NIACIN - niacin tablet, extended release
Aurobindo Pharma Limited

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NIACIN EXTENDED-RELEASE TABLETS safely and effectively. See full prescribing information for NIACIN EXTENDED-RELEASE TABLETS.

NIACIN film-coated, extended-release tablets for oral use

Initial U.S. Approval: 1997

RECENT MAJOR CHANGES

Indications and Usage, Combination With a Statin – removal (1) 4/2015
Dosage and Administration, Combination With a Statin – removal (2) 4/2015

INDICATIONS AND USAGE

Niacin extended-release tablets contain extended-release niacin (nicotinic acid), and is indicated:

- To reduce elevated TC, LDL-C, Apo B and TG, and to increase HDL-C in patients with primary hyperlipidemia and mixed dyslipidemia. (1)
- To reduce the risk of recurrent nonfatal myocardial infarction in patients with a history of myocardial infarction and hyperlipidemia. (1)
- In combination with a bile acid binding resin:
  - Slows progression or promotes regression of atherosclerotic disease in patients with a history of coronary artery disease (CAD) and hyperlipidemia. (1)
  - As an adjunct to diet to reduce elevated TC and LDL-C in adult patients with primary hyperlipidemia. (1)
- To reduce TG in adult patients with severe hypertriglyceridemia. (1)

Limitations of use:
Addition of niacin extended-release tablets did not reduce cardiovascular morbidity or mortality among patients treated with simvastatin in a large, randomized controlled trial (5.1).

DOSAGE AND ADMINISTRATION

- Niacin extended-release tablets should be taken at bedtime with a low-fat snack. (2)
- Dose range: 500 mg to 2000 mg once daily. (2)
- Therapy with niacin extended-release tablets must be initiated at 500 mg at bedtime in order to reduce the incidence and severity of side effects which may occur during early therapy and should not be increased by more than 500 mg in any four week period. (2)
- Maintenance dose: 1000 mg to 2000 mg once daily. (2)
- Doses greater than 2000 mg daily are not recommended. (2)

DOSAGE FORMS AND STRENGTHS

Unscored film-coated tablets for oral administration: 500 mg, 750 mg and 1000 mg niacin extended-release. (3)

CONTRAINDICATIONS

- Active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels. (4, 5.3)
- Active peptic ulcer disease. (4)
- Arterial bleeding. (4)
- Known hypersensitivity to product components. (4, 6.1)

WARNINGS AND PRECAUTIONS

- Severe hepatic toxicity has occurred in patients substituting sustained-release niacin for immediate-release niacin at equivalent doses. (5.3)
- Myopathy has been reported in patients taking niacin extended-release tablets. The risk for myopathy and rhabdomyolysis are increased among elderly patients; patients with diabetes, renal failure, or uncontrolled hypothyroidism; and patients being treated with a statin. (5.2)
- Liver enzyme abnormalities and monitoring: Persistent elevations in hepatic transaminase can occur. Monitor liver enzymes before and during treatment. (5.3)
- Use with caution in patients with unstable angina or in the acute phase of an MI. (5)
- Niacin extended-release tablets can increase serum glucose levels. Glucose levels should be closely monitored in diabetic or potentially diabetic patients particularly during the first few months of use or dose adjustment. (5.4)

ADVERSE REACTIONS

Most common adverse reactions (incidence >5% and greater than placebo) are flushing, diarrhea, nausea, vomiting, increased cough, and pruritus. (6.1)
Flushing of the skin may be reduced in frequency or severity by pretreatment with aspirin (up to the recommended dose of 325 mg taken 30 minutes prior to niacin extended-release tablets dose). (2)

To report SUSPECTED ADVERSE REACTIONS, contact Aurobindo Pharma USA, Inc. at 1-800-850-2876 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Statins: Caution should be used when prescribing niacin with statins as these agents can increase risk of myopathy/rhabdomyolysis. (5.2, 7.1)
- Bile Acid Sequestrants: Bile acid sequestrants have a high niacin-binding capacity and should be taken at least 4 to 6 hours before niacin extended-release tablets administration. (7.2)

USE IN SPECIFIC POPULATIONS

- Renal impairment: Niacin extended-release tablets should be used with caution in patients with renal impairment. (5, 8.6)
- Hepatic impairment: Niacin extended-release tablets are contraindicated in active liver disease or significant or unexplained hepatic dysfunction or unexplained elevations of serum transaminases. (4,5, 5.3, 8.7)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 9/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Therapy with lipid-altering agents should be only one component of multiple risk factor intervention in individuals at significantly increased risk for atherosclerotic vascular disease due to hyperlipidemia. Niacin therapy is indicated as an adjunct to diet when the response to a diet restricted in saturated fat and cholesterol and other nonpharmacologic measures alone has been inadequate.

