Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:
Resiliva 80

2. Qualitative and quantitative composition
Each film coated tablet contains Resmetirom 80 mg.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Film-coated tablet (tablet).

4. Clinical particulars

4.1 Therapeutic indications
Resmetirom is indicated in conjunction with diet andexercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).

4.2 Posology and method of 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.

4.3 Contraindications
None

4.4 Special warnings and precautions for use

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, andobstructive 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.

4.5 Interaction with other medicinal products and other forms of interaction

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 coadministered with CYP2C8 substrates where minimal concentration changes may lead to serious adverse reactions.

4.6 Pregnancy and Lactation

Pregnancy

There are no available data on Resmetirom use inpregnant 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.

4.7 Effects on ability to drive and use machines

Resmetirom INN has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The common side effects of Resmetirom are:

- Diarrhea
- Nausea
- Vomiting
- Abdominal pain
- Dizziness
- Pruritus
- Constipation

Summary of safety profile

Resmetirom's safety profile, based on clinical trials involving 2019 patients, shows a higher incidence of adverse reactions compared to placebo, particularly gastrointestinal issues like diarrhea and nausea, which were the main reasons for discontinuation. Other common side effects included pruritus, vomiting, constipation, and abdominal pain. The drug was associated with transient liver enzyme elevations, mild hypersensitivity reactions, and slight increases in gallbladder-related issues. While most adverse events were mild to moderate, Resmetirom groups experienced higher discontinuation rates than placebo. One case of hepatotoxicity was reported in an additional safety trial. Despite these concerns, the overall safety profile was consistent across different patient populations, with most side effects being manageable and resolving over time.

Adverse reactions with their respective frequency

Table 1 displays EAIRs per 100 PY for the common adverse reactions that occurred in at least 5% of patients with F2 or F3 fibrosis treated in either drug arm with Resmetirom and were greater than that reported for placebo.

Adverse Reaction	Placebo N=294 n (EAIRd)	Resmetirom 80 mg Once Daily N=298 n (EAIRd)	Resmetirom 100 mg Once Daily N=296 n (EAIRd)
Diarrhea	52 (14)	78 (23)	98 (33)
Nausea	36 (9)	65 (18)	51 (15)
Pruritus	18 (4)	24 (6)	36 (10)
Vomiting	15 (4)	27 (7)	30 (8)
Constipation	18 (4)	20 (5)	28 (8)
Abdominal pain	18 (4)	22 (5)	27 (7)
Dizziness	6 (1)	17 (4)	17 (4)

Common Adverse Reactions

Diarrhea: Most common side effect, usually mild to moderate, typically starting early in treatment and lasting about 20 days.
Nausea: Second most common, also mild to moderate, occurring early in treatment and lasting 26- 28 days on average.
Pruritus: Itching, more frequent with Resmetirom than placebo.
Vomiting: Mild to moderate in severity.
Constipation: More common in Resmetirom groups than placebo.
Abdominal pain: Mild to moderate in severity.
Dizziness: Reported more frequently in Resmetirom groups.
Hypersensitivity reactions: Including urticaria (hives) and rash.
Gallbladder-related issues: Slightly increased risk of cholelithiasis, acute cholecystitis, and obstructive pancreatitis.
Liver enzyme elevations: Transient increases in ALT and AST, typically resolving by week 8.
Thyroid function changes: Decrease in free T4 levels, but without clinical significance. Less common effects: Decreased appetite, flatulence, abnormal feces, taste changes (dysgeusia), vertigo, arrhythmia, palpitations, depression, skin redness (erythema), low blood sugar (hypoglycemia), tendon problems, and abnormal uterine bleeding.
Hepatotoxicity: One case reported in an additional safety trial.

Use on Special Population

Pregnancy

There are no human data on the use of resmetirom in pregnancy, but risks to the mother and fetus may arise from underlying NASH with liver fibrosis. In animal studies, high doses of resmetirom in pregnant rabbits caused fetal loss and reduced weight, linked to maternal toxicity, while no such effects were seen at lower doses. Rats showed increased stillbirths and pup mortality at 37 times the recommended dose, with significant drops in maternal thyroid hormones. However, lower doses did not affect development. The metabolite MGL-3623 showed no adverse effects in rats. The background risk of birth defects or

miscarriage in the general population is estimated at 2-4% and 15-20%, respectively.

Pediatric Use
The safety and effectiveness of Resmetirom have not been established in pediatric patients.

Geriatric Use
In Trial 1, of the 594 patients with NASH who received at least one dose of Resmetirom, 149 (25%) were 65 years of age and older and 13 (2%) were 75 years of age and older. 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 Cmax 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 of Resmetirom have not been established in patients with NASH cirrhosis.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via National Pharmacovigilance Electronic Reporting Systems' to the respective National Regulatory Authorities.

