Orfoxen

Orforglipron Calcium INN

Everest

COMPOSITION

Orfoxen 0.8 Tablet: Each film coated tablet contains Orforglipron Calcium INN equivalent to Orforglipron 0.8 mg.

Orfoxen 2.5 Tablet: Each film coated tablet contains Orforglipron Calcium INN equivalent to Orforglipron 2.5 mg.

Orfoxen 5.5 Tablet: Each film coated tablet contains Orforglipron Calcium INN equivalent to Orforglipron 5.5 mg.

Orfoxen 9 Tablet: Each film coated tablet contains Orforglipron Calcium INN equivalent to Orforglipron 9 mg.

Orfoxen 14.5 Tablet: Each film coated tablet contains Orforglipron Calcium INN equivalent to Orforglipron 14.5 mg.

Orfoxen 17.2 Tablet: Each film coated tablet contains Orforglipron Calcium INN equivalent to Orforglipron 17.2 mg.

PHARMACOLOGY

Orforglipron is a GLP-1 receptor agonist that binds to and activates the human GLP-1 receptor. GLP-1 is a physiological regulator of appetite and caloric intake. GLP-1 receptors are present in brain regions that regulate appetite. In animal studies, orforglipron distributed to and activated neurons in brain regions that regulate appetite and food intake.

INDICATION

Orforglipron is a GLP-1 receptor agonist indicated in combination with a reduced-calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition.

Limitations of Use

- Concomitant use of Orforglipron with another GLP-1 receptor agonist is not recommended.
- Orforglipron is contraindicated in patients with Medullary Thyroid Carcinoma or Multiple Endocrine Neoplasia type 2.

DOSAGE AND ADMINISTRATION

- The starting dosage is 0.8 mg orally once daily. After at least 30 days on the 0.8 mg dosage, increase the dosage to 2.5 mg once daily.
- After at least 30 days on the 2.5 mg dosage, increase the dosage to 5.5 mg once daily.
- The dosage may be increased to the next dosage level (9 mg, 14.5 mg, or 17.2 mg once daily) after at least 30 days on the current dosage, based on treatment response and tolerability.
- The maximum dosage of Orforglipron is 17.2 mg once daily.

Take Orforglipron once daily orally with or without food; swallow whole (no crushing/chewing) and do not exceed one tablet per day.

Dose Modification

Strong CYP3A4 Inhibitors

Avoid strong CYP3A4 inhibitors that also inhibit OATP1B when taking Orforglipron. The maximum dosage of Orforglipron is 9 mg once daily when used concomitantly with a strong CYP3A4 inhibitor.

Strong and Moderate CYP3A4 Inducers

Avoid strong CYP3A4 inducers when taking Orforglipron. Monitor Orforglipron effectiveness when concomitantly using moderate CYP3A4 inducers and escalate Orforglipron dosage as needed.

Recommendations Regarding Missed Dose

If a dose of Orforglipron is missed, it should be taken as soon as possible without doubling the next dose. If 7 or more consecutive doses are missed, therapy should be reinitiated at a lower dose to reduce the risk of gastrointestinal adverse effects.

CONTRAINDICATION

- A personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- Known serious hypersensitivity to Orforglipron or any of the excipients in Orforglipron. Serious hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with GLP-1 receptor agonists.

ADVERSE REACTION

The following serious adverse reactions have been reported with Orforglipron:

Risk of thyroid C-cell tumors, acute pancreatitis, severe gastrointestinal reactions, acute kidney injury due to volume depletion, hypoglycemia, hypersensitivity reactions, diabetic retinopathy complications in patients with type 2 diabetes, acute gallbladder disease, and pulmonary aspiration during general anesthesia or deep sedation.

WARNINGS AND PRECAUTION

Risk of Thyroid C-Cell Tumors

GLP-1 receptor agonists cause thyroid C-cell tumors in rodents, but Orforglipron showed no tumors in animals; however, the relevance to humans remains uncertain. Postmarketing cases with Liraglutide are inconclusive. Orforglipron is contraindicated in patients with Medullary Thyroid Carcinoma or Multiple Endocrine Neoplasia type 2, and patients should be counseled on tumor symptoms. Routine calcitonin or ultrasound screening has limited value and may lead to unnecessary procedures, though elevated calcitonin or thyroid nodules warrant further evaluation.

Acute Pancreatitis

Acute pancreatitis has been reported in patients treated with Orforglipron. Fatal and non-fatal hemorrhagic or necrotizing pancreatitis have been observed in patients treated with GLP-1 receptor agonists. After initiation of Orforglipron, observe patients carefully for signs and symptoms of acute pancreatitis, which may include persistent or severe abdominal pain (sometimes radiating to the back) and which may or may not be accompanied by nausea or vomiting. If pancreatitis is suspected, discontinue Orforglipron and initiate appropriate management.

Severe Gastrointestinal Reactions

Use of Orforglipron has been associated with gastrointestinal adverse reactions, sometimes severe. In clinical trials, severe gastrointestinal adverse reactions were reported more frequently among patients treated with Orforglipron (approximately 3%) than patients who received placebo (1%). Severe gastrointestinal adverse reactions have also been reported postmarketing with GLP-1 receptor agonists. Orforglipron is not recommended in patients with severe gastroparesis.