1. Niacin extended-release tablets are indicated to reduce elevated TC, LDL-C, Apo B and TG levels, and to increase HDL-C in patients with primary hyperlipidemia and mixed dyslipidemia.
2. In patients with a history of myocardial infarction and hyperlipidemia, niacin is indicated to reduce the risk of recurrent nonfatal myocardial infarction.
3. In patients with a history of coronary artery disease (CAD) and hyperlipidemia, niacin, in combination with a bile acid binding resin, is indicated to slow progression or promote regression of atherosclerotic disease.
4. Niacin extended-release tablets in combination with a bile acid binding resin is indicated to reduce elevated TC and LDL-C levels in adult patients with primary hyperlipidemia.
5. Niacin is also indicated as adjunctive therapy for treatment of adult patients with severe hypertriglyceridemia who present a risk of pancreatitis and who do not respond adequately to a determined dietary effort to control them.

Limitations of Use

Addition of niacin extended-release tablets did not reduce cardiovascular morbidity or mortality among patients treated with simvastatin in a large, randomized controlled trial (AIM-HIGH) *[see Warnings and Precautions (5.1)]*.

2 DOSAGE AND ADMINISTRATION

Niacin extended-release tablets should be taken at bedtime, after a low-fat snack, and doses should be individualized according to patient response. Therapy with niacin extended-release tablets must be initiated at 500 mg at bedtime in order to reduce the incidence and severity of side effects which may occur during early therapy. The recommended dose escalation is shown in Table 1 below.

Table 1. Recommended Dosing

	Week(s)	Daily dose	Niacin Extended-Release Tablets Dosage
INITIAL TITRATION SCHEDULE	1 to 4	500 mg	1 Niacin extended-release 500 mg tablet at bedtime
	5 to 8	1000 mg	1 Niacin extended-release 1000 mg tablet or 2 Niacin extended-release 500 mg tablets at bedtime
	*	1500 mg	2 Niacin extended-release 750 mg tablets or 3 Niacin extended-release 500 mg tablets at bedtime
	*	2000 mg	2 Niacin extended-release 1000 mg tablets or 4 Niacin extended-release 500 mg tablets at bedtime
* After Week 8, titrate to patient response and tolerance. If response to 1000 mg daily is inadequate, increase dose to 1500 mg daily; may subsequently increase dose to 2000 mg daily. Daily dose should not be increased more than 500 mg in a 4-week period, and doses above 2000 mg daily are not recommended. Women may respond at lower doses than men.			

Maintenance Dose

The daily dosage of niacin extended-release tablets should not be increased by more than 500 mg in any 4-week period. The recommended maintenance dose is 1000 mg (two 500 mg tablets or one 1000 mg tablet) to 2000 mg (two 1000 mg tablets or four 500 mg tablets) once daily at bedtime. Doses greater than 2000 mg daily are not recommended. Women may respond at lower niacin extended-release tablets doses than men *[see Clinical Studies (14.2)]*.

Single-dose bioavailability studies have demonstrated that two of the 500 mg and one of the 1000 mg tablet strengths are interchangeable but three of the 500 mg and two of the 750 mg tablet strengths are not interchangeable.

Flushing of the skin *[see Adverse Reactions (6.1)]* may be reduced in frequency or severity by pretreatment with aspirin (up to the recommended dose of 325 mg taken 30 minutes prior to niacin extended-release tablets dose). Tolerance to this flushing develops rapidly over the course of several weeks. Flushing, pruritus, and gastrointestinal distress are also greatly reduced by slowly increasing the dose of niacin and avoiding administration on an empty stomach. Concomitant alcoholic, hot drinks or spicy foods may increase the side effects of flushing and pruritus and should be avoided around the time of niacin extended-release tablets ingestion.

Equivalent doses of niacin extended-release tablets should not be substituted for sustained-release (modified-release, timed-release) niacin preparations or immediate-release (crystalline) niacin *[see Warnings and Precautions (5)]*. Patients previously receiving other niacin products should be started with the recommended niacin extended-release tablets titration schedule (see Table 1), and the dose should subsequently be individualized based on patient response.

If niacin extended-release tablets therapy is discontinued for an extended period, reinstitution of therapy should include a titration phase (see Table 1).

Niacin extended-release tablets should be taken whole and should not be broken, crushed or chewed

before swallowing.

Dosage in Patients with Renal or Hepatic Impairment

Use of niacin extended-release tablets in patients with renal or hepatic impairment has not been studied. Niacin extended-release tablets are contraindicated in patients with significant or unexplained hepatic dysfunction. Niacin extended-release tablets should be used with caution in patients with renal impairment *[see Warnings and Precautions (5)]*.

