OLBETAM®

250 mg
ACIPIMOX

Olbetam (acipimox or 5-methylpyrazinecarboxylic acid-4-oxide) is a novel lipid-lowering agent synthesized in the Pharmacia & Upjohn Research Laboratories. Olbetam is indicated in lipid disorders characterized by hypertriglyceridaemia and/or hypercholesterolaemia. Elevated plasma lipids are an acknowledged risk factor in the pathogenesis of atherosclerosis and related cardiovascular complications.

PHARMACOLOGY

Olbetam has a marked lipid-lowering effect which reduces plasma levels of free fatty acids and triglycerides. The drug acts on adipose tissue by reducing mobilisation of lipids (lipolysis) and by stimulating lipoprotein-lipase, thus accelerating catabolism of the very low density lipoproteins (VLDL).

TOXICOLOGY

Toxicity studies in various animal species (mouse, rat and dog) have shown that Olbetam has very low acute toxicity. Prolonged treatment (up to two years) has shown that the compound has good systemic and gastric safety.

Reproductive studies did not demonstrate adverse effects of the drug on fertility, embryogenesis or lactation.

Chronic toxicity

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and repeat-dose toxicity. Biochemical and histological investigations revealed no sign of an effect on the peroxisomes in the liver cell.

Carcinogenicity

In vivo carcinogenicity studies in mice and rats revealed no evidence of any kind of oncogenic properties for acipimox.

Mutagenicity

In none of the mutagenicity studies conducted was there any evidence that acipimox can cause mutagenic effects.

PHARMACOKINETICS

In man, Olbetam is rapidly and completely absorbed after oral administration, reaching peak plasma levels within two hours. The half-life is about two hours.

The compound does not bind to plasma proteins. It is not significantly metabolized and is eliminated almost completely intact by the urinary route.

CLINICAL USE

Olbetam inhibits the release of fatty acids from adipose tissue and reduces the blood concentrations of very low density lipoproteins (VLDL or Pre-beta) and low density lipoproteins (LDL or beta) with a subsequent overall reduction in triglyceride and cholesterol levels.

Olbetam also has a favorable effect on high density lipoproteins (HDL or alpha), which increase during treatment.

Improvement in the plasma lipids picture is usually seen within the first month of therapy.

INDICATIONS

Treatment of lipid disorders characterized, according to Fredrickson, by elevated plasma levels of triglycerides (type IV hyperlipoproteinaemia), of cholesterol (type IIa hyperlipoproteinaemia) and of triglycerides and cholesterol (type IIb, III and V hyperlipoproteinaemia).

Olbetam should be prescribed only for patients with lipid or lipoprotein abnormalities demonstrated by laboratory tests and where diet alone is insufficient to correct the condition.

CONTRAINDICATIONS

Confirmed individual hypersensitivity towards the drugs.

Peptic ulcer.

Severe renal impairment (creatinine clearance less than 30 mL/min).

DOSAGE

The daily dosage may be adjusted individually depending on plasma triglyceride and cholesterol levels. The average daily dose is one 250 mg capsule two or three times daily to be taken with or after meals. One capsule twice daily is recommended in type IV hyperlipoproteinaemia and one capsule three times daily in types II, III and V.

In particularly severe cases doses can be increased at the physician’s discretion. Daily dosages of up to 1200 mg have been safely administered for long periods.

For patients with moderate to severe renal impairment (creatinine clearance values between 60 and 30 mL/min) the dose needs to be reduced accordingly to one 250 mg capsule 1 or 2 times daily to be taken with or after meals.

WARNING AND PRECAUTIONS

As for other drugs of the same therapeutic class, low-cholesterol and low-fat diets, exercise and weight loss in case of obesity are preferable therapeutic approaches, to be tried before starting treatment with Olbetam.

During prolonged treatment in particular, all baseline values, including lipid profile, should be measured before treatment and periodic checks should be made of blood lipids and lipoproteins and hepatic and renal function to confirm that the desired therapeutic effect has been achieved.

Acipimox is structurally related to nicotinic acid. The risk of muscle toxicity is increased when nicotinic acid is administered concomitantly with a statin (i.e., a 3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitor). In one study, Chinese patients taking niacin plus laropiprant concomitantly with simvastatin were reported to have a higher incidence of myopathy and rhabdomyolysis compared to Caucasians.

Keep out of the reach of children.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

The risk of the myopathy may be increased when nicotinic acid is administered concomitantly with a statin. As acipimox is structurally related to nicotinic acid caution is recommended when administering both drugs together (see WARNING AND PRECAUTIONS).

No interaction has been shown with digoxin, warfarin and cholestyramine.

FERTILITY, PREGNANCY AND LACTATION

As the product's safety in pregnancy has not yet been ascertained and it is not known whether acipimox is secreted in human milk, it should not be administered to presumed or confirmed pregnant women or during breast-feeding.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effect of Olbetam on ability to drive or use machinery has not been studied, but based on its pharmacodynamic properties and overall safety profile it is unlikely to have an effect.

ADVERSE REACTIONS

Long-term clinical trials on a large number of patients have confirmed the experimental results and shown that the drug is well tolerated. Clinical and laboratory assessment showed that the drug did not give rise to toxicity in the principal organs and did not interfere with other metabolic pathways (such as glucose and uric acid metabolisms).

Immune system disorders: Anaphylactoid reactions

Nervous system disorders: Headache

Vascular disorders: Flushing, Vasodilatation

Respiratory, thoracic and mediastinal disorders: Bronchospasm

Gastrointestinal disorders: Dyspepsia, Abdominal pain upper, Nausea, Diarrhea

Skin and subcutaneous tissue disorders: Pruritus, Rash, Erythema, Urticaria, Angioedema

Musculoskeletal and connective tissue disorders: Myositis, Myalgia, Arthralgia

General disorders and administration site conditions: Feeling hot, Malaise, Asthenia

The drug may induce vasodilation giving rise to a sensation of heat, flushing or pruritus, especially at the beginning of therapy, and also rash and erythema. These reactions usually disappear rapidly during the first days of treatment.

In such cases, Olbetam should be discontinued and appropriate therapeutic measures instituted.

OVERDOSE
If toxic effects are observed, supportive care and symptomatic treatment should be administered.

PRESENTATION
250 mg capsules: Packs of 30 capsules.

LPD reference: OLB-SIN-0613/1
Date of Last Revision: November 2013