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ZEPBOUND® APPEALS AND COMPOSING A LETTER OF MEDICAL NECESSITY

Composing A Letter Of Medical Necessity

The following information is presented as a guide for informational purposes only and is not intended to provide reimbursement or legal advice. Laws, regulations, and policies concerning reimbursement are complex and are updated frequently. Eli Lilly and Company, with the use of the information contained herein, does not guarantee success in obtaining insurance payments. While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. Providers are encouraged to contact third-party payers for specific information on their coverage policies. For more information, please visit zepbound.lilly.com/hcp for additional help and resources.

Many health plans require a Letter of Medical Necessity when appealing a coverage determination or prior authorization for a patient's plan.* The purpose of a Letter of Medical Necessity is to explain the prescribing healthcare provider's (HCP's) rationale and clinical decision-making when choosing a treatment.

This resource, **Zepbound Appeals and Composing a Letter of Medical Necessity,** provides information on the process of drafting a Letter of Medical Necessity. Included on the following page is a list of considerations that can be followed when creating a Letter of Medical Necessity. In addition, 2 sample letters are attached to this document and include information that plans often require. Note that some plans have specific Coverage Authorization Forms that must be used to document a Letter of Medical Necessity.

Follow the patient's plan requirements when requesting Zepbound; otherwise, treatment may be delayed.

For guidance completing the initial Prior Authorization for a patient, see the **Zepbound PA Resource Guide**.

*For Medicare beneficiaries, specific requirements must be met for the HCP to be considered a legal representative of the patient in an appeal. For additional information, please visit https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/downloads/cms1696.pdf.

Indication

Zepbound is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obesity) or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea, or cardiovascular disease).

Limitations of Use

- Zepbound contains tirzepatide. Coadministration with other tirzepatide-containing products or with any glucagon-like peptide-1 (GLP-1) receptor agonist is not recommended.
- The safety and efficacy of Zepbound in combination with other products intended for weight management, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.
- Zepbound has not been studied in patients with a history of pancreatitis.

Select Important Safety Information

WARNING: RISK OF THYROID C-CELL TUMORS

In rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether Zepbound causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined.

Zepbound is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of Zepbound and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Zepbound.

Contraindications

Zepbound is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with known serious hypersensitivity to tirzepatide or any of the excipients in Zepbound. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with tirzepatide.

Please see Important Safety Information including Boxed Warning about possible thyroid tumors, including thyroid cancer, on pages 5-6 and click for Prescribing Information and Medication Guide for Zepbound.

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Composing A Letter Of Medical Necessity

Letter of Medical Necessity Considerations

1. If required and following patient's consent, include the patient's full name, date of birth, plan identification number, and case identification number if a decision has already been rendered.

2. Add the prescribing HCP's National Provider Identifier (NPI) number and specialty.

3. Provide a copy of the patient's records with the following details: patient's history (including relevant clinical and progress notes), diagnosis with specific International Classification of Diseases (ICD) code, and condition.

4. Note the severity of the patient's condition.

5. Document prior treatments, the duration of each, and the rationale for discontinuation. It may be beneficial to include Common Procedural Terminology (CPT)-4 and/or J-codes to define prior services/treatments, so that the health plan can conduct research and make a timely determination.

6. Attach documentation that supports your recommendation such as chart notes or, if applicable, information in Zepbound Prescribing Information and/or clinical peer reviewed literature, etc.
Disclaimer: may not be all-encompassing.

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ZEPBOUND APPEALS AND COMPOSING A LETTER OF MEDICAL NECESSITY

Sample Letter of Medical Necessity

HCPs can follow this format FOR PATIENTS WHO ARE NOT CURRENTLY RECEIVING TREATMENT with Zepbound (tirzepatide) injection.

[Date]
[Medical director]
[Name of health plan]
[Mailing address]

Re: **[Patient's name]**
[Plan identification number]
[Date of birth]
[Case identification number]

To Whom It May Concern:

We have reviewed and recognize your guidelines for the responsible management of medications within this class. We are requesting that you reassess your recent denial of Zepbound coverage. We understand that the reason for your denial is **[copy reason verbatim from the plan's denial letter].** However, we believe that Zepbound **[dose, frequency]** is the appropriate treatment for the patient. In support of our recommendation for Zepbound treatment, we have provided an overview of the patient's relevant clinical history below.

Patient's history, diagnosis, condition, and symptoms:
Patient must have a diagnosis consistent with the indication for Zepbound.

[Please consider including relevant patient's medical records, inclusive of diagnosis, patient weight and BMI history, trial and/or failure of other medications, lifestyle modification attempts and outcomes, and any supporting documentation.]

Past Treatment(s)	Start/Stop Dates	Reason(s) for Discontinuation
[Drug name, strength, dosage]		

[Please detail all that apply and add additional lines as needed.]