3 DOSAGE FORMS AND STRENGTHS

- 500 mg tablets are white to off-white, film-coated, capsule shaped biconvex tablets debossed with 'T' on one side and '65' on other side.
- 750 mg tablets are white to off-white, film-coated, capsule shaped biconvex tablets debossed with 'T' on one side and '66' on other side.
- 1000 mg tablets are white to off-white, film-coated, oval shaped biconvex tablets debossed with 'T' on one side and '67' on other side.

4 CONTRAINDICATIONS

Niacin extended-release tablets are contraindicated in the following conditions:

- Active liver disease or unexplained persistent elevations in hepatic transaminases *[see Warnings and Precautions (5.3)]*
- Patients with active peptic ulcer disease
- Patients with arterial bleeding
- Hypersensitivity to niacin or any component of this medication *[see Adverse Reactions (6.1)]*

5 WARNINGS AND PRECAUTIONS

Niacin extended-release tablet preparations should not be substituted for equivalent doses of immediate-release (crystalline) niacin. For patients switching from immediate-release niacin to niacin extended-release tablets, therapy with niacin extended-release tablets should be initiated with low doses (i.e., 500 mg at bedtime) and the niacin extended-release tablets dose should then be titrated to the desired therapeutic response *[see Dosage and Administration (2)]*.

Caution should also be used when niacin extended-release tablets are used in patients with unstable angina or in the acute phase of an MI, particularly when such patients are also receiving vasoactive drugs such as nitrates, calcium channel blockers, or adrenergic blocking agents.

Niacin is rapidly metabolized by the liver, and excreted through the kidneys. Niacin extended-release tablets are contraindicated in patients with significant or unexplained hepatic impairment *[see Contraindications (4) and Warnings and Precautions (5.3)]* and should be used with caution in patients with renal impairment. Patients with a past history of jaundice, hepatobiliary disease, or peptic ulcer should be observed closely during niacin extended-release tablets therapy.

5.1 Mortality and Coronary Heart Disease Morbidity

Niacin extended-release tablets have not been shown to reduce cardiovascular morbidity or mortality among patients already treated with a statin.

The Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH) trial was a randomized placebo-controlled trial of 3414 patients with stable, previously diagnosed cardiovascular disease. Mean baseline lipid levels were LDL-C 74 mg/dL, HDL-C 35 mg/dL, non-HDL-C 111 mg/dL and median triglyceride level of 163 to

177 mg/dL. Ninety-four percent of patients were on background statin therapy prior to entering the trial. All participants received simvastatin, 40 to 80 mg per day, plus ezetimibe 10 mg per day if needed, to maintain an LDL-C level of 40 to 80 mg/dL, and were randomized to receive niacin extended-release tablets 1500 to 2000 mg/day (n=1718) or matching placebo (IR Niacin, 100 to 150 mg, n=1696). On-treatment lipid changes at two years for LDL-C were -12.0% for the simvastatin plus niacin extended-release tablets group and -5.5% for the simvastatin plus placebo group. HDL-C increased by 25.0% to 42 mg/dL in the simvastatin plus niacin extended-release tablets group and by 9.8% to 38 mg/dL in the simvastatin plus placebo group (P<0.001). Triglyceride levels decreased by 28.6% in the simvastatin plus niacin extended-release tablets group and by 8.1% in the simvastatin plus placebo group. The primary outcome was an ITT composite of the first study occurrence of coronary heart disease death, nonfatal myocardial infarction, ischemic stroke, hospitalization for acute coronary syndrome or symptom-driven coronary or cerebral revascularization procedures. The trial was stopped after a mean follow-up period of 3 years owing to a lack of efficacy. The primary outcome occurred in 282 patients in the simvastatin plus niacin extended-release tablets group (16.4%) and in 274 patients in the simvastatin plus placebo group (16.2%) (HR 1.02 [95% CI, 0.87 to 1.21], P=0.79. In an ITT analysis, there were 42 cases of first occurrence of ischemic stroke reported, 27 (1.6%) in the simvastatin plus niacin extended-release tablets group and 15 (0.9%) in the simvastatin plus placebo group, a non-statistically significant result (HR 1.79, [95%CI = 0.95 to 3.36], p=0.071). The on-treatment ischemic stroke events were 19 for the simvastatin plus niacin extended-release tablets group and 15 for the simvastatin plus placebo group *[see Adverse Reactions (6.1)]*.

5.2 Skeletal Muscle

Cases of rhabdomyolysis have been associated with concomitant administration of lipid-altering doses (≥1 g/day) of niacin and statins. Elderly patients and patients with diabetes, renal failure, or uncontrolled hypothyroidism are particularly at risk. Monitor patients for any signs and symptoms of muscle pain, tenderness, or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration. Periodic serum creatine phosphokinase (CPK) and potassium determinations should be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy.

5.3 Liver Dysfunction

Cases of severe hepatic toxicity, including fulminant hepatic necrosis, have occurred in patients who have substituted sustained-release (modified-release, timed-release) niacin products for immediate-release (crystalline) niacin at equivalent doses.

