Nicotinic Acid

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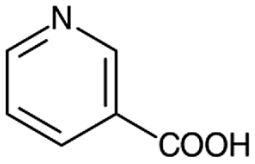
PRODUCT INFORMATION

NAME OF THE MEDICINE

Active ingredient: Nicotinic acid BP 250 mg.

Structural formula:



Molecular weight: 123.1

CAS Registry no.: 59-67-6

DESCRIPTION

Inactive ingredients: lactose, starch-wheat, povidone, talc and magnesium stearate.

PHARMACOLOGY

Pharmacodynamics

Nicotinic acid is a water-soluble B complex vitamin which is able to reduce serum lipids. It lowers serum cholesterol and triglyceride concentrations by inhibiting the synthesis of very low density lipoproteins (VLDL) which are the precursors to the formation of low-density lipoproteins, the principal carrier of blood cholesterol. Several possible modes of action have been proposed, including inhibition of hepatic synthesis of lipoproteins containing apolipoprotein B-100, promotion of lipoprotein lipase activity, and reduction of free fatty acid mobilisation from adipose tissue with an increase in faecal output of sterols. Oral therapy produces reduced triglyceride concentrations within several hours and reduced cholesterol concentrations within several days.

Nicotinic acid also has a vasodilation effect when administered in large doses, identified by flushing of the skin while plasma nicotinic acid levels are rising. This process is believed to be mediated by prostacyclin. Vasodilation occurs within 20 minutes of an oral dose and persists for about 20-60 minutes.

Nicotinic acid has been reported to stimulate histamine release resulting in increased gastric motility and acid production which may activate peptic ulcer. Reports have also indicated that large doses of nicotinic acid may decrease uric acid excretion and impair glucose tolerance. These effects may result in precipitation of an episode of gout in susceptible patients and may necessitate adjustment of diet and anti-hyperglycaemic

therapy in diabetic patients.

The normal physiological role of nicotinic acid is as a component of the coenzymes NAD and NADP which are essential for oxidation-reduction reactions in tissue respiration. Nicotinamide, a metabolite of nicotinic acid, possesses similar function as a vitamin but has no pharmacological value in reducing lipids.

Pharmacokinetics

Nicotinic acid is readily absorbed from the gastrointestinal tract following oral administration and is widely distributed in the body tissues. It is metabolised in the liver to nicotinamide when taken in physiological doses but when therapeutic doses are taken only a portion is converted to nicotinamide with the remainder eventually being excreted unchanged in the urine. Nicotinamide is widely distributed in the body and is further metabolised in the liver to N-methylnicotinamide and the 2-pyridone and 4-pyridone derivatives with some nicotinuric acid also being formed before being excreted in the urine. The elimination half-life is approximately 45 minutes, and time to peak serum concentration after oral administration is also 45 minutes.

INDICATIONS

1. The treatment of hyperlipidaemia, hypertriglyceridaemia and Frederickson-Lees Levy hyperlipoproteinaemia type II, IIB, III, IV and V (as adjunctive therapy in addition to diet and other measures); and
2. Pellagra (note: pellagra in Australia is limited to special situations not typical of the general lifestyle. A variety of other non-nutritional factors may also lead to the development of the disease).

CONTRAINDICATIONS

Nicotinic acid may exacerbate hepatic dysfunction and large doses may exacerbate peptic ulcer, overt diabetes mellitus, gout or hyperuricaemia.

Large doses of Nicotinic acid should not be used by persons with heart or gallbladder disease, arterial bleeding or glaucoma.

Contraindicated in cases of recent myocardial infarction.

Nicotinic acid is contraindicated in patients with severe idiosyncratic reactions to it or those who exhibit a sudden fall in peripheral vascular resistance.

WARNINGS

Antihypertensive Drugs. Patients taking antihypertensive drugs should consult a physician before taking Nicotinic acid.

Myocardial Infarction. Nicotinic acid therapy should be withdrawn if the patient has a myocardial infarction.

PRECAUTIONS

Antihypertensive Drugs. Antihypertensive drugs may have an additive vasodilating effect and produce postural hypotension.

Liver Function. Frequent monitoring of liver function should be performed during therapy to ascertain that the drug has no adverse effects.

Glucose Tolerance. As decreased glucose tolerance may occur, glucose tolerance tests should be performed regularly. Adjustment of diet and/or hypoglycaemic therapy may be necessary.

Serum Uric Acid Levels. Frequent monitoring of serum uric acid levels is advised as elevated uric acid levels may occur during long-term therapy.

