PATIENT INFORMATION LEAFLET

Niaspan™ Prolonged-Release Tablets

MERCK

Nicotinic acid

COMPOSITION

Niaspan™ 500 mg Prolonged-Release 28 tablets:
Each prolonged-release tablet contains 500 mg nicotinic acid as active ingredient. Reg Lebanon 195262
Niaspan™ 750 mg Prolonged-Release 28 tablets:
Each prolonged-release tablet contains 750 mg nicotinic acid as active ingredient. Reg Lebanon 195263
Niaspan™ 1000 mg Prolonged-Release 28 tablets:
Each prolonged-release tablet contains 1000 mg nicotinic acid as active ingredient. Reg Lebanon 195264

Excipients: hypromellose, povidone, stearic acid

PROPERTIES

Niaspan contains nicotinic acid in a prolonged-release form. Nicotinic acid is a B-complex vitamin and a natural ingredient of food. Used for medicinal purposes, nicotinic acid can improve blood fats (lipids) such as cholesterol and triglycerides and thus help to reduce the risk for stroke and heart disease.
Nicotinic acid reduces total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and increases high-density lipoprotein cholesterol (HDL-C). The magnitude of the individual lipid response may be influenced by the severity and type of the underlying lipid abnormality. Nicotinic acid treatment also decreases serum levels of apolipoprotein B-100 (Apo B), the major protein component of the very low-density lipoprotein (VLDL) and LDL fractions, and of lipoprotein a (Lp(a)), a variant form of LDL independently associated with risk for heart disease.
Following oral administration of Niaspan, nicotinic acid is rapidly and extensively absorbed (bioavailability 60-76% of dose). The individual Niaspan tablet strengths show differing rates of absorption. Thus, the tablet strengths are not interchangeable. Administration with food increases bioavailability, and the time to reach maximum effect is significantly increased from 2-3 hours fast to 5-6 hours with a light meal.
The pharmacokinetics of Niaspan are not proportional to dose. Metabolism involves two metabolic pathways, one of which is saturable, explaining the non-linear relationship between nicotinic acid dose and plasma concentrations. Nicotinic acid and its metabolites are rapidly eliminated in the urine.

INDICATIONS

Treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia, characterised by elevated levels of LDL-cholesterol and triglycerides and low HDL-cholesterol, and in patients with primary hypercholesterolaemia. Niaspan should be used in patients in combination with statins (HMG-CoA reductase inhibitors), when the cholesterol lowering effect of statin monotherapy is inadequate. Niaspan can be used as monotherapy in patients who do not tolerate statins. Diet and other non-pharmacological treatments (e.g., exercise, weight reduction) should be continued during therapy with Niaspan.

CONTRAINDICATIONS

Niaspan must not be used in patients with:
- Hypersensitivity to nicotinic acid or to any of the excipients (see 'Composition'),
- Significant liver dysfunction
- Active peptic ulcer disease
- Arterial bleeding

Pregnancy and lactation

Niaspan should not be taken by pregnant women unless strictly necessary. It is not known whether nicotinic acid at doses typically used for lipid disorders can cause foetal harm when administered to pregnant women or whether it can affect reproductive capacity. Animal studies are incomplete.
Niaspan must not be used by breast-feeding women because nicotinic acid can pass into breast milk.

SPECIAL WARNINGS AND PRECAUTIONS

Liver

Severe liver dysfunction, including fulminant hepatic necrosis, has occurred in patients who have taken long-acting nicotinic acid products in place of immediate-release nicotinic acid. Since the pharmakokinetics of Niaspan are different to other nicotinic acid preparations, Niaspan must not be replaced with other preparations, see 'Dosage and administration'. See also the product information of the statin used.
Caution is advised when Niaspan is used in patients who consume substantial quantities of alcohol and/or have a history of liver disease. Elevated liver transaminases have been observed with Niaspan therapy. However, transaminase elevations were reversible upon discontinuation of Niaspan. Liver tests including AST and ALT must be performed periodically in all patients during therapy with Niaspan and prior to treatment in case of history and/or symptoms of hepatic dysfunction (e.g. jaundice, nausea, fever, and/or malaise).
If the transaminase levels show evidence of progression, particularly if they rise to three times the upper limit of normal, the drug must be discontinued.

