

Sample Letter of Medical Necessity for Rezdiffra™ (resmetirom)

This template is offered as a resource for a healthcare provider to potentially use when responding to a request from a patient's health benefits company with a letter of medical necessity for prescribing Rezdiffra. Use of the letter does not guarantee that the insurance company will provide coverage for Rezdiffra and is not intended to be a substitute for or an influence on the independent medical judgment of the healthcare provider.

This page should not be included when submitting a Prior Authorization to a payor.

Attachments that may be included with the letter of medical necessity are:

- ☐ Prior Authorization (PA) or appeal form recommended by the health plan
- ☐ Chart notes
 - Date of initial diagnosis
 - Patient's age, Rx details, NDC
 - MASH, stage (F2 or F3)
 - Noncirrhotic state
 - Relevant health conditions or symptoms
 - Date and results of diagnostic test to assess fibrosis, including but not limited to imaging such as elastography and magnetic resonance elastography (MRE), and blood tests such as fibrosis-4 (FIB-4) and enhanced liver fibrosis (ELF)
 - Documentation of conjoint prescription with diet and exercise
 - ICD-10 CM Code (K75.81, consistent with F2 or F3)
- ☐ Explanation of medical necessity, including why the patient's diagnosis, severity of condition, and impact of disease warrant treatment with Rezdiffra
- ☐ Previous management of MASH if applicable
- ☐ Rezdiffra Prescribing Information (PI)

If you need additional references, please contact the Madrigal Medical Information team at:
1-800-905-0324.

Please see Indication and Important Safety Information on pages 3 and 4 and accompanying full [Prescribing Information](#) for Rezdiffra.

EXAMPLE

Date: [Date]
Plan Name: [Plan Name]
Plan Address: [Plan Address]
City, State, ZIP Code: [City, State, ZIP Code]

Name: [Patient Name]
Date of Birth: [Patient Date of Birth]
Policy Number: [Policy Number]
Group Number: [Number]

Dear [Name of the contact person at the insurance company]:

I am writing on behalf of my patient, [Patient Full Name], who has been diagnosed with [diagnosis] (ICD-10 CM Code: [insert code]) to document the medical necessity of Rezdiffra™ (resmetirom).

Rezdiffra is a thyroid hormone receptor beta (THR-β) agonist indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).

This indication is approved under accelerated approval based on improvement of MASH and fibrosis. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitations of Use

Avoid use of Rezdiffra in patients with decompensated cirrhosis.

The Prescribing Information for Rezdiffra is enclosed. This letter provides information about the patient's medical history and diagnosis, along with a statement summarizing my treatment rationale.

Summary of Patient Medical History and Diagnosis

- [Provide a brief description of the patient's age, medical condition, i.e., noncirrhotic MASH, (F2 or F3), relevant health conditions or symptoms, Rx details, NDC]
- [Date of initial diagnosis]
- [Include date and results of patient's recent diagnostic tests as applicable, including but not limited to imaging such as elastography and magnetic resonance elastography (MRE), and blood tests such as fibrosis-4 (FIB-4) and enhanced liver fibrosis (ELF)]
- [Previous management of MASH if applicable]
- [Include conjoint prescription with diet and exercise]

Summary of Treatment Rationale

- [Explain why you believe it is medically necessary for patient to receive Rezdiffra]
- [Describe the potential consequences for the patient if they do not receive Rezdiffra]

To conclude, Rezdiffra is medically necessary for this patient's medical condition. Please contact me if any additional information is required to ensure the prompt approval of Rezdiffra.

Sincerely,

[Provider name, contact information, and signature]

References: [Include Rezdiffra Prescribing Information] [Include other relevant references and publications regarding Rezdiffra]

Enclosures: [List and attach additional documents to support your treatment rationale, see checklist on previous page]

INDICATION

Rezdiffra is indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).