Niacin extended-release tablets should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease. Active liver diseases or unexplained transaminase elevations are contraindications to the use of niacin extended-release tablets.

Niacin preparations have been associated with abnormal liver tests. In three placebo-controlled clinical trials involving titration to final daily niacin extended-release tablets doses ranging from 500 to 3000 mg, 245 patients received niacin extended-release tablets for a mean duration of 17 weeks. No patient with normal serum transaminase levels (AST, ALT) at baseline experienced elevations to more than 3 times the upper limit of normal (ULN) during treatment with niacin extended-release tablets. In these studies, fewer than 1% (2/245) of niacin extended-release tablets patients discontinued due to transaminase elevations greater than 2 times the ULN.

Liver-related tests should be performed on all patients during therapy with niacin extended-release tablets. Serum transaminase levels, including AST and ALT (SGOT and SGPT), should be monitored before treatment begins, every 6 to 12 weeks for the first year, and periodically thereafter (e.g., at approximately 6-month intervals). Special attention should be paid to patients who develop elevated

serum transaminase levels, and in these patients, measurements should be repeated promptly and then performed more frequently. If the transaminase levels show evidence of progression, particularly if they rise to 3 times ULN and are persistent, or if they are associated with symptoms of nausea, fever, and/or malaise, the drug should be discontinued.

5.4 Laboratory Abnormalities

Increase in Blood Glucose: Niacin treatment can increase fasting blood glucose. Frequent monitoring of blood glucose should be performed to ascertain that the drug is producing no adverse effects. Diabetic patients may experience a dose-related increase in glucose intolerance. Diabetic or potentially diabetic patients should be observed closely during treatment with niacin extended-release tablets, particularly during the first few months of use or dose adjustment; adjustment of diet and/or hypoglycemic therapy may be necessary.

Reduction in platelet count: Niacin extended-release tablets have been associated with small but statistically significant dose-related reductions in platelet count (mean of -11% with 2000 mg). Caution should be observed when Niacin extended-release tablets are administered concomitantly with anticoagulants; platelet counts should be monitored closely in such patients.

Increase in Prothrombin Time (PT): Niacin extended-release tablets have been associated with small but statistically significant increases in prothrombin time (mean of approximately +4%); accordingly, patients undergoing surgery should be carefully evaluated. Caution should be observed when niacin extended-release tablets are administered concomitantly with anticoagulants; prothrombin time should be monitored closely in such patients.

Increase in Uric Acid: Elevated uric acid levels have occurred with niacin therapy, therefore use with caution in patients predisposed to gout.

Decrease in Phosphorus: In placebo-controlled trials, niacin extended-release tablets has been associated with small but statistically significant, dose-related reductions in phosphorus levels (mean of -13% with 2000 mg). Although these reductions were transient, phosphorus levels should be monitored periodically in patients at risk for hypophosphatemia.

6 ADVERSE REACTIONS

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

6.1 Clinical Studies Experience

In the placebo-controlled clinical trials database of 402 patients (age range 21 to 75 years, 33% women, 89% Caucasians, 7% Blacks, 3% Hispanics, 1% Asians) with a median treatment duration of 16 weeks, 16% of patients on niacin extended-release tablets and 4% of patients on placebo discontinued due to adverse reactions. The most common adverse reactions in the group of patients treated with niacin extended-release tablets that led to treatment discontinuation and occurred at a rate greater than placebo were flushing (6% vs. 0%), rash (2% vs. 0%), diarrhea (2% vs. 0%), nausea (1% vs. 0%), and vomiting (1% vs. 0%). The most commonly reported adverse reactions (incidence >5% and greater than placebo) in the niacin extended-release tablets controlled clinical trial database of 402 patients were flushing, diarrhea, nausea, vomiting, increased cough and pruritus.

In the placebo-controlled clinical trials, flushing episodes (i.e., warmth, redness, itching and/or tingling) were the most common treatment-emergent adverse reactions (reported by as many as 88% of patients) for niacin extended-release tablets. Spontaneous reports suggest that flushing may also be accompanied

by symptoms of dizziness, tachycardia, palpitations, shortness of breath, sweating, burning sensation/skin burning sensation, chills, and/or edema, which in rare cases may lead to syncope. In pivotal studies, 6% (14/245) of niacin extended-release tablets patients discontinued due to flushing. In comparisons of immediate-release (IR) niacin and niacin extended-release tablets, although the proportion of patients who flushed was similar, fewer flushing episodes were reported by patients who received niacin extended-release tablets. Following 4 weeks of maintenance therapy at daily doses of 1500 mg, the incidence of flushing over the 4-week period averaged 8.6 events per patient for IR niacin versus 1.9 following niacin extended-release tablets.

Other adverse reactions occurring in ≥5% of patients treated with niacin extended-release tablets and at an incidence greater than placebo are shown in Table 2 below.

