

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Olbetam 250 mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Acipimox 250.00 mg

For the full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Red-brown/dark pink bard gelatin capsules, size no. 1, containing a white to cream powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Olbetam is indicated as alternative or adjunct treatment to reduce triglyceride levels in patients who have not responded adequately to other treatments such as statin or fibrate treatment for:

- hypertriglyceridaemia (Fredrickson type IV hyperlipoproteinaemia);
- hypercholesterolaemia and hypertriglyceridaemia (Fredrickson type IIB hyperlipoproteinaemia).

Olbetam should be used after other measures have been taken such as dietary changes and other non-pharmacological treatment (e.g. exercise, weight reduction).

It has not been shown that treatment of hyperlipoproteinaemia with acipimox leads to a reduction of cardiac morbidity or mortality.

4.2 Posology and method of administration

Posology

The daily dosage should be adjusted individually depending on plasma triglyceride and cholesterol levels.

The recommended dosage is one 250 mg capsule 2 or 3 times daily to be taken with or after meals. The lower dose is advised in type IV and the higher dose in type IIB hyperlipoproteinaemias.

Daily dosages of up to 1200 mg have been safely administered for long periods.

Improvement in the plasma lipid's picture is usually seen within the first month of therapy.

Renal impairment

In patients with slight renal impairment (creatinine clearance values > 60 ml/min) no dose reduction is required. 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. Acipimox is eliminated entirely through the kidneys, therefore, accumulation can be expected and is related to the degree of renal impairment. It is advised that longer intervals are left between doses of the drug in patients with renal impairment.

Method of administration

To be given orally.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients and those with peptic ulceration listed in section 6.1.

Acipimox should not be given to patients with severe renal impairment (creatinine clearance < 30 ml/min).

4.4 Special warnings and precautions for use

Modification of hyperlipidaemia is recommended only for patients with hyperlipoproteinaemia of a degree and type considered appropriate for treatment.

Low cholesterol and low-fat diets, together with cessation of alcohol consumption, exercise and weight loss, in case of obesity are preferable therapeutic approaches to be tried before starting treatment with acipimox.

Since long term administration of acipimox is recommended, all baseline values, including lipid profile, should be measured before treatment and periodic determinations of serum lipids should be obtained 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 nicotinic acid plus laropiprant concomitantly with simvastatin were reported to have a higher incidence of myopathy and rhabdomyolysis compared to Caucasians.

Hepatic and renal functions should be monitored.

The absorption of acipimox is not affected by the concomitant administration of colestyramine

Evidence of clinical efficacy in the prevention of heart disease has not been established.

The possible beneficial and adverse, long-term consequences of some drugs used in the hyperlipidaemias are still the subject of scientific discussion.

Excipient Information:

Olbetam contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction has been shown with other lipid lowering agents. However, the combination with statins or fibrates should be used with caution due to reports of an increased risk of musculoskeletal events with nicotinic acid (a structural analogue of acipimox) when used in combination with such lipid-lowering agents.

No interaction has been shown with digoxin and warfarin.

4.6. Fertility, pregnancy and lactation

Fertility

No human data on the effect of acipimox on fertility are available. In rats, there was no effect on mating or fertility with acipimox treatment.

Pregnancy

There is only limited experience to date of administration of acipimox to humans therefore epidemiological data is not available. Animal studies have shown reproductive toxicity at high doses (see section 5.3). Taking into account the present experience of administration to humans of acipimox and that the safety of acipimox in human pregnancy has not yet been ascertained, it is recommended, therefore, that acipimox not be administered to women who are, or may be pregnant.

Breast-feeding

In the absence of animal data on the levels of acipimox excreted in milk, acipimox should not be administered to women who are breast-feeding.

4.7 Effects on ability to drive and use machines

The effect of acipimox 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.

4.8 Undesirable effects

The following undesirable effects have been observed from the clinical and post-marketing experience and reported during treatment with acipimox with the following frequencies: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$); Not Known (cannot be estimated from the available data).

MedDRA System Organ Class	Frequency	Undesirable Effects
Eye Disorders	Not Known	Eye symptoms (dry or gritty eyes)
Immune System Disorders	Uncommon	Anaphylactoid reaction*
Nervous System Disorders	Very Common	Headache
Vascular Disorders	Very Common	Flushing
	Not Known	Vasodilatation**
Respiratory Thoracic and Mediastinal Disorders	Uncommon	Bronchospasm*
Gastrointestinal Disorders	Very Common	Dyspepsia
	Common	Abdominal pain upper
	Uncommon	Nausea*
	Not Known	Diarrhoea**
Skin and Subcutaneous Tissue Disorders	Common	Urticaria
	Uncommon	Angioedema*, Pruritus*, Rash*, Erythema*
Musculoskeletal and Connective Tissue Disorders	Uncommon	Myositis*, Myalgia*, Arthralgia*
General Disorders and Administration Site Conditions	Common	<i>Asthenia</i>
	Uncommon	<i>Feeling hot*</i> , <i>Malaise*</i>

* AE frequency estimated from post-marketing safety database

** AE frequency cannot be estimated from the available data

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nicotinic acid and derivatives, ATC code: C10AD06

Acipimox 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.

Acipimox also has a favourable effect on high density lipoproteins (HDL or alpha) which increase during treatment.

5.2 Pharmacokinetic properties

Acipimox is rapidly and completely absorbed orally, reaching peak plasma levels within two hours. The half-life is about two hours. It does not bind to plasma proteins; it is not significantly metabolised and is eliminated almost completely intact by the urinary route.

5.3. Preclinical safety data

Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and repeat-dose toxicity, carcinogenicity and mutagenicity.

There is no evidence from the animal studies that acipimox is teratogenic. However, a higher incidence of immature and underweight foetuses was seen in pregnant animals given higher doses of acipimox. This effect may be due to maternal toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Physically modified corn starch (STA-RX 1500)
Silica gel (Syloid 244)
Magnesium stearate
Sodium lauryl sulfate

Hard gelatin capsules shell:
Gelatin
Titanium dioxide (E171)
Iron oxide red (E172)
Iron oxide yellow (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store below 30°C in the original container to protect from moisture.

6.5 Nature and contents of container

Packed in blisters of 10 capsules per strip, inside cartons. Each carton contains 90 capsules.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00057/1022

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2 May 2003

10 DATE OF REVISION OF THE TEXT

16/08/2023