Hypoglycemia

Orforglipron lowers blood glucose and may cause hypoglycemia (2% vs 0.2% with placebo; higher risk with sulfonylureas or insulin), therefore, requiring patient education, regular glucose monitoring, and possible dose reduction of concomitant insulin or insulin secretagogues to minimize risk.

Hypersensitivity Reactions

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with GLP-1 receptor agonists. If hypersensitivity reactions occur, advise the patient to promptly seek medical attention and discontinue

use of Orforglipron. Orforglipron is contraindicated in patients with a prior serious hypersensitivity reaction to orforglipron or to any of the excipients in Orforglipron. Use caution in a patient with a history of anaphylaxis or angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to these reactions with Orforglipron.

Diabetic Retinopathy Complications in Patients with Type 2 Diabetes

Temporary worsening of diabetic retinopathy has been reported with rapid improvement in glucose control. Orforglipron has not been studied in patients with diabetic retinopathy and/or macular edema requiring acute treatment. Monitor patients with a history of diabetic retinopathy for progression of diabetic retinopathy.

Acute Gallbladder Disease

Treatment with Orforglipron and GLP-1 receptor agonists is associated with an increased occurrence of acute gallbladder disease. In a pool of two clinical trials for weight reduction (Trials 1 and 2), cholelithiasis was reported in 1% of patients treated with Orforglipron once daily and 0.7% of placebo-treated patients, and acute cholecystitis was reported in 0.4% of patients treated with Orforglipron once daily and 0.3% of placebo-treated patients. Acute gallbladder events were associated with weight reduction. If cholecystitis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated.

Pulmonary Aspiration During General Anesthesia or Deep Sedation

Orforglipron delays gastric emptying and has rare reports of pulmonary aspiration during anesthesia despite fasting; risk mitigation is unclear, so patients should inform healthcare providers before any surgery or procedure.

USE IN SPECIFIC POPULATIONS

Pregnancy

Weight loss offers no benefit to a pregnant patient and may cause fetal harm. When a pregnancy is recognized, advise the pregnant patient of the risk to a fetus and discontinue Orforglipron.

Lactation

Orforglipron is not recommended for nursing women.

Females and Males of Reproductive Potential

Contraception

Based on animal studies, Orforglipron may pose fetal risk; women should use effective contraception, and due to delayed gastric emptying potentially affecting oral contraceptive absorption, switch to non-oral methods or add barrier protection for 30 days after initiation and each dose escalation.

Pediatric Use

Safety and effectiveness of Orforglipron have not been established in pediatric patients.

Hepatic Impairment

Orforglipron is not recommended for use in patients with severe hepatic impairment (Child-Pugh Class C). No dosage modification of Orforglipron is recommended in patients with mild or moderate hepatic impairment (Child-Pugh Class A and B, respectively).

Renal Impairment

No dosage modification of Orforglipron is recommended for patients with renal impairment. In subjects with renalimpairment including end-stage renal disease (ESRD), no change in Orforglipron pharmacokinetics (PK) was observed. Monitor renal function in patients reporting adverse reactions to Orforglipron that could lead to volume depletion.

OVERDOSE

In case of overdose with Orforglipron, seek guidance from Poison Control or a medical toxicologist and provide supportive care based on symptoms, with monitoring as needed due to its prolonged half-life.

DRUG INTERACTIONS

- Concomitant use of strong CYP3A4 inhibitors (e.g., Ritonavir) can increase exposure to Orforglipron, raising the risk of adverse effects; dose limits or avoidance may be required.
- Strong CYP3A4 inducers (e.g., Rifampin) can decrease Orforglipron levels, potentially reducing its effectiveness. Coadministration should generally be avoided.
- Moderate CYP3A4 inducers may also lower Orforglipron exposure; monitor clinical response and adjust the dose if needed.
- When used with Simvastatin, Orforglipron can increase Simvastatin levels, so the Simvastatin dose should not exceed 20 mg daily.
- Combining Orforglipron with insulin or insulin secretagogues (e.g., sulfonylureas) increases the risk of hypoglycemia; dose reduction of the other antidiabetic agents should be considered.

PHARMACEUTICAL INFORMATION

Storage

Store below 25°C in a cool and dry place. Keep away from light & out of the reach of children.

HOW SUPPLIED

Orfoxen 0.8 Tablet: Each HDPE container contains 30 tablets (each tablets contains Orforglipron 0.8 mg), a silica gel desiccant and polyester coil with child resistant closure.

Orfoxen 2.5 Tablet: Each HDPE container contains 30 tablets (each tablets contains Orforglipron 2.5 mg), a silica gel desiccant and polyester coil with child resistant closure.

Orfoxen 5.5 Tablet: Each HDPE container contains 30 tablets (each tablets contains Orforglipron 5.5 mg), a silica gel desiccant and polyester coil with child resistant closure.

Orfoxen 9 Tablet: Each HDPE container contains 30 tablets (each tablets contains Orforglipron INN 9 mg), a silica gel desiccant and polyester coil with child resistant closure.

Orfoxen 14.5 Tablet: Each HDPE container contains 30 tablets (each tablets contains Orforglipron 14.5 mg), a silica gel desiccant and polyester coil with child resistant closure.

Orfoxen 17.2 Tablet: Each HDPE container contains 30 tablets (each tablets contains Orforglipron 17.2 mg), a silica gel desiccant and polyester coil with child resistant closure.

Manufactured by
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