This indication is approved under accelerated approval based on improvement of MASH and fibrosis. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitation of Use: Avoid use in patients with decompensated cirrhosis.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Hepatotoxicity has been observed with the use of Rezdiffra. One patient developed substantial elevations of liver biochemistries that resolved when treatment was interrupted. *Please see full Prescribing Information for more details on this specific case of Hepatotoxicity [see Warnings and Precautions (5.1)].*

Monitor for elevations in liver tests, liver-related adverse reactions, and symptoms/signs of hepatotoxicity (eg, fatigue, nausea, vomiting, right upper quadrant pain or tenderness, jaundice, fever, rash, and/or eosinophilia [$>5\%$]). If hepatotoxicity is suspected, discontinue Rezdiffra and monitor. If laboratory values return to baseline, weigh the potential risks against the benefits of restarting Rezdiffra. If laboratory values do not return to baseline, consider drug-induced autoimmune-like hepatitis (DI-ALH) or autoimmune liver disease in the evaluation of elevations in liver tests.

Gallbladder-Related Adverse Reactions

Cholelithiasis, acute cholecystitis, and obstructive pancreatitis (gallstone) were observed more often in Rezdiffra-treated patients than in placebo-treated patients. The exposure-adjusted incidence rates (EAIRs) for these events were less than 1 per 100 person-years (PY) for all treatment arms. If cholelithiasis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated. If an acute gallbladder event is suspected, interrupt treatment until the event is resolved.

Drug Interaction with Certain Statins

An increase in exposure of atorvastatin, pravastatin, rosuvastatin and simvastatin was observed when concomitantly administered with Rezdiffra, which may increase the risk of adverse reactions related to these drugs.

Dosage adjustment for certain statins is recommended. Monitor for statin-related adverse reactions including, but not limited to, elevation of liver tests, myopathy, and rhabdomyolysis. *Please see the upcoming Drug Interactions section of the Important Safety Information for more details.*

ADVERSE REACTIONS

The most common adverse reactions with Rezdiffra (reported in $\geq 5\%$ of patients and higher compared to placebo) are diarrhea, nausea, pruritus, vomiting, constipation, abdominal pain, and dizziness. Diarrhea and nausea were the most common causes of treatment discontinuation.

Please see the Important Safety Information continued on page 4.

IMPORTANT SAFETY INFORMATION (cont.)

DRUG INTERACTIONS

Clinically Significant Interactions Affecting Rezdifra

- Concomitant use with strong CYP2C8 inhibitors (eg, gemfibrozil) is not recommended. Reduce dosage if used concomitantly with a moderate CYP2C8 inhibitor (eg, clopidogrel).
- Concomitant use with OATP1B1 or OATP1B3 inhibitors (eg, cyclosporine) is not recommended.

Clinically Significant Interactions Affecting Other Drugs

- **Statins:** Limit daily rosuvastatin and simvastatin dosage to 20 mg. Limit pravastatin and atorvastatin dosage to 40 mg.
- **CYP2C8 Substrates:** Monitor patients more frequently for substrate-related adverse reactions if Rezdifra is co-administered with CYP2C8 substrates where minimal concentration changes may lead to serious adverse reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no available data on Rezdifra use in pregnant women. Report pregnancies to Madrigal Pharmaceuticals, Inc.'s Adverse Event reporting line at 1-800-905-0324 and <https://www.madrigalpharma.com/contact/>.

Lactation

There is no information regarding the presence of Rezdifra in human or animal milk, the effects on the breast-fed 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 Rezdifra and any potential adverse effects on the breastfed infant from Rezdifra or from the underlying maternal condition.

Geriatric Use

Numerically higher incidence of adverse reactions have been observed in patients ≥ 65 years of age compared to younger adult patients.

Renal Impairment

Rezdifra has not been studied in patients with severe renal impairment.

Hepatic Impairment

Avoid use in patients with decompensated cirrhosis (consistent with moderate to severe hepatic impairment). Moderate or severe hepatic impairment (Child-Pugh Class B or C) may increase the risk of adverse reactions.

The safety and effectiveness have not been established in patients with cirrhosis.

Please see accompanying full [Prescribing Information](#) for Rezdifra.