Table 2. Treatment-Emergent Adverse Reactions by Dose Level in ≥ 5% of Patients and at an Incidence Greater than Placebo; Regardless of Causality Assessment in Placebo-Controlled Clinical Trials

Placebo-Controlled Studies Niacin Extended-Release Tablets Treatment[@]					
	Recommended Daily Maintenance Doses[†]				
	Placebo (n = 157) %	500 mg[‡] (n = 87) %	1000 mg (n = 110) %	1500 mg (n = 136) %	2000 mg (n = 95) %
Gastrointestinal Disorders					
Diarrhea	13	7	10	10	14
Nausea	7	5	6	4	11
Vomiting	4	0	2	4	9
Respiratory					
Cough, Increased	6	3	2	< 2	8
Skin and Subcutaneous Tissue Disorders					
Pruritus	2	8	0	3	0
Rash	0	5	5	5	0
Vascular Disorders					
Flushing[&]	19	68	69	63	55

Note: Percentages are calculated from the total number of patients in each column.
[†] Adverse reactions are reported at the initial dose where they occur.
[@] Pooled results from placebo-controlled studies; for niacin extended-release tablets, n = 245 and median treatment duration = 16 weeks.
Number of niacin extended-release tablet patients (n) are not additive across doses.
[‡] The 500 mg/day dose is outside the recommended daily maintenance dosing range *[see Dosage and Administration (2)]*.
[&] 10 patients discontinued before receiving 500 mg, therefore they were not included.

In general, the incidence of adverse events was higher in women compared to men.

Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH)

In AIM-HIGH involving 3414 patients (mean age of 64 years, 15% women, 92% Caucasians, 34% with diabetes mellitus) with stable, previously diagnosed cardiovascular disease, all patients received simvastatin, 40 to 80 mg per day, plus ezetimibe 10 mg per day if needed, to maintain an LDL-C level of 40 to 80 mg/dL, and were randomized to receive niacin extended-release tablets 1500 to 2000 mg/day (n=1718) or matching placebo (IR Niacin, 100 to 150 mg, n=1696). The incidence of the adverse reactions of "blood glucose increased" (6.4% vs. 4.5%) and "diabetes mellitus" (3.6% vs. 2.2%) was significantly higher in the simvastatin plus niacin extended-release tablets group as compared to the simvastatin plus placebo group. There were 5 cases of rhabdomyolysis reported, 4 (0.2%) in the simvastatin plus niacin extended-release tablets group and one (<0.1%) in the simvastatin plus placebo group *[see Warnings and Precautions (5.1)]*.

6.2 Postmarketing Experience

Because the below reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following additional adverse reactions have been identified during post-approval use of niacin extended-release tablets:

Hypersensitivity reactions, including anaphylaxis, angioedema, urticaria, flushing, dyspnea, tongue edema, larynx edema, face edema, peripheral edema, laryngismus, and vesiculobullous rash; maculopapular rash; dry skin; tachycardia; palpitations; atrial fibrillation; other cardiac arrhythmias; syncope; hypotension; postural hypotension; blurred vision; macular edema; peptic ulcers; eructation; flatulence; hepatitis; jaundice; decreased glucose tolerance; gout; myalgia; myopathy; dizziness; insomnia; asthenia; nervousness; paresthesia; dyspnea; sweating; burning sensation/skin burning sensation; skin discoloration, and migraine.

Clinical Laboratory Abnormalities

Chemistry: Elevations in serum transaminases *[see Warnings and Precautions (5.3)]*, LDH, fasting glucose, uric acid, total bilirubin, amylase and creatine kinase, and reduction in phosphorus.

Hematology: Slight reductions in platelet counts and prolongation in prothrombin time *[see Warnings and Precautions (5.4)]*.

7 DRUG INTERACTIONS

7.1 Statins

Caution should be used when prescribing niacin (≥1 gm/day) with statins as these drugs can increase risk of myopathy/rhabdomyolysis *[see Warnings and Precautions (5) and Clinical Pharmacology (12.3)]*.

7.2 Bile Acid Sequestrants

An *in vitro* study results suggest that the bile acid-binding resins have high niacin binding capacity. Therefore, 4 to 6 hours, or as great an interval as possible, should elapse between the ingestion of bile acid-binding resins and the administration of niacin extended-release tablets *[see Clinical Pharmacology (12.3)]*.

7.3 Aspirin

Concomitant aspirin may decrease the metabolic clearance of nicotinic acid. The clinical relevance of this finding is unclear.

7.4 Antihypertensive Therapy

Niacin may potentiate the effects of ganglionic blocking agents and vasoactive drugs resulting in postural hypotension.

7.5 Other

Vitamins or other nutritional supplements containing large doses of niacin or related compounds such as nicotinamide may potentiate the adverse effects of niacin extended-release tablets.

