Black 100%

Rezna Tablets

(Resmetirom)

ریزنا ٹیبلیٹس

(ریسمی ٹیروم)

COMPOSITION:
Rezna 60mg Tablets
Each film coated tablet contains: Resmetirom ..... 60mg.

Rezna 80mg Tablets
Each film coated tablet contains: Resmetirom ..... 80mg.

Rezna 100mg Tablets
Each film coated tablet contains: Resmetirom ..... 100mg.
[Innovator's Specs.]

DESCRIPTION: Rezna contain resmetirom, a thyroid hormone receptor-beta agonist.

INDICATIONS: Rezna 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).
Limitations of Use: Avoid use of **Rezna** in patients with decompensated cirrhosis

DOSAGE AND ADMINISTRATION:
Recommended Dosage and Administration: The recommended dosage of Resmetirom is based on actual body weight. For patients weighing:
• <100kg, the recommended dosage is 80mg orally once daily.
• ≥100 kg, the recommended dosage is 100mg orally once daily.
Administer Resmetirom with or without food.

Dosage Modifications for CYP2C8 Inhibitors: Concomitant use of Resmetirom with strong CYP2C8 inhibitors (e.g., gemfibrozil) is not recommended. If Resmetirom is used concomitantly with a moderate CYP2C8 inhibitor (e.g., clopidogrel).
• <100kg, reduce the dosage of RESMETIROM to 60mg once daily.
• ≥100kg, reduce the dosage of RESMETIROM to 80mg once daily.

CLINICAL PHARMACOLOGY: Mechanism of Action: Resmetirom is a partial agonist of the thyroid hormone receptor-beta (THR-β). Resmetirom produced 83.8% of the maximum response compared to triiodothyronine (T3), with an EC50 of 0.21μM in an in vitro functional assay for THR-β activation. The same functional assay for thyroid hormone receptoralpha (THR-α) agonism showed 48.6% efficacy for resmetirom relative to T3, with an EC50 of 3.74μM. THR-β is the major form of THR in the liver, and stimulation of THR-β in the liver reduces intrahepatic triglycerides, whereas actions of thyroid hormone outside the liver, including in heart and bone, are largely mediated through THR-α.

Pharmacokinetics:
Absorption: The resmetirom median time to maximum plasma concentration (Tmax) is approximately 4 hours following multiple daily doses of resmetirom 80mg or 100mg.
Effect of Food: No clinically significant differences in resmetirom pharmacokinetics were observed following administration with a high-fat meal (approximately 150, 250, and 500-600 calories from protein, carbohydrate, and fat, respectively). Concomitant food administration resulted in a 33% decrease in C_{max}, an 11% decrease in AUC, and a delay in median T_{max} by about 2 hours compared to under fasted condition.
Distribution: Resmetirom apparent volume of distribution (Vd/F) at steady-state is 68 (227%) L. Resmetirom is greater than 99% protein-bound.
Metabolism: Resmetirom is metabolized by CYP2C8 and is not metabolized by other CYP enzymes in vitro. MGL-3623 is a major metabolite with a 28-times lower potency for THR-β than resmetirom. MGL-3623 represents 33% to 51% of resmetirom AUC at steady state following administration of 100mg once daily.
Elimination: Resmetirom median terminal plasma half-life ($t_{½}$) is 4.5 hours and the steady state apparent clearance (CL/F) is 17.5 (56.3%) L/h.

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS: Hepatotoxicity: Hepatotoxicity has been observed with use of RESMETIROM. One patient had normal alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TB) levels at baseline, who received RESMETIROM 80mg daily, developed substantial elevations of liver biochemistries that resolved when treatment was interrupted. After reinitiating RESMETIROM, the patient had elevations of ALT, AST, and TB.
Gallbladder-Related Adverse Reactions: In clinical trials, cholelithiasis, acute cholecystitis, and obstructive pancreatitis (gallstone) were observed more often in RESMETIROM-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 RESMETIROM treatment until the event is resolved.

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

SIDE EFFECTS: The following are the side effects as described below: Diarrhea, nausea, pruritus, vomiting, constipation, abdominal pain & dizziness.

DRUG INTERACTIONS:
Effects of Other Drugs on Resmetirom: Strong or Moderate CYP2C8 Inhibitors:
Clinical Impact: Resmetirom is a CYP2C8 substrate. Concomitant use with a strong or moderate CYP2C8 inhibitor can increase resmetirom C_{max} and AUC, which may increase the risk of RESMETIROM adverse reactions.

Intervention: Concomitant use of Resmetirom with strong CYP2C8 inhibitors (e.g., gemfibrozil) is not recommended. Reduce Resmetirom dosage if used concomitantly with a moderate CYP2C8 inhibitor (e.g., clopidogrel).

Organic Anion-Transporting Polypeptides (OATP) 1B1 and OATP1B3 Inhibitors:
Clinical Impact: Resmetirom is an OATP1B1 and OATP1B3 substrate. Concomitant use with OATP1B1 and OATP1B3 inhibitors may increase resmetirom Cmax and AUC.
Intervention: Concomitant use of Resmetirom with OATP1B1 or OATP1B3 inhibitors (e.g., cyclosporine) is not recommended.

Effects of Resmetirom on Other Drugs:
Statins (Atorvastatin, Pravastatin, Rosuvastatin, or Simvastatin):
Clinical Impact: Resmetirom increased plasma concentrations of some statins (atorvastatin,pravastatin, rosuvastatin and simvastatin), which may increase the risk of adverse reactions related to these drugs.
Intervention:
Rosuvastatin and simvastatin: Limit daily statin dosage to 20mg.
Pravastatin and atorvastatin: Limit daily statin dosage to 40mg.

CYP2C8 Substrates: Clinical Impact: Resmetirom is a weak CYP2C8 inhibitor. Resmetirom increases exposure of CYP2C8 substrates, which may increase the risk of adverse reactions related to these substrates.

Intervention: Monitor patients more frequently for substrate-related adverse reactions if Resmetirom is co-administered with CYP2C8 substrates where minimal concentration changes may lead to serious adverse reactions.

USE IN SPECIFIC POPULATIONS:
Pregnancy: Risk Summary: There are no available data on RESMETIROM 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.
Lactation: Risk Summary: There is no information regarding the presence of RESMETIROM in human or animal milk, the effects on the breast-fed infant, or the effects on milk production.

Pediatric Use: The safety and effectiveness of RESMETIROM 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 and older 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. RESMETIROM has not been studied in patients with severe renal impairment

Hepatic Impairment: Avoid use of RESMETIROM 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.

OVERDOSE: In cases of overdose contact with your healthcare provider.

INSTRUCTIONS: Store below 30° C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION:
Rezna 60mg Tablets are available in pack size of 14's
Rezna 80mg Tablets are available in pack size of 14's
Rezna 100mg Tablets are available in pack size of 14's

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
NABIQASIM INDUSTRIES (PVT.) LTD.
PHARMA 17/24, Korangi Industrial Area, Karachi-Pakistan.

Rev: 03-25/0

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