

## APO-NICOTINIC ACID

Nicotinic Acid 25mg, 50mg, 100mg and 500mg Tablets

---

### Presentation

APO-NICOTINIC ACID 25mg tablets are white, round, 6.5mm in diameter, flat faced with beveled edges. Each tablet contains 25mg nicotinic acid and typically weighs 75mg.

APO-NICOTINIC ACID 50mg tablets are white, round, 7mm in diameter, flat faced with beveled edges. Engraved 'APO' and scored on one side and engraved 'NIC' over '50' on the other side. Each tablet contains 50mg nicotinic acid and typically weighs 130mg.

APO-NICOTINIC ACID 100mg tablets are white, round, biconvex tablets, 8.7mm in diameter. Each tablet contains 100mg nicotinic acid and typically weighs 260mg.

APO-NICOTINIC ACID 500mg tablets are white, round, biconvex tablets, 13mm in diameter. Engraved 'APO' over 'N500' on one side, other side plain. Each tablet contains 500mg nicotinic acid and typically weighs 623mg.

### Uses

#### Actions

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 with 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

Apo-Nicotinic Acid is indicated as a direct vitamin supplement, to treat conditions caused by nicotinic acid deficiency such as pellagra, and for the treatment of hyperlipidaemia. It is recommended for use only in patients with primary hyperlipidaemia (type IIa, IIb, III, IV or V hyperlipoproteinaemia).

### Dosage and Administration

**Hyperlipidaemia** - a common regimen in the treatment of hyperlipidaemia begins with an oral dose of 100mg three times daily, which is gradually increased to an average dose of 1g three times daily with a maximum dose of 6 to 9 grams.

**Nicotinic Acid Deficiency** - a dose of up to 500mg per day has been used in the treatment and prevention of pellagra, and a dose of 10mg - 20mg per day is suggested for the treatment of nicotinic acid deficiency.

### Contraindications

Previous allergic reaction to nicotinic acid, niacin or nicotinamide is a contraindication.

Risk/benefit considerations should be taken into account when the following medical problems exist:

**Arterial bleeding or haemorrhage, glaucoma** - these conditions may be exacerbated.

**Diabetes mellitus** - large doses of nicotinic acid may cause impaired glucose tolerance

**Gout** - large doses of nicotinic acid may cause hyperuricaemia.

**Hepatic disease** - large doses of nicotinic acid may cause hepatic damage.

**Hypotension** - may worsen due to vasodilating effects of nicotinic acid.

**Peptic Ulcer** - large doses may activate peptic ulcer.

### Warnings and Precautions

Patients with gallbladder disease or history of jaundice, liver disease or peptic ulcer should be monitored closely while taking nicotinic acid. Liver function tests should be conducted frequently in the initial stages of therapy and periodically thereafter.

Nicotinic acid may cause hyperglycaemia. Periodic blood glucose monitoring is advised especially in the early phase of therapy.

Elevated uric acid levels have occurred therefore nicotinic acid should be used with caution in patients predisposed to gout.

Patients prone to gastric irritation or with a history of peptic ulcer should be closely supervised.

### Use in Pregnancy

Category B2.

Problems in humans have not been documented with intake of normal daily requirements of nicotinic acid. However, studies have not been conducted in either animals or humans and use in pregnancy should be avoided.

### Use in Lactation

Nicotinic acid is distributed into breast milk. Problems have not been reported with intake at normal daily requirements but there is no information pertaining to higher doses used in the treatment of hyperlipidemia.

### Use in Children

Normal daily vitamin requirements vary according to age. Appropriate studies of nicotinic acid as an antihyperlipidaemic have not been performed in children. Use of nicotinic acid in children under 2 years of age is not recommended since cholesterol is required for normal development.

### Adverse Effects

The following adverse effects may occur:

**Haematological** - abnormalities in blood glucose levels.

**Cardiovascular** - atrial fibrillation, other arrhythmias, hypotension.

**Gastrointestinal** - stimulation of peptic ulcer, jaundice, nausea, vomiting, abdominal pain, diarrhoea. Taking nicotinic acid with meals may alleviate these gastrointestinal effects.

**Kidney/Genitourinary** - in patients with non-insulin dependent diabetes mellitus with dyslipidaemia, nicotinic acid treatment may induce a deterioration of glycaemic control and a consistent increase in plasma uric acid levels.

**Liver** - increases in aspartate aminotransferase and alkaline phosphatase which are dose related. Severe hepatotoxicity is rare.

**Skin** - severe generalised flushing and a sensation of warmth, particularly in the area of the face, neck and ears may occur soon after ingestion. The flushing resolves when plasma nicotinic acid levels are steady or falling. Administration of 325mg to 650mg of aspirin or indomethacin one hour prior to nicotinic acid is recommended to reduce flushing. Keratosis nigrican, pruritis, skin rash and dry skin with itching and tingling may also occur.

### Interactions

**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 hyperglycaemia 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.

**Chenodial/Ursodiol** - the effect of nicotinic acid as an antihyperlipidaemic may be decreased with concurrent use of chenodiol or ursodiol, which tend to increase cholesterol saturation of bile.

**Chlorpropamide** - Nicotinic acid may produce hyperglycaemia and lead to loss of glucose control in patients on oral hypoglycaemics.

**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 or 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 for.

**Nicotine** - if nicotinic acid and transdermal nicotine are used concurrently flushing and dizziness after each nicotinic acid dose may occur.

# APO-NICOTINIC ACID

Nicotinic Acid 25mg, 50mg, 100mg and 500mg Tablets

---

**Tolazamide** - nicotinic acid may antagonise the hypoglycaemic effects of tolazamide.

**Alcohol/Ethanol** - in one case report concomitant ethanol and nicotinic acid therapy resulted in delirium (paranoid ideation and asterixis) and lactic acidosis.

**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.

## Overdosage

### Symptoms:

Cutaneous flush, pruritis, vomiting, diarrhoea, dyspepsia, syncope, severe abdominal cramps.

Chronic administration of large doses of nicotinic acid have been associated with cystoid maculopathy and cholestatic and hepatocellular liver toxicity.

### Treatment:

Discontinue nicotinic acid and institute general supportive measures.

## Pharmaceutical Precautions

Store below 30°C. Protect from heat, light and moisture.

Keep container tightly closed.

## Medicine Classification

Prescription Only Medicine for 500mg tablets

General Sale Medicine for 25mg, 50mg, 100mg

## Package Quantities

APO-NICOTINIC ACID 25mg tablets: Bottles of 500 tablets.

APO-NICOTINIC ACID 50mg tablets: Bottles of 100 and 500 tablets

APO-NICOTINIC ACID 100mg tablets: Bottles of 100 and 500 tablets

APO-NICOTINIC ACID 500mg tablets: Bottles of 100 and 500 tablets

## Further Information

Tablets contains lactose

## Name and Address

Apotex NZ Ltd.  
32 Hillside Road  
Glenfield  
Private Bag 102995  
North Shore  
North Shore City 0745  
Tel: (09) 444-2073  
Fax: (09) 444-2951

## Date of Preparation

09 November 2010