[Provide clinical rationale for this treatment; consider including chart notes or, if applicable, information in Zepbound Prescribing Information and/or clinical peer reviewed literature, etc.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Zepbound.]

Please feel free to contact me, **[HCP's name]**, at **[office phone number]** for any additional information you may require. We look forward to receiving your timely response and approval of this claim.

Sincerely,

_____ _____

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI #]
[Physician's practice name]
[Phone #]
[Fax #]

[Patient's name and signature]
Encl: Medical records
Clinical trial information

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ZEPBOUND APPEALS AND COMPOSING A LETTER OF MEDICAL NECESSITY

Sample Letter of Medical Necessity

HCPs can follow this format FOR PATIENTS WHO HAVE BEEN TREATED with Zepbound (tirzepatide) injection and have had treatment interruption.

[Date]
[Medical director]
[Name of health plan]
[Mailing address]

Re: **[Patient's name]**
[Plan identification number]
[Date of birth]
[Case identification number]

To Whom It May Concern:

I am writing to provide additional information to support my claim for **[patient's name]**'s treatment of chronic weight management **[ICD code]** with Zepbound. In brief, continued treatment with Zepbound **[dose, frequency]**, is medically appropriate and necessary for this patient. This letter includes the patient's medical history, previous treatments, and disease severity **[if applicable]** that support my recommendation for treatment with Zepbound.

Patient's history, diagnosis, condition, and symptoms:
Patient must have a diagnosis consistent with the indication for Zepbound.

[Please consider including relevant patient's medical records, inclusive of diagnosis, patient weight and BMI history, trial and/or failure of other medications, lifestyle modification attempts and outcomes, and any supporting documentation.]

Past Treatment(s)	Start/Stop Dates	Reason(s) for Discontinuation
[Drug name, strength, dosage]		

[Please detail all that apply and add additional lines as needed.]

[Provide clinical rationale for this treatment; consider including chart notes or, if applicable, information in Zepbound Prescribing Information and/or clinical peer reviewed literature, etc.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Zepbound.]

Please feel free to contact me, **[HCP's name]**, at **[office phone number]** for any additional information you may require. We look forward to receiving your timely response and approval of this claim.

Sincerely,

_____ _____

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI #]
[Physician's practice name]
[Phone #]
[Fax #]

[Patient's name and signature]
Encl: Medical records
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ZEPBOUND APPEALS AND COMPOSING A LETTER OF MEDICAL NECESSITY

IMPORTANT SAFETY INFORMATION FOR ZEPBOUND® (TIRZEPATIDE) INJECTION

WARNING: RISK OF THYROID C-CELL TUMORS

In rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether Zepbound causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined.

Zepbound is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of Zepbound and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Zepbound.

Contraindications: Zepbound is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with known serious hypersensitivity to tirzepatide or any of the excipients in Zepbound. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with tirzepatide.

Risk of Thyroid C-cell Tumors: Counsel patients regarding the potential risk for MTC with the use of Zepbound and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Zepbound. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin values may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

Severe Gastrointestinal Disease: Use of Zepbound has been associated with gastrointestinal adverse reactions, sometimes severe. In clinical trials, severe gastrointestinal adverse reactions were reported more frequently among patients receiving Zepbound (5 mg 1.7%, 10 mg 2.5%, 15 mg 3.1%) than placebo (1.0%). Zepbound has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and is therefore not recommended in these patients.

Acute Kidney Injury: Use of Zepbound has been associated with acute kidney injury, which can result from dehydration due to gastrointestinal adverse reactions to Zepbound, including nausea, vomiting, and diarrhea. In patients treated with GLP-1 receptor agonists, there have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function in patients reporting adverse reactions to Zepbound that could lead to volume depletion.

Acute Gallbladder Disease: Treatment with Zepbound and GLP-1 receptor agonists is associated with an increased occurrence of acute gallbladder disease. In clinical trials of Zepbound, cholelithiasis was reported in 1.1% of Zepbound-treated patients and 1.0% of placebo-treated patients, cholecystitis was reported in 0.7% of Zepbound-treated patients and 0.2% of placebo-treated patients, and cholecystectomy was reported in 0.2% of Zepbound-treated patients and no placebo-treated patients. Acute gallbladder events were associated with weight reduction. If cholecystitis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated.

Acute Pancreatitis: Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists or tirzepatide. In clinical trials of tirzepatide for a different indication, 14 events of acute pancreatitis were confirmed by adjudication in 13 tirzepatide-treated patients (0.23 patients per 100 years of exposure) versus 3 events in 3 comparator-treated patients (0.11 patients per 100 years of exposure). In Zepbound clinical trials, 0.2% of Zepbound-treated patients had acute pancreatitis confirmed by adjudication (0.14 patients per 100 years of exposure) versus 0.2% of placebo-treated patients (0.15 patients per 100 years of exposure). Zepbound has not been studied in patients with a prior history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on Zepbound. Observe patients for signs and symptoms of pancreatitis, including persistent severe abdominal pain sometimes radiating to the back, which may or may not be accompanied by vomiting. If pancreatitis is suspected, discontinue Zepbound and initiate appropriate management. If the diagnosis of pancreatitis is confirmed, Zepbound should not be restarted.