4.9 Overdose

If someone has overdosed and has serious symptoms such as passing out or trouble breathing, take the patient to emergency center right away.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Liver Fat Content: Resmetirom decreases liver fat content as measured by magnetic resonance imaging-protein density fat fraction (MRI-PDFF) or FibroScan controlled attenuation parameter (CAP). Reductions in liver fat content by MRI-PDFF were observed at 16 (the first assessment) and 52 weeks of treatment. Reductions in liver fat content by CAP were observed at 52 weeks of treatment.

Prohormone FT4: Resmetirom decreased concentrations of prohormone FT4 were observed at the first assessment at 4 weeks of treatment. Similar decreases in FT4 were observed during the treatment.

Sex Hormone Binding Globulin (SHBG): Resmetirom increased concentrations of sex hormone binding globulin (SHBG) were observed at the first assessment at 4 weeks of treatment, and at longer durations of treatment. The clinical significance of this change is unknown.

Cardiac Electrophysiology: At a dose two times the maximum recommended dose, RESILIVA does not prolong the QT interval to any clinically relevant extent.

5.2 Pharmacokinetic properties

Absorption

The resmetirom median time to maximum plasma concentration (Tmax) is approximately 4 hours following multiple daily doses of resmetirom 80 mg or 100 mg. 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 Cmax, an 11% decrease in AUC, and a delay in median Tmax 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.

Elimination

Resmetirom median terminal plasma half-life (t½) is 4.5 hours and the steady state apparent clearance (CL/F) is 17.5 (56.3%) L/h. 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 100 mg once daily.

Excretion

Following oral administration of a 100 mg radio-labeled dose of resmetirom, approximately 67% of the total radioactive dose was recovered in the feces, mostly as metabolites and 24% of the total radioactive dose was recovered in the urine. Unchanged labeled resmetirom was not detected in feces and accounted for 1% of the dose recovered in urine. A metabolite MGL-3623 accounted for 3.3% and 16% of the dose recovered in feces and urine, respectively. Oxalic acid metabolite was observed in plasma but not in urine.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

Carcinogenesis

In a 2-year study in CD-1 mice, resmetirom produced leiomyoma or leiomyosarcoma in the uterus at a dose of 100 mg/kg/day (51 times the maximum recommended dose based on AUC). No tumorigenic effects were observed in female mice at doses of up to 30 mg/kg/day (14 times the maximum recommended dose based on AUC) or in male mice at doses of up to 100 mg/kg/day (35 times the maximum recommended dose based on AUC). In a 2-year study in Sprague-Dawley rats, resmetirom produced benign fibroadenoma in the mammary gland of males at a dose of 30 mg/kg/day (6.5 times the maximum recommended dose based on AUC). No tumorigenic effects were observed in male rats at doses of up to 6 mg/kg/day (3.7 times the maximum recommended dose based on AUC) or in female rats at doses of up to 30 mg/kg/day (3.4 times the maximum recommended dose based on AUC).

Fertility, reproductive and developmental toxicity

In a fertility and early embryonic development study in male and female rats, there were no adverse effects of resmetirom on male or female fertility, reproductive organs, reproductive function or early embryonic development at oral doses up to 30 mg/kg/day (6.9 and 2.6 times the maximum recommended dose based on AUC, for males and females respectively). No effects on embryo-fetal development were observed in pregnant rats treated orally with up to 100 mg/kg/day (21 times the maximum recommended dose based on AUC) or in pregnant rabbits treated orally with up to 30 mg/kg/day (2.8 times the maximum recommended dose based on AUC) during the period of organogenesis.

6. Pharmaceutical Particulars

6.1 List of Excipients

Microcrystalline Cellulose (Avicel PH 101) BP
Povidone K-30 (Polyvinyl Pyrrolidone) BP
Sodium Starch Glycolate BP
Sodium Lauryl Sulphate BP
Magnesium Stearate BP
Opadry II White 85G68918 Ph. Grade
Opadry II Pink 85G84846 Ph. Grade
Opadry II Blue 85G50642 Ph. Grade
Purified Water USP

6.2 Incompatibilities

None

6.3 Shelf-Life

2 years.

6.4 Special Precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and Content of container

Each HDPE container contains 30 film coated tablets, a silica gel desiccant and polyester coil with a child-resistant closure.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

Zinaya Pharmaceuticals Ltd,
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Mayfair Business Centre, 5th floor, Parklands Road, Nairobi. Kenya.

8. Marketing Authorization Number

H2025/CTD12263/26953

9. Date of first authorization/renewal of the authorization

08/10/2025

10. Date of revision of the text

08/10/2025