ORLIRISE CAPSULE
(ORLISTAT)

DESCRIPTION:

ORLIRISE is a lipase inhibitor for obesity management that acts by inhibiting the absorption of dietary fats. ORLIRISE works in intestines, where it blocks some of the fat from being absorbed. This undigested fat is then eliminated in bowel movements. ORLIRISE should be used together with a reduced calorie diet recommended by the doctor.

COMPOSITION:

Each capsule contains:
Orlistat……120mg

PHARMACOLOGICAL PROPERTIES:

Pharmacodynamic Properties:
ORLIRISE is a potent, specific and reversible long acting inhibitor of gastrointestinal lipases. It exerts its therapeutic activity in the lumen of the stomach and the small intestine by forming a covalent bond with the serine residue of the active site of gastric and pancreatic lipases. The inactivated enzyme is thus unable to hydrolyse dietary fat, in the form of triglycerides, into absorbable free fatty acids and monoglycerides. As undigested triglycerides are not absorbed, the resulting caloric deficit has a positive effect on the weight control.

Pharmacokinetic properties:
ORLIRISE is non-systemically acting drug that works locally. About 2% of ORLIRISE is absorbed and this is mostly metabolized within the gastrointestinal wall. Most of the drug is excreted unchanged in faeces.

INDICATIONS:

ORLIRISE is indicated in conjunction with a mildly hypocaloric diet for the treatment of obese patients with a body mass index (BMI) greater or equal to 30 kg/m^2, or overweight patients (BMI $\geq$ 28 kg/m^2) with associated risk factors such as type II diabetes, hyperlipidemia and hypertension.
In non-diabetic patients, treatment with ORLIRISE should be started only if diet alone has previously produced a weight loss of at least 2.5kg over a period of 4 consecutive weeks. Treatment with ORLIRISE should be discontinued after 12 weeks if patients have been unable to lose at least 5 % of the body weight as measured at the start of therapy.

CONTRAINDICATIONS:

- Hypersensitivity to the active substance or to any of the excipients.
- Chronic malabsorption syndrome.
- Cholestasis.
- Breast-feeding.

INTERACTIONS:

Cyclosporine

A decrease in cyclosporine plasma levels has been observed. This can lead to a decrease of immunosuppressive efficacy. Therefore the combination is not recommended.

Acarbose

In the absence of pharmacokinetic interaction studies, the concomitant administration of ORLIRISE with acarbose should be avoided.

Oral anticoagulants

When warfarin or other anticoagulants are given in combination with ORLIRISE, international normalised ratio (INR) values should be monitored.

Fat soluble vitamins

Treatment with ORLIRISE may potentially impair the absorption of fat-soluble vitamins (A, D, E and K).

In order to ensure adequate nutrition, patients on a weight control diet should be advised to have a diet rich in fruit and vegetables and use of a multivitamin supplement could be considered.

Amiodarone

A small decrease in plasma levels of amiodarone, when given as a single dose, has been observed in a limited number of healthy volunteers. In patients receiving concomitant amiodarone treatment, reinforcement of clinical and ECG monitoring is warranted.

Lack of interactions

No interactions with amitriptyline, atorvastatin, biguanides, digoxin, fibrates, fluoxetine, losartan, phenytoin, phentermine, pravastatin, nifedipine, Gastrointestinal Therapeutic System (GITS), nifedipine slow release, sibutramine or alcohol have been observed.

ORLIRISE may indirectly reduce the availability of oral contraceptives and lead to unexpected pregnancies in some individual cases. An additional contraceptive method is recommended in case of severe diarrhoea.

PRECAUTIONS:

- Organic causes of obesity, such as hypothyroidism, should be excluded before prescribing ORLIRISE.
- ORLIRISE should be stopped after 3 months if the patient has not lost 5% of body weight and stopped after 6 months if the patient has not lost 10% of body weight.

- The daily intake of fat should be distributed over three main meals. If ORLIRISE is taken with any one meal very high in fat, the possibility of gastrointestinal effects may increase.
- Weight loss induced by ORLIRISE accompanied by improved metabolic control in type II diabetics might require reduction in the dose of hypoglycaemic medication (e.g. sulfonylureas).

Pregnancy and lactation:

For ORLIRISE no clinical data on exposed pregnancies are available.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
Caution should be exercised when prescribing to pregnant women.
As it is not known whether ORLIRISE is secreted into human milk, ORLIRISE is contra-indicated during breast-feeding.

ADVERSE REACTIONS :

Gastrointestinal disturbances, including faecal urgency and incontinence, flatulence, and fatty stools or discharge are the most frequently reported adverse effects during treatment with ORLIRISE. They may be minimized by limiting the amount of fat in the diet. Other reported effects are headache, anxiety, fatigue and menstrual irregularities.

DOSAGE AND ADMINISTRATION:

Adults:
The recommended dose of ORLIRISE is one 120 mg capsule taken with water immediately before, during or up to one hour after each main meal. If a meal is missed or contains no fat, the dose of ORLIRISE should be omitted.
The patient should be on a nutritionally balanced, mildly hypocaloric diet that contains approximately 30 % of calories from fat. It is recommended that the diet should be rich in fruit and vegetables. The daily intake of fat, carbohydrate and protein should be distributed over three main meals.
Doses of ORLIRISE above 120 mg three times daily have not been shown to provide additional benefit.
The effect of ORLIRISE results in an increase in faecal fat as early as 24 to 48 hours after dosing. Upon discontinuation of therapy, faecal fat content usually returns to pre-treatment levels, within 48 to 72 hours.

Special populations:
The effect of ORLIRISE in patients with hepatic and/or renal impairment, children and elderly patients has not been studied.
There is no relevant indication for use of ORLIRISE in children.

OVERDOSAGE:

Single doses of 800 mg ORLIRISE and multiple doses of up to 400 mg three times daily for 15 days have been studied in normal weight and obese subjects without significant adverse findings. In addition, doses of 240 mg tid have been administered to obese patients for 6 months. The majority of ORLIRISE overdose cases received during post-marketing reported either no adverse events or adverse events that are similar to those reported with recommended dose.

INSTRUCTIONS:

- To be sold on the prescription of a registered medical practitioner only.
- Store below 25^{o}C.
- Protect from sunlight and moisture.
- Keep out of the reach of children.

PRESENTATION

ORLIRISE 120 mg capsules are available in the blister packs of 1 x 10's.

MANUFACTURED BY:

OBS PAKISTAN (PVT) LIMITED
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