Skeletal muscle

Single reports on rhabdomyolysis in patients on combined therapy with Niaspan and statins have been received from spontaneous reporting. Doctors contemplating combined therapy with statins and Niaspan should carefully weigh the potential benefits and risks and should carefully monitor patients for any symptoms of rhabdomyolysis, e.g., muscle pain, tenderness, or weakness, particularly during the initial months of therapy and during any periods of dose escalation of either agent. Periodic serum creatine phosphokinase (CPK) and potassium determinations should be considered in such situations.
A CPK level should be measured before starting such a combination in patients with pre-disposing factors for rhabdomyolysis, as follows:
- renal impairment
- hypothyroidism
- alcohol abuse
- age > 70 years
- personal or family history of hereditary muscular disorders
- previous history of muscular toxicity with a fibrate or a statin

Muscle damage must be considered in any patient presenting with diffuse myalgia, muscle tenderness and/or marked increase in muscle CK levels (> 5 x ULN); under these conditions treatment must be discontinued.

The product information of the statin should be consulted.

Further monitoring recommendations

Unstable angina and acute myocardial infarction:
Caution is advised when Niaspan is used in patients with unstable angina or in the acute phase of myocardial infarction, particularly when such patients are also receiving vasoactive drugs such as nitrates, calcium channel blockers, or adrenergic blocking agents.
Coagulation:
Patients undergoing surgery or receiving anti-coagulants must be monitored closely, as Niaspan may reduce platelet count and increase prothrombin time.
Glucose intolerance:
Adjustment of diet and/or blood-sugar-lowering therapy may become necessary because Niaspan may increase glucose intolerance.
Uric acid:
Monitoring of patients predisposed to gout is recommended. Elevated uric acid levels have occurred with Niaspan therapy.
Hypophosphataemia:
In patients at risk of hypophosphataemia, monitoring of phosphorous levels is recommended. Niaspan has been associated with reductions in phosphorous levels.
Other:
Patients with a past history of jaundice, hepatobiliary disease, or peptic ulcer should be observed closely.
Effects on the ability to drive and use machines:
Niaspan has no or negligible influence on the ability to drive and use machines.

ADVERSE EFFECTS

In the placebo-controlled clinical trials, flushing episodes (i.e., warmth, redness, itching and/or tingling) were the most common treatment-emergent adverse events for Niaspan (reported by 88% of patients). In these studies fewer than 6% of Niaspan patients discontinued due to flushing. In comparisons of immediate-release (IR) nicotinic acid and Niaspan, although the number of patients who flushed was similar, fewer flushing episodes were reported by patients who received Niaspan. Following four weeks of maintenance therapy with Niaspan at daily doses of 1500 mg, the frequency of flushing over the four week period averaged 1.88 events per patient.
Tolerance to flushing usually develops over the course of several weeks. Flushing may be accompanied by symptoms such as dizziness, rapid heart beat, palpitations, shortness of breath, sweating, chills, and/or oedema, which in rare cases may lead to fainting.
The following adverse reactions have been observed in clinical studies or in routine patient management, in patients receiving the recommended daily maintenance doses (1000, 1500, and 2000 mg) of Niaspan.
Flushing episodes are very common (>1/10 patients).
Commonly reported adverse reactions (>1/100 and <1/10 patients) are diarrhoea, nausea, vomiting, abdominal pain, dyspepsia, itching, rash.
Uncommon adverse reactions (>1/1000 and <1/100 patients) are dizziness, headache, rapid heart beat, palpitations, shortness of breath, sweating, pain, asthenia, chills, peripheral oedema, changes in laboratory tests (elevation of liver transaminases [AST, ALT], alkaline phosphatase, total bilirubin, LDH, amylase, fasting glucose, uric acid, reduction of platelet count, prolongation of prothrombin time, reduction in phosphorus).