7.6 Laboratory Test Interactions

Niacin may produce false elevations in some fluorometric determinations of plasma or urinary catecholamines. Niacin may also give false-positive reactions with cupric sulfate solution (Benedict's reagent) in urine glucose tests.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C.

Animal reproduction studies have not been conducted with niacin or with niacin extended-release tablets. It is also not known whether niacin at doses typically used for lipid disorders can cause fetal harm when administered to pregnant women or whether it can affect reproductive capacity. If a woman receiving niacin for primary hyperlipidemia becomes pregnant, the drug should be discontinued. If a woman being treated with niacin for hypertriglyceridemia conceives, the benefits and risks of continued therapy should be assessed on an individual basis.

8.3 Nursing Mothers

Niacin is excreted into human milk but the actual infant dose or infant dose as a percent of the maternal dose is not known. Because of the potential for serious adverse reactions in nursing infants from lipid-altering doses of nicotinic acid, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. No studies have been conducted with niacin extended-release tablets in nursing mothers.

8.4 Pediatric Use

Safety and effectiveness of niacin therapy in pediatric patients (≤16 years) have not been established.

8.5 Geriatric Use

Of 979 patients in clinical studies of niacin extended-release tablets, 21% of the patients were age 65 and over. No overall differences in safety and effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

No studies have been performed in this population. Niacin extended-release tablets should be used with caution in patients with renal impairment *[see Warnings and Precautions (5)]*.

8.7 Hepatic Impairment

No studies have been performed in this population. Niacin extended-release tablets should be used with caution in patients with a past history of liver disease and/or who consume substantial quantities of alcohol. Active liver disease, unexplained transaminase elevations and significant or unexplained

hepatic dysfunction are contraindications to the use of niacin extended-release tablets *[see Contraindications (4) and Warnings and Precautions (5.3)]*.

8.8 Gender

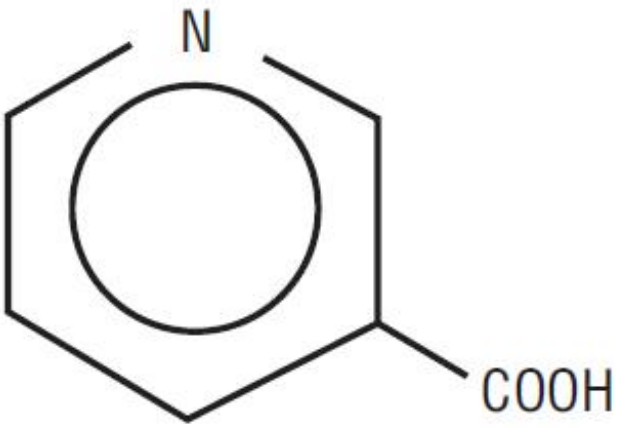
Data from the clinical trials suggest that women have a greater hypolipidemic response than men at equivalent doses of niacin extended-release tablets.

10 OVERDOSAGE

Supportive measures should be undertaken in the event of an overdose.

11 DESCRIPTION

Niacin extended-release tablets USP, contain niacin, USP, which at therapeutic doses is an antihyperlipidemic agent. Niacin USP (nicotinic acid, or 3-pyridinecarboxylic acid) is white crystals or crystalline powder, sparingly soluble in water, soluble in boiling alcohol, freely soluble in boiling water and in solutions of alkali hydroxides and carbonates. Very slightly soluble in ether, with the following structural formula:



$C_6H_5NO_2$ M.W. = 123.11

Niacin extended-release tablets USP are white to off-white, film-coated tablets for oral administration and are available in three tablet strengths containing 500 mg, 750 mg, and 1000 mg niacin, USP. Niacin extended-release tablets USP also contain the inactive ingredients: colloidal silicon dioxide, hydrogenated castor oil, hypromellose, lactose monohydrate, magnesium stearate, polyethylene glycol, titanium dioxide.

USP dissolution test is pending.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism by which niacin alters lipid profiles has not been well defined. It may involve several actions including partial inhibition of release of free fatty acids from adipose tissue, and increased lipoprotein lipase activity, which may increase the rate of chylomicron triglyceride removal from plasma. Niacin decreases the rate of hepatic synthesis of VLDL and LDL, and does not appear to affect fecal excretion of fats, sterols, or bile acids.

12.3 Pharmacokinetics

Absorption

Due to extensive and saturable first-pass metabolism, niacin concentrations in the general circulation are dose dependent and highly variable. Time to reach the maximum niacin plasma concentrations was about 5 hours following niacin extended-release tablets. To reduce the risk of gastrointestinal (GI) upset, administration of niacin extended-release tablets with a low-fat meal or snack is recommended.

Single-dose bioavailability studies have demonstrated that the 500 mg and 1000 mg tablet strengths are dosage form equivalent but the 500 mg and 750 mg tablet strengths are not dosage form equivalent.

