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Presented by

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9:30-10:15 AM
DDW Theater 1

INDICATION AND IMPORTANT SAFETY INFORMATION

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.

WARRANTS 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 discontinuation of Rezdiffra or autotransplant liver disease in the evaluation of elevations in liver tests.

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.

Hyersensitivity Reactions
Reactions such as urticaria and rash may occur 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 CYP3A4 and P-gp inhibitor: Resmetirom is a CYP3A4 substrate. Concomitant use with potent CYP3A4 inhibitors (e.g., ketoconazole) is recommended. Reduce dose of Rezdiffra (consistent with moderate to severe hepatic impairment) by 50%.

- Organic Anion-Transporting Polypeptides (OATP) B1 and OATP1B1 Inhibitors: Resmetirom is an OATP1B1 inhibitor. Concomitant use with OATP1B1 inhibitors (e.g., atorvastatin) is 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 is 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 risk 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 visit 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.

Pediatic 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 CLr 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 accompanying full Prescribing Information for Rezdiffra or visit www.madrigalpharma.com/Rezdiffra-USPI.

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