Hypersensitivity Reactions: There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) in patients treated with tirzepatide. In Zepbound clinical trials, 0.1% of Zepbound-treated patients had severe hypersensitivity reactions compared to no placebo-treated patients. If hypersensitivity reactions occur, advise patients to promptly seek medical attention and discontinue use of Zepbound. Do not use in patients with a previous serious hypersensitivity reaction to tirzepatide or any of the excipients in Zepbound. Use caution in patients with a history of angioedema or anaphylaxis with a GLP-1 receptor agonist because it is unknown if such patients will be predisposed to these reactions with Zepbound.

Please see Important Safety Information including Boxed Warning about possible thyroid tumors, including thyroid cancer, on pages 5-6 and click for Prescribing Information and Medication Guide for Zepbound.

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IMPORTANT SAFETY INFORMATION (cont'd)

Hypoglycemia: Zepbound lowers blood glucose and can cause hypoglycemia. In a trial of patients with type 2 diabetes mellitus and BMI ≥27 kg/m^2, hypoglycemia (plasma glucose <54 mg/dL) was reported in 4.2% of Zepbound-treated patients versus 1.3% of placebo-treated patients. In this trial, patients taking Zepbound in combination with an insulin secretagogue (e.g., sulfonylurea) had increased risk of hypoglycemia (10.3%) compared to Zepbound-treated patients not taking a sulfonylurea (2.1%). Hypoglycemia has also been associated with Zepbound and GLP-1 receptor agonists in adults without type 2 diabetes mellitus. There is also increased risk of hypoglycemia in patients treated with tirzepatide in combination with insulin. Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In patients with diabetes mellitus, monitor blood glucose prior to starting Zepbound and during Zepbound treatment. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogue) or insulin.

Diabetic Retinopathy Complications in Patients with Type 2 Diabetes Mellitus: Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. Tirzepatide has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular edema. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

Suicidal Behavior and Ideation: Suicidal behavior and ideation have been reported in clinical trials with other chronic weight management products. Monitor patients treated with Zepbound for the emergence or worsening of depression, suicidal thoughts or behaviors, and/or any unusual changes in mood or behavior. Discontinue Zepbound in patients who experience suicidal thoughts or behaviors. Avoid Zepbound in patients with a history of suicidal attempts or active suicidal ideation.

Most Common Adverse Reactions: The most common adverse reactions, reported in ≥5% of patients treated with Zepbound are: nausea, diarrhea, vomiting, constipation, abdominal pain, dyspepsia, injection site reactions, fatigue, hypersensitivity reactions, eructation, hair loss, and gastroesophageal reflux disease.

Drug Interactions: Zepbound lowers blood glucose. When initiating Zepbound, consider reducing the dose of concomitantly administered insulin secretagogues (e.g., sulfonylureas) or insulin to reduce the risk of hypoglycemia. Zepbound delays gastric emptying and thereby has the potential to impact the absorption of concomitantly administered oral medications. Caution should be exercised when oral medications are concomitantly administered with Zepbound. Monitor patients on oral medications dependent on threshold concentrations for efficacy and those with a narrow therapeutic index (e.g., warfarin) when concomitantly administered with Zepbound.

Pregnancy: Advise pregnant patients that weight loss is not recommended during pregnancy and to discontinue Zepbound when a pregnancy is recognized. Available data with tirzepatide in pregnant patients are insufficient to evaluate for a drug-related risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Based on animal reproduction studies, there may be risks to the fetus from exposure to tirzepatide during pregnancy. There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Zepbound (tirzepatide) during pregnancy. Pregnant patients exposed to Zepbound and healthcare providers are encouraged to contact Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979).

Lactation: There are no data on the presence of tirzepatide or its metabolites in animal or human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Zepbound and any potential adverse effects on the breastfed infant from Zepbound or from the underlying maternal condition.

Females and Males of Reproductive Potential: Use of Zepbound may reduce the efficacy of oral hormonal contraceptives due to delayed gastric emptying. This delay is largest after the first dose and diminishes over time. Advise patients using oral hormonal contraceptives to switch to a non-oral contraceptive method or add a barrier method of contraception, for 4 weeks after initiation with Zepbound and for 4 weeks after each dose escalation.

Pediatric Use: The safety and effectiveness of Zepbound have not been established in pediatric patients less than 18 years of age.

Please click to access Prescribing Information, including Boxed Warning about possible thyroid tumors, including thyroid cancer, and Medication Guide.

Please see Instructions for Use.

ZP HCP ISI 08NOV2023

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