Orlifit™

اورلیفِٹ

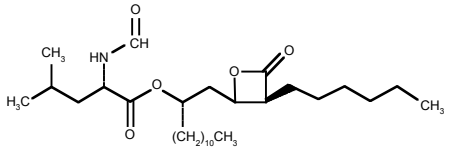
(ORLISTAT)

Capsules 60mg, 120mg

DESCRIPTION

ORLIFIT (Orlistat) is the first drug in a new class of non-systemically acting anti-obesity drugs known as lipase inhibitors.

Chemically orlistat is (S)-2-formylamino-4-methyl-pentanoic acid (S)-1-[[(2S, 3S)-3-hexyl-4-oxo-2-oxetanyl] methyl]-dodecyl ester. The molecular formula is $C_{29}H_{53}NO_5$ and the structural formula is:



Orlistat

QUALITATIVE & QUANTITATIVE COMPOSITION

ORLIFIT (Orlistat) is available for oral administration as:

1. ORLIFIT Capsules 60mg
   Each capsule contains:
   Orlistat …60mg

2. ORLIFIT Capsules 120mg
   Each capsule contains:
   Orlistat …120mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Orlistat is a potent, specific and reversible long-acting inhibitor of gastrointestinal lipases. It exerts its therapeutic activity in the lumen of the stomach and 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.

Pharmacokinetics

Absorption

Orlistat is minimally absorbed after oral doses. Systemic absorption of the drug is therefore not needed for the activity.

Distribution

The volume of distribution cannot be determined because orlistat is minimally absorbed. *In vitro* orlistat is > 99% bound to plasma proteins (lipoproteins and albumin were the major binding proteins). Orlistat minimally partitions into erythrocytes.

Elimination

Approximately 97% of the administered dose is excreted in feces and 83% of that as unchanged orlistat. The cumulative renal excretion of total orlistat-related materials was <2% of the given dose. The time to reach complete excretion (fecal+urinary) is 3 to 5 days.

THERAPEUTIC INDICATIONS

ORLIFIT (Orlistat) is used together with dietary modification (reduced calorie diet) in the management of obesity, i.e. in patients with a BMI of 30Kg/m^2 or greater. It may also be used in overweight patients with BMI of 27Kg/m^2 or more with associated risk factors e.g., (hypertension, diabetes, dyslipidemia).

DOSAGE & ADMINISTRATION

Adults

The recomeded dose of ORLIFIT (Orlistat) is 1 capsule of 60mg or 120mg to be taken three times daily, immediately before, during or up to 1 hour after meals. If a meal is missed or contains no fat, the dose can be omitted. Not more than 3 capsules of 60mg or 120mg should be taken in 24 hours. It is recommended that the diet should be rich in fruits and vegetables.

Treatment should not exceed 6 months. If patients have been unable to loose weight after 12 weeks of treatment, they should consult their doctor or a pharmacist. It may be necessary to discontinue treatment.

The diet and exercise programme should continue to be followed when treatment with ORLIFIT (Orlistat) is stopped.

ORLIFIT (Orlistat) should be taken with a low-calorie diet containing less than 30% of calories from fat.

Special population

There is no relevent use of orlistat in children. Since orlistat is minimally absorbed, no dosage adjustment is necessary in elderly and in individuals with/without hepatic impairment.

ADVERSE REACTIONS

Adverse reaction to orlistat are largely gastrointestinal in nature and related to the pharmacological effect of the medicinal product on preventing the absorption of ingested fat. The frequency of adverse reaction during use of orlistat are as follows:

Very common

Headache, upper respiratory infection, abdominal pain, oily spotting from the rectum, flatus with discharge, fecal urgency, fatty stool, flatulence, liquid stool, influenza, oily evacuation and increased defecation.

Common

Lower respiratory infection, rectal pain, soft stools, fecal incontinence, tooth disorder, gingival disorder, urinary tract infection, fatigue, menstrual irregularity and anxiety.

CONTRAINDICATIONS

Orlistat is contraindicated in:

- Patients with known hypersensitivity to orlistat or any of the other components contained in the medicinal product.
- Patients with chronic malabsorption syndrome, cholestasis.
- Pregnant women and nursing mothers.

PRECAUTIONS

- Organic causes of obesity, such as hypothyroidism, should be excluded before prescribing orlistat.
- Orlistat should be stopped after 3 months if the patient has not lost 5% of body weight and stopped at 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 orlistat is taken with any one meal very high in fat, the possibility of gastrointestinal effects may increase.
- Weight loss induced by orlistat accompanied by improved metabolic control in type 2 diabetics might require reduction in the dose of hypoglycemic medication (e.g., sulfonylureas).
- Weight loss may be accompanied by an improvement in blood pressure and cholesterol levels. Patients who are taking a medicinal product for hypertension or hypercholesterolemia should consult a doctor or pharmacist when taking orlistat, in case it is necessary to adjust the dose of these medicinal products.

Drug Interactions

Cyclosporine

A decrease in cyclosporine plasma levels has been observed, when orlistat was administered concomitantly. Therefore the combination is not recommended. However, if such concomitant use is unavoidable, to reduce the chance of drug-drug interaction cyclosporine should be taken 2 hours after or before orlistat. In addition more frequent monitoring of cyclosporine blood levels should be performed both after addition of orlistat and upon discontinuation of orlistat in cyclosporine treated patients. Cyclosporine blood levels should be monitored until stabilised.

Fat soluble vitamins

Decrease in the absorption of fat soluble vitamins and β-carotene have been observed when co-administered with orlistat.

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. If a multivitamin supplement is recommended, it should be taken at least two hours after the administration of orlistat or at bedtime.

Oral Anticoagulants

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

Acarbose

The concomitant administration of orlistat with acarbose should be avoided.

Oral contraceptives

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

Amiodarone

In patient receiving concomitant amiodarone treatment, reinforcement of clinical ECG monitoring is warranted.

OVERDOSAGE

Single dose of 800mg orlistat and multiple dose of up to 400mg three times a day for 15 days in normal weight and obese subjects showed no significant adverse findings. If a significant overdose of orlistat occur, it is recommended that the patient be observed for 24 hours. The systemic effects attributable to the lipase-inhibiting properties of orlistat should be rapidly reversible.

STORAGE

Store at 25°C (Excursions permitted between 15°C-30°C)
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

ORLIFIT (Orlistat) Capsules 60mg are available in blister pack of 10's.
ORLIFIT (Orlistat) Capsules 120mg are available in blister pack of 10's.

Keep out of reach of children.

To be sold on the prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
Getz pharma (PVT) LIMITED
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