Gastrointestinal Irritation or Peptic Ulcer History. Nicotinic acid causes release of histamine from the mast cells to stimulate gastric secretion of hydrochloric acid. Therefore, patients prone to gastrointestinal irritation or with a history of peptic ulcer should be closely supervised.

Use in Pregnancy (Category B2)

Contraindicated.

Use in Lactation

Contraindicated.

Interactions with Other Medicines

Adrenergic blocking agents. Due to an additive vasodilating effect, postural hypotension may occur when nicotinic acid is added to the regimen of patients taking adrenergic blocking agents.

Anti-hyperglycaemic therapy. Because nicotinic acid can cause hyperglycaemic, dosage adjustment of insulin or oral anti-hyperglycaemic therapy may be required in diabetic patients.

Aspirin. Concurrent use of aspirin and nicotinic acid may result in a reduction of the warmth and flushing associated with nicotinic acid use. Also, concurrent use of aspirin may result in an increased and prolonged nicotinic acid concentration, and so the potential for nicotinic acid toxicity may exist.

Clonidine. Concomitant nicotinic acid and clonidine has been reported to result in reduction in flushing of skin secondary to nicotinic acid.

Colestipol. Nicotinic acid absorption may be affected by administration with colestipol. Combined use of these two drugs resulted in lower plasma cholesterol concentrations than were achieved with colestipol alone.

Glipizide. Concomitant administration of glipizide and nicotinic acid may result in loss of blood glucose control since nicotinic acid can cause hyperglycaemia.

Isoniazid. Concomitant administration of isoniazid and nicotinic acid may cause nicotinic acid requirements to be increased, but pellagra is rare, only occurring in patients with an underlying nicotinic acid deficiency.

Lovastatin/Pravastatin/Simvastatin. The concurrent use of lovastatin, pravastatin or simvastatin and

nicotinic acid may be associated with myopathy and an increased risk of rhabdomyolysis, and acute renal failure. Symptoms of myopathy and rhabdomyolysis should be monitored.

Nicotine. If nicotinic acid and transdermal nicotine are used concurrently, flushing and dizziness after each nicotinic acid dose may occur.

Alcohol. In one case report concomitant alcohol and nicotinic acid therapy resulted in delirium (paranoid ideation and asterixis) and lactic acidosis.

Effects on Laboratory Tests

Nicotinic acid may cause false elevation in fluorometric determinations of urinary catecholamines and false positive tests for urinary glucose when Benedict's reagent is used. Nicotinic acid has also been reported to give false positive results for blood bilirubin tests.

ADVERSE REACTIONS

Cardiovascular. Acute flush, pounding in the head, sensation of heat, headache, hypotension. Atrial fibrillation and other arrhythmias in patients with CHD.

Dermatological. Pruritus, dryness with mild epidermal exfoliation, brown pigmentation, hyperkeratosis, urticaria, furunculosis, rash. All these adverse reactions are reversible on cessation of drug therapy.

Endocrine. Increased insulin requirements in diabetic patients, hypothyroidism.

Gastrointestinal. Nausea, vomiting, diarrhoea, heartburn, flatulence, activation of peptic ulcer.

Hepatic. Cholestatic jaundice, elevated liver function tests, ascites, hepatomegaly, patchy fibrosis, areas of necrosis, cholestasis and lymphocyte infiltration around the bile ducts.

Nervous system. Nervousness.

Others. Hyperuricemia, Toxic amblyopia.

DOSAGE AND ADMINISTRATION

In adults:

Pellagra: 250mg (one tablet) twice a day.

Hypercholesterolaemia, hypertriglyceridaemia: 250mg three times daily increased by 250mg increments every fourth day until a final daily dose of 3 to 4.5 g is reached.

Individual dosage is recommended because lipid reduction is dose related. Initially plasma cholesterol and triglyceride levels should be monitored.

Tablets should be taken orally after meals.

Following oral administration, nicotinic acid induced vasodilation occurs within 20 minutes and persists for about 20 to 60 minutes.

OVERDOSAGE

Symptoms: Cutaneous flush, pruritus, vomiting, diarrhoea, dyspepsia, syncope, severe abdominal cramps.

Treatment: Discontinue drug and institute general supportive measures.

PRESENTATION AND STORAGE CONDITIONS

Tablets (white, with a single score on one side), 250 mg; Available in bottles of 100's or 200's*.

* Not marketed in Australia.

Store below 30^{o}C.

POISON SCHEDULE OF THE MEDICINE

S3 – Pharmacist only medicine

NAME AND ADDRESS OF THE SPONSOR

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DATE OF APPROVAL

Grandfather product: no TGA approval date.

Date of most recent amendment: 24 August 2011.