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Rare adverse reactions (>1/10 000 and <1/1000 patients) are decreased glucose tolerance, insomnia, fainting, low blood pressure, drop in blood pressure when sitting up, rhinitis, muscle disorders, muscle pain and muscle weakness.
Very rare adverse reactions (<1/10 000 patients and isolated reports) include loss of appetite.
In addition, eye disorders (toxic amblyopia, cystoid macular oedema), heart disorders (artrial fibrillation, other arrhythmias), gastro-intestinal disorders (activation of peptic ulcers, peptic ulceration), urticaria, dry skin, hyperpigmentation, acanthosis nigricans, jaundice, migraine, and gout have been reported during treatment with other nicotinic acid products.
Please consult your doctor if you notice any unwanted or unexpected effect. To prevent serious reactions, speak to your doctor immediately, if an effect is severe, occurs suddenly, or gets worse rapidly.

INTERACTIONS

Concomitant alcohol or hot drinks may increase undesirable flushing and pruritus and should be avoided around the time of Niaspan ingestion.
Bile acid sequestrants (resins) bind to other orally administered medicinal products and should be taken separately, see also the product information of the resin.
Nicotinic acid may reduce platelet count and increase prothrombin time. When Niaspan is administered concomitantly with anti-coagulants, platelet count and prothrombin time must be monitored closely.
Nicotinic acid may also potentiate the blood-pressure-lowering effect of ganglionic blocking agents e.g., transdermal nicotine or vasoactive drugs such as nitrates, calcium channel blockers, or adrenergic blocking agents.
Nicotinic acid may cause false results in laboratory tests for catecholamines or urine glucose.
For combined use of Niaspan and statins, see 'Special warnings and precautions'.

DOSAGE AND ADMINISTRATION

Initial treatment
Niaspan must be used as directed by a doctor. Treatment must begin with a low dose that is gradually increased. This applies also when therapy with Niaspan has been discontinued for a longer time period or when the patient has previously been treated with other nicotinic acid products.
Niaspan doses must not be replaced with other nicotinic acid preparations.
The following dose escalation schedule is recommended over the course of seven weeks:

- One tablet Niaspan 500 mg daily at bedtime in week 1
- One tablet Niaspan 750 mg daily at bedtime in week 2
- Two tablets Niaspan 500 mg daily at bedtime in weeks 3, 4, 5, 6, and 7.

Please note that Niaspan tablet strengths are not interchangeable, e.g., do not replace 2 x 500 mg dose by 1 x 1000 mg.

Maintenance treatment
After week 7, the doctor will decide on the appropriate individual dose and the further duration of treatment. The recommended maintenance dose is 1000 mg (two 500 mg tablets) to 2000 mg (two 1000 mg tablets) once daily at bedtime depending on the patient's response and tolerance. If response to 1000 mg is inadequate, the dose may be increased to 1500 mg daily (two 750 mg tablets), and subsequently to 2000 mg daily. The daily dose should not be increased by more than 500 mg in any four week period. The maximum daily dose is 2000 mg.

SPECIAL POPULATIONS

Women may respond at lower doses than men.
In elderly patients, no dose adjustment is necessary.
Use in children and adolescents is not recommended.
No studies have been performed in patients with impaired renal function, Niaspan must be used with caution in patients with renal disease.
No studies have been performed in patients with impaired hepatic function. Niaspan must be used with caution in patients with a history of liver disease and who consume substantial quantities of alcohol, see 'Special warnings and precautions'. Niaspan is contraindicated in patients with significant hepatic dysfunction, see 'Contraindications'.
No studies have been performed in patients with kidney or liver dysfunction. Niaspan must be used with caution in patients with kidney or liver dysfunction Niaspan is contraindicated in patients with significant liver dysfunction, see 'Contraindications'.

ADMINISTRATION

Niaspan is taken at bedtime after a light meal. Niaspan tablets must be swallowed whole. The tablets must not be broken, crushed or chewed before swallowing.
Alcohol or hot drinks may increase undesirable flushing and itching when taken together with Niaspan.

OVERDOSE

The signs and symptoms of an acute overdose are expected to be those mentioned in section 'Adverse effects' and may require treatment by a doctor. Insufficient information is available on the dialysis potential of nicotinic acid.

Storage and Stability

Do not store above 25°C.

Blister: Store in the original package to protect from moisture.

Do not use after the expiry date.

Keep medicines out of the reach of children.

PRESENTATIONS

28 prolonged-release tablets in blisters

Date of Information
January 2004

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