Rezdiffra™
(resmetirom) tablets

CODING RESOURCE GUIDE

THIS INFORMATION IS PROVIDED FOR EDUCATIONAL PURPOSES ONLY AND IS NOT A GUARANTEE OF COVERAGE. IT IS THE SOLE RESPONSIBILITY OF THE HEALTHCARE PROVIDER TO ENSURE ALL CODING IS ACCURATE AND DOCUMENTED IN THE MEDICAL RECORD BASED UPON THE PATIENT'S CONDITION.

10 Digit National Drug Codes (NDC)

Dosage Form and Strengths	Code
60-mg tablets, 30-ct bottle	82576-060-30
80-mg tablets, 30-ct bottle	82576-080-30
100-mg tablets, 30-ct bottle	82576-100-30

11 Digit National Drug Codes (NDC)[1]

Dosage Form and Strengths	Code
60-mg tablets, 30-ct bottle	82576-0060-30
80-mg tablets, 30-ct bottle	82576-0080-30
100-mg tablets, 30-ct bottle	82576-0100-30

Diagnosis Codes

ICD-10	Description
K75.81	Nonalcoholic steatohepatitis (NASH)
K74.0	Hepatic fibrosis

Noninvasive Test CPT Codes[2]

CPT	Description
81517	Enhanced liver fibrosis (ELF) score
91200	Liver elastography without imaging
76391	Magnetic resonance elastography (MRE)
80076	Hepatic function panel

The table above lists some potential CPT codes for your reference.

Questions? We can help

Call 1-877-219-7770
Monday – Friday, 8 AM – 8 PM ET

Madrigal Patient Support

INDICATION

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

This indication is approved under accelerated approval based on improvement of NASH 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 in one patient. *Please see full Prescribing Information for more details on this specific case of Hepatotoxicity [see Warnings and Precautions (5.1)].*

Monitor patients during treatment for elevations in liver tests and for the development of liver-related adverse reactions. Monitor for symptoms and signs of hepatotoxicity (e.g., fatigue, nausea, vomiting, right upper quadrant pain or tenderness, jaundice, fever, rash, and/or eosinophilia [>5%]). If hepatotoxicity is suspected, discontinue Rezdiffra and continue to monitor the patient. 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 DI-ALH or autoimmune liver disease in the evaluation of elevations in liver tests.

IMPORTANT SAFETY INFORMATION continued on page 2.

Please see full Prescribing Information for Rezdiffra.

Go to RezdiffraHCP.com for product information.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Gallbladder-Related Adverse Reactions

In clinical trials, cholelithiasis, acute cholecystitis, and obstructive pancreatitis (gallstone) were observed more often in Rezdiffra-treated patients than in placebo-treated patients. If cholelithiasis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated. If an acute gallbladder event is suspected, interrupt Rezdiffra treatment until the event is resolved.

Drug Interaction with Certain Statins

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 Interaction *section of the Important Safety Information for more details.*

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.

Hypersensitivity Reactions

Reactions such as urticaria and rash, which may reflect drug hypersensitivity, were observed in patients receiving Rezdiffra.

Laboratory Abnormalities

Increases in mean ALT and AST levels were observed in the first 4 weeks after initiating treatment with Rezdiffra. The mean elevation in ALT and AST values was less than 1.5 times baseline at 4 weeks after treatment initiation. These values returned to baseline around 8 weeks after initiating treatment.

DRUG INTERACTIONS

Clinically Significant Interactions Affecting Rezdiffra

- **Strong or Moderate CYP2C8 Inhibitors:** Resmetirom is a CYP2C8 substrate. Concomitant use with strong CYP2C8 inhibitors (e.g., gemfibrozil) is not recommended. Reduce dosage if used concomitantly with a moderate CYP2C8 inhibitor (e.g., clopidogrel).
- **Organic Anion-Transporting Polypeptides (OATP) 1B1 and OATP1B3 Inhibitors:** Resmetirom is an OATP1B1 and OATP1B3 substrate. Concomitant use with OATP1B1 or OATP1B3 inhibitors (e.g., cyclosporine) is not recommended.

Clinically Significant Interactions Affecting Other Drugs

- Statins
  - Limit daily rosuvastatin and simvastatin dosage to 20 mg
  - Limit daily pravastatin and atorvastatin dosage to 40 mg
- **CYP2C8 Substrates:** Resmetirom is a weak CYP2C8 inhibitor. 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. There are risks to the mother and fetus related to underlying NASH with liver fibrosis, such as increased risks of gestational diabetes, hypertensive complications, preterm birth, and postpartum hemorrhage. 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 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.

Pediatric Use

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

Geriatric Use

No overall differences in effectiveness but 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 in patients with mild or moderate renal impairment is the same as in patients with normal kidney function. Rezdiffra 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) increases resmetirom C_{max} and AUC, which may increase the risk of adverse reactions.

No dosage adjustment is recommended for patients with mild hepatic impairment (Child-Pugh Class A).

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

Please see full Prescribing Information for Rezdiffra or visit madrigalpharma.com/Rezdiffra-USPI.

References: 1. Chun J. *Format of the National Drug Code*. U.S. Food & Drug Administration. https://www.fda.gov/media/173715/download. Accessed March 4, 2024. **2.** American Medical Association. *CPT® 2024 Professional Edition*. American Medical Association; 2023:556, 611, 666, 766.