its mechanism of action, ZYNYZ can cause fetal harm when administered to a pregnant woman. There are no available data on the use of ZYNYZ in pregnant women. Human IgG4 immunoglobulins are known to cross the placenta; therefore, retifanlimab-dlwr has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to a fetus.

There is no information regarding the presence of retifanlimab-dlwr in human milk, or its effects on the breastfed child or on milk production. 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 of ZYNYZ.

ZYNYZ can cause fetal harm when administered to a pregnant woman.

Verify pregnancy status in females of reproductive potential prior to initiating ZYNYZ.

Advise females of reproductive potential to use effective contraception during treatment with ZYNYZ and for 4 months after the last dose.

The safety and effectiveness of ZYNYZ have not been established in pediatric patients.

Of the 65 patients with metastatic or recurrent locally advanced MCC treated with ZYNYZ, 79% were ≥ 65 years, and 37% were ≥ 75 years. Clinical studies of ZYNYZ did not include sufficient numbers of younger adult patients to determine if patients ≥ 65 years of age respond differently than younger adult patients.

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 for ZYNYZ for additional Important Safety Information.

ZYNYZ™
retifanlimab-dlwr
Injection 500 mg

ZYNYZ™

retifanlimab-dlwr

Injection 500 mg