Resiliva
Resmetirom INN

Everest

## COMPOSITION

**RESILIVA 80 mg tablet:** Each film coated tablet contains Resmetirom INN 80 mg.

**RESILIVA 100 mg tablet:** Each film coated tablet contains Resmetirom INN 100 mg.

## PHARMACOLOGY

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 $EC_{50}$ of 0.21 μM in an in vitro functional assay for THR-β activation. The same functional assay for thyroid hormone receptor alpha (THR-α) agonism showed 48.6% efficacy for Resmetirom relative to T3, with an $EC_{50}$ of 3.74 μM. THR-β is the major form of THR in the liver, and stimulation of THR-β in the liver reduces intrahepatic triglycerides, whereas action of thyroid hormone outside the liver, including the head and bone, are largely mediated through THR-α.

## INDICATION

Resmetirom 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).

## DOSAGE & ADMINISTRATION

The recommended dose of Resmetirom is based on actual body weight. For patients weighing:

- <100 kg, the recommended dose is 80 mg orally once daily.
- ≥100 kg, the recommended dose is 100 mg orally once daily.

The recommended dose of Resmetirom with moderate CYP2C8 inhibitor

For patients weighing:
- <100 kg, the recommended dose is 60 mg orally once daily.
- ≥100 kg, the recommended dose is 80 mg orally once daily.

Resmetirom can be administered with or without food.

## CONTRAINDICATIONS

- None.

## WARNINGS & PRECAUTION

### Hepatotoxicity

Hepatotoxicity has been observed with use of Resmetirom. Monitoring of patient is required during treatment with Resmetirom for elevations in liver tests, for the development of liver-related adverse reactions and for sign & symptoms of hepatotoxicity. If hepatotoxicity is suspected, Resmetirom should be discontinued and monitoring of the patient should be continued. If laboratory values return to baseline, the potential risks against the benefits of restarting Resmetirom should be considered. If laboratory values do not return to baseline, DI-ALH or autoimmune liver disease should be considered in the evaluation of elevations in liver tests.

### Gallbladder-Related Adverse Reactions

In clinical trials, cholelithiasis, acute cholecystitis, and obstructive pancreatitis (gallstone) were observed in Resmetirom-treated patients. If cholelithiasis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated. If an acute gallbladder event is suspected, Resmetirom treatment should be interrupted 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 Resmetirom, which may increase the risk of adverse reactions related to these drugs. Dosage adjustment for certain statins is recommended.

## SIDE EFFECTS

The common side effects of Resmetirom are:
- Diarrhea
- Nausea
- Vomiting
- Abdominal pain
- Dizziness
- Pruritus
- Constipation.

## DRUG INTERACTIONS

**Effects of Other Drugs on Resmetirom:**

- **Strong or Moderate CYP2C8 Inhibitors:** Concomitant use of Resmetirom with a strong or moderate CYP2C8 inhibitor can increase the risk of Resmetirom adverse reactions. Concomitant use of Resmetirom with strong CYP2C8 inhibitors (e.g., Gemfibrozil) is not recommended. Resmetirom dose should be reduced if used concomitantly with a moderate CYP2C8 inhibitor (e.g., Clopidogrel).

• **Organic Anion-Transporting Polypeptides (OATP) 1B1 and OATP1B3 Inhibitors:** Concomitant use with OATP1B1 and OATP1B3 inhibitors may increase the risk of Resmetirom adverse reactions. 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):** Resmetirom increases plasma concentrations of some statins (Atorvastatin, Pravastatin, Rosuvastatin and Simvastatin), which may increase the risk of adverse reactions related to these drugs. Dose adjustment of statins is recommended. Rosuvastatin and Simvastatin: Maximum daily statin dose should be 20 mg. Pravastatin and Atorvastatin: Maximum daily statin dose should be 40 mg.

• **CYP2C8 Substrates:** Resmetirom increases exposure of CYP2C8 substrates (e.g., Pioglitazone), which may increase the risk of adverse reactions related to these substrates. Patients should be monitored 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**

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.

**Lactation**

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. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Resmetirom and any potential adverse effects on the breastfed infant from Resmetirom or from the underlying maternal condition.

**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 who received Resmetirom compared to younger adult patients.

**Renal Impairment**

The recommended dose of Resmetirom 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**

Use of Resmetirom in patients with decompensated cirrhosis (consistent with moderate to severe hepatic impairment) should be avoided. Moderate or severe hepatic impairment (Child-Pugh Class B or C) may increase the risk of adverse reactions of Resmetirom. No dose adjustment is recommended for patients with mild hepatic impairment (Child-Pugh Class A).

**PHARMACEUTICAL INFORMATION**

**Storage Condition**

Store below 30°C, in a cool and dry place. Keep away from light. Keep out of the reach of children.

**HOW SUPPLIED**

**RESILIVA 80 mg tablet:** Each HDPE container contains 30 film coated tablets, a silica gel desiccant and polyester coil with a child-resistant closure.

**RESILIVA 100 mg tablet:** Each HDPE container contains 30 film coated tablets, a silica gel desiccant and polyester coil with a child-resistant closure.

Manufactured by
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