Metabolism

The pharmacokinetic profile of niacin is complicated due to extensive first-pass metabolism that is dose-rate specific and, at the doses used to treat dyslipidemia, saturable. In humans, one pathway is through a simple conjugation step with glycine to form nicotinuric acid (NUA). NUA is then excreted in the urine, although there may be a small amount of reversible metabolism back to niacin. The other pathway results in the formation of nicotinamide adenine dinucleotide (NAD). It is unclear whether nicotinamide is formed as a precursor to, or following the synthesis of, NAD. Nicotinamide is further metabolized to at least N-methylnicotinamide (MNA) and nicotinamide-N-oxide (NNO). MNA is further metabolized to two other compounds, N-methyl-2-pyridone-5-carboxamide (2PY) and N-methyl-4-pyridone- 5-carboxamide (4PY). The formation of 2PY appears to predominate over 4PY in humans. At the doses used to treat hyperlipidemia, these metabolic pathways are saturable, which explains the nonlinear relationship between niacin dose and plasma concentrations following multiple-dose niacin extended-release tablets administration.

Nicotinamide does not have hypolipidemic activity; the activity of the other metabolites is unknown.

Elimination

Following single and multiple doses, approximately 60 to 76% of the niacin dose administered as niacin extended-release tablets was recovered in urine as niacin and metabolites; up to 12% was recovered as unchanged niacin after multiple dosing. The ratio of metabolites recovered in the urine was dependent on the dose administered.

Pediatric Use

No pharmacokinetic studies have been performed in this population (≤16 years) *[see Use in Specific Populations (8.4)]*.

Geriatric Use

No pharmacokinetic studies have been performed in this population (> 65 years) *[see Use in Specific Populations (8.5)]*.

Renal Impairment

No pharmacokinetic studies have been performed in this population. Niacin extended-release tablets should be used with caution in patients with renal disease *[see Warnings and Precautions (5)]*.

Hepatic Impairment

No pharmacokinetic studies have been performed in this population. Active liver disease, unexplained transaminase elevations and significant or unexplained hepatic dysfunction are contraindications to the use of niacin extended-release tablets *[see Contraindications (4) and Warnings and Precautions (5.3)]*.

Gender

Steady-state plasma concentrations of niacin and metabolites after administration of niacin extended-release tablets are generally higher in women than in men, with the magnitude of the difference varying with dose and metabolite. This gender differences observed in plasma levels of niacin and its metabolites may be due to gender-specific differences in metabolic rate or volume of distribution. Recovery of niacin and metabolites in urine, however, is generally similar for men and women, indicating that absorption is similar for both genders *[see Gender (8.8)]*.

Drug interactions

Fluvastatin

Niacin did not affect fluvastatin pharmacokinetics *[see Drug Interactions (7.1)]*.

Lovastatin

When niacin extended-release tablets 2000 mg and lovastatin 40 mg were co-administered, niacin extended-release tablets increased lovastatin C_{max} and AUC by 2% and 14%, respectively, and decreased lovastatin acid C_{max} and AUC by 22% and 2%, respectively. Lovastatin reduced niacin extended-release tablets bioavailability by 2 to 3% *[see Drug Interactions (7.1)]*.

Simvastatin

When niacin extended-release tablets 2000 mg and simvastatin 40 mg were co-administered, niacin extended-release tablets increased simvastatin C_{max} and AUC by 1% and 9%, respectively, and simvastatin acid C_{max} and AUC by 2% and 18%, respectively. Simvastatin reduced niacin extended-release tablets bioavailability by 2% *[see Drug Interactions (7.1)]*.

Bile Acid Sequestrants

An *in vitro* study was carried out investigating the niacin-binding capacity of colestipol and cholestyramine. About 98% of available niacin was bound to colestipol, with 10 to 30% binding to cholestyramine *[see Drug Interactions (7.2)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Niacin administered to mice for a lifetime as a 1% solution in drinking water was not carcinogenic. The mice in this study received approximately 6 to 8 times a human dose of 3000 mg/day as determined on a mg/m^2 basis. Niacin was negative for mutagenicity in the Ames test. No studies on impairment of fertility have been performed. No studies have been conducted with niacin extended-release tablets regarding carcinogenesis, mutagenesis, or impairment of fertility.

