Madrigal patient SUPPORT

Rezdiffra® resmetirom tablets
60 mg · 80 mg · 100 mg

Checklist for Coverage Exception Requests

This checklist is designed to help support completion of a **formulary exception or tiering exception request for Rezdiffra® (resmetirom).** It is intended to be informational and for administrative support purposes only and does not direct clinical decision-making or guarantee coverage or approval. Always verify payer guidelines before submission. This checklist should accompany, not replace, payer-specific forms. This checklist is not intended for direct submission to payers unless explicitly requested.

PATIENT AND PROVIDER INFORMATION

Patient name _____ Date of birth (MM/DD/YYYY) _____

Insurance plan _____ Policy # _____

Provider name _____ National Provider Identifier # _____

Office contact name _____ Phone # _____

Specialty: ○ Gastroenterology ○ Hepatology ○ Endocrinology ○ Other _____

REQUEST TYPE — Select the appropriate request category based on payer requirements

○ Formulary Exception Request ○ Tiering Exception Request ○ Letter of Medical Necessity (LMN)

INDICATION AND IMPORTANT SAFETY INFORMATION

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.

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.

Please see the Important Safety Information on the page 3 and 4.

Please see full Prescribing Information for Rezdiffra. **Go to RezdiffraHCP.com for product information.**

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Rationale for treatment

Consider including clinical rationale for requesting Rezdiffra® (resmetirom):

- ☐ Documentation supporting diagnosis of metabolic dysfunction-associated steatohepatitis with F2 to F3 fibrosis, as required by payer or consistent with payer-specific diagnostic criteria (e.g., biopsy, FibroScan/ Vibration-Controlled Transient Elastography, Enhanced Liver Fibrosis, Magnetic Resonance Imaging Proton Density Fat Fraction)
- ☐ Severity of the patient's current condition
- ☐ Relevant comorbidities
- ☐ Documentation of contraindications, prior intolerance, or failure of formulary alternatives
- ☐ Documentation of step therapy requirements and outcomes, if applicable
- ☐ Clinical rationale for lack of response, intolerance, or contraindication to formulary alternatives
- ☐ Clinical rationale supporting medical necessity, consistent with the FDA-approved indication
- ☐ Supporting clinical data or society guidelines, if available

Administrative documentation

Ensure administrative records are maintained to support processing and appeals including:

- ☐ Submission dates, fax confirmations, and payer reference numbers
- ☐ Names and titles of payer representatives contacted
- ☐ Appeal deadlines and documentation of communications
- ☐ Copies of all correspondence and decision letters
- ☐ Use of a payer interaction log or case-ID tracker for internal documentation

Additional supporting documentation

You may attach the following items as applicable:

- ☐ Signed and dated payer forms
- ☐ FDA approval letter, if required by the payer
- ☐ Full Prescribing Information (PI)
- ☐ Relevant clinical records
- ☐ Payer denial letter (if appealing or submitting additional information)
- ☐ Provider's LMN (if not included within the payer form)
- ☐ Supporting literature or clinical guidelines, if applicable and consistent with the FDA-approved indication
- ☐ Patient authorization on file prior to submitting Protected Health Information

Summary of patient's treatment history

Consider including a concise overview of the patient's previous therapies:

- ☐ Prior treatments and duration
- ☐ Clinical response or lack of response
- ☐ Documentation of failed, contraindicated, or intolerant therapies
- ☐ Relevant labs and diagnostic testing
- ☐ Notes supporting disease severity and need for Rezdiffra

This checklist is intended as a general guide only and does not guarantee coverage or approval. Requirements may vary by payer and plan.

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INDICATION

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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.

IMPORTANT SAFETY INFORMATION continued on page 4.

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IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

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.

ADVERSE REACTIONS

The most common adverse reactions with Rezdiffra (reported in ≥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.

DRUG INTERACTIONS

Clinically Significant Interaction Effects of Strong or Moderate CYP2C8 Inhibitors on Rezdiffra

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

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 Rezdiffra 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 Rezdiffra use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Report pregnancies to Madrigal Pharmaceuticals, Inc. Adverse Event Reporting line at 1-800-905-0324 and visit https://pregnancyregistry.madrigalpharma.com for information about a pregnancy safety study.

Lactation
There is no information regarding the presence of Rezdiffra 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 Rezdiffra and any potential adverse effects on the breastfed infant from Rezdiffra 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
The recommended dosage of Rezdiffra in patients with mild, moderate, or severe renal impairment is the same as in patients with normal kidney function.

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 of Rezdiffra have not been established in patients with cirrhosis.

Please see full Prescribing Information for Rezdiffra.

For questions or additional support, contact Madrigal Patient Support®

CALL 1-877-219-7770, Monday–Friday, 9 AM–7 PM ET

VISIT MadrigalPatientSupport.com/hcp

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