



APO-NICOTINIC ACID

1. APO-NICOTINIC ACID (50mg & 500mg tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Name and strength of the active substance

Nicotinic acid 50 mg

Nicotinic acid 500 mg

Excipient with known effect

Lactose

Apo-Nicotinic acid contain Lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Apo-Nicotinic acid is gluten free.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

APO-NICOTINIC ACID 50mg tablets are white, round, 7mm in diameter, flat faced with beveled edged. Each tablet contains 50mg nicotinic acid and typically weighs 130mg.

APO-NICOTINIC ACID 500mg tablets are white, round, biconvex tablets, 12.5mm in diameter. Each tablet contains 500mg nicotinic acid and typically weighs 623mg.

4. CLINICAL PARTICULARS

4.1 Therapeutic 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).

4.2 Dose and method of administration

Dose

Hyperlipidaemia

For treatment regime begin 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. A dose of 10mg - 20mg per day is suggested for the treatment of nicotinic acid deficiency.

Use of nicotinic acid in children under 2 years of age is not recommended since cholesterol is required for normal development.

Method of administration

Maximum Tolerated Daily Dose

For treatment of Hyperlipidemia begin 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.

A dose of 10mg-20mg per day is suggested for the treatment of nicotinic acid deficiency.

Liver function tests should be conducted frequently in the initial stages of therapy and periodically thereafter.

Periodic blood glucose monitoring is advised especially in the early phase of therapy.

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

4.3 Contraindications

Previous allergic reaction to nicotinic acid, niacin or nicotinamide is a contraindication or to any of the excipients listed in section 6.1.

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 vasodilation effects of nicotinic acid.

Peptic ulcer- large doses may activate peptic ulcer.

4.4 Special warnings and precautions for use

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 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.

Contains Ethanol

This medicinal product contains small amounts of ethanol (alcohol), less than 100 mg per dose.

4.5 Interaction with other medicines and other forms of interaction

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.

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.

4.6 Fertility, pregnancy and lactation

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.

Breast-feeding

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.

4.7 Effects on ability to drive and use machines

Presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

4.8 Undesirable 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 glycemic 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 nigricans, pruritis, skin rash and dry skin with itching and tingling may also occur.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions

<https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: peripheral vasodilators

ATC code: C04AC Includes low strength preparations (e.g. nicotinic acid tablets 50 mg). C10AD Nicotinic acid preparations in high strength (e.g. nicotinic acid tablets 500 mg) is used as a cholesterol reducer.

Mechanism of Action

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.

5.2 Pharmacokinetic properties

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.

5.3 Preclinical safety data

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Apo –Nicotinic acid 50 mg tablet contains the following excipients:

- Povidone
- Lactose
- Ethanol
- Aerosil
- Magnesium Stearate

Apo-Nicotinic acid 500 mg tablets contains the following excipients:

- Povidone
- Ethanol
- Colloidal Silicon Dioxide
- Croscarmellose Sodium
- Lactose monohydrate
- Magnesium Stearate

Apo-Nicotinic acid 50 mg and 500 mg tablets contain Lactose and small amounts of ethanol. Apo-Nicotinic acid is gluten free.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

48 months from the date of manufacture.

6.4 Special Precautions

Store below 30°C

Protect from heat, light and moisture.

6.5 Nature and contents of container

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

APO-NICOTINIC ACID 500mg tablets: HDPE Bottles of 100 or 500 tablets

Not all pack sizes maybe marketed

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Only Medicine for 500mg tablets

General Sale Medicine for 50mg tablets

8. SPONSOR

Apotex NZ Ltd.
32 Hillside Road
Glenfield
AUCKLAND 0627

Telephone: (09) 444 2073

Fax: (09) 444 2951

E-mail: NZcustomerservice@apotex.com

9. DATE OF FIRST APPROVAL

31 December 1969

10. DATE OF REVISION OF THE TEXT

01 March 2017

Summary Table of Changes

Section changed	Summary of new information
Whole data sheet	Reformatted as per Medsafe new data sheet. Removal of references to 25mg and 100mg strengths as the approval has lapsed.
6.1	Additional information as per Medsafe requirements Apo-Nicotinic acid 50 mg and 500 mg tablets contain Lactose and small amounts of ethanol.