14 CLINICAL STUDIES

14.1 Niacin Clinical Studies

Niacin's ability to reduce mortality and the risk of definite, nonfatal myocardial infarction (MI) has been assessed in long-term studies. The Coronary Drug Project, completed in 1975, was designed to assess the safety and efficacy of niacin and other lipid-altering drugs in men 30 to 64 years old with a history

of MI. Over an observation period of 5 years, niacin treatment was associated with a statistically significant reduction in nonfatal, recurrent MI. The incidence of definite, nonfatal MI was 8.9% for the 1,119 patients randomized to nicotinic acid versus 12.2% for the 2,789 patients who received placebo ($p<0.004$). Total mortality was similar in the two groups at 5 years (24.4% with nicotinic acid versus 25.4% with placebo; p=N.S.). At the time of a 15-year follow-up, there were 11% (69) fewer deaths in the niacin group compared to the placebo cohort (52.0% versus 58.2%; $p=0.0004$). However, mortality at 15 years was not an original endpoint of the Coronary Drug Project. In addition, patients had not received niacin for approximately 9 years, and confounding variables such as concomitant medication use and medical or surgical treatments were not controlled.

The Cholesterol-Lowering Atherosclerosis Study (CLAS) was a randomized, placebo-controlled, angiographic trial testing combined colestipol and niacin therapy in 162 non-smoking males with previous coronary bypass surgery. The primary, per-subject cardiac endpoint was global coronary artery change score. After 2 years, 61% of patients in the placebo cohort showed disease progression by global change score (n=82), compared with only 38.8% of drug-treated subjects (n=80), when both native arteries and grafts were considered ($p<0.005$); disease regression also occurred more frequently in the drug-treated group (16.2% versus 2.4%; $p=0.002$). In a follow-up to this trial in a subgroup of 103 patients treated for 4 years, again, significantly fewer patients in the drug-treated group demonstrated progression than in the placebo cohort (48% versus 85%, respectively; $p<0.0001$).

The Familial Atherosclerosis Treatment Study (FATS) in 146 men ages 62 and younger with Apo B levels ≥125 mg/dL, established coronary artery disease, and family histories of vascular disease, assessed change in severity of disease in the proximal coronary arteries by quantitative arteriography. Patients were given dietary counseling and randomized to treatment with either conventional therapy with double placebo (or placebo plus colestipol if the LDL-C was elevated); lovastatin plus colestipol; or niacin plus colestipol. In the conventional therapy group, 46% of patients had disease progression (and no regression) in at least one of nine proximal coronary segments; regression was the only change in 11%. In contrast, progression (as the only change) was seen in only 25% in the niacin plus colestipol group, while regression was observed in 39%. Though not an original endpoint of the trial, clinical events (death, MI, or revascularization for worsening angina) occurred in 10 of 52 patients who received conventional therapy, compared with 2 of 48 who received niacin plus colestipol.

14.2 Niacin Extended-Release Tablets Clinical Studies

Placebo-Controlled Clinical Studies in Patients with Primary Hyperlipidemia and Mixed Dyslipidemia: In two randomized, double-blind, parallel, multi-center, placebo-controlled trials, niacin extended-release tablets dosed at 1000, 1500 or 2000 mg daily at bedtime with a low-fat snack for 16 weeks (including 4 weeks of dose escalation) favorably altered lipid profiles compared to placebo (Table 3). Women appeared to have a greater response than men at each niacin extended-release tablets dose level (see *Gender Effect*, below).

Table 3. Lipid Response to Niacin Extended-Release Tablets Therapy

		Mean Percent Change from Baseline to Week 16*				
Treatment	**n**	**TC**	**LDL-C**	**HDL-C**	**TG**	**Apo B**
Niacin extended-release tablets 1000 mg at bedtime	41	-3	-5	+18	-21	-6
Niacin extended-release tablets 2000 mg at bedtime	41	-10	-14	+22	-28	-16
Placebo	40	0	-1	+4	0	+1
Niacin extended-release tablets 1500 mg at bedtime	76	-8	-12	+20	-13	-12

Placebo	73	+2	+1	+2	+12	+1

n = number of patients at baseline;
* Mean percent change from baseline for all niacin extended-release tablet doses was significantly different ($p < 0.05$) from placebo.

In a double-blind, multi-center, forced dose-escalation study, monthly 500 mg increases in niacin extended-release tablets dose resulted in incremental reductions of approximately 5% in LDL-C and Apo B levels in the daily dose range of 500 mg through 2000 mg (Table 4). Women again tended to have a greater response to niacin extended-release tablets than men (see *Gender Effect*, below).

Table 4. Lipid Response in Dose-Escalation Study

		Mean Percent Change from Baseline*				
Treatment	**n**	**TC**	**LDL-C**	**HDL-C**	**TG**	**Apo B**
Placebo‡	44	-2	-1	+5	-6	-2
Niacin extended-release tablets	87					
500 mg at bedtime		-2	-3	+10	-5	-2
1000 mg at bedtime		-5	-9	+15	-11	-7
1500 mg at bedtime		-11	-14	+22	-28	-15
2000 mg at bedtime		-12	-17	+26	-35	-16

n = number of patients enrolled;
‡Placebo data shown are after 24 weeks of placebo treatment.
* For all niacin extended-release tablet doses except 500 mg, mean percent change from baseline was significantly different ($p < 0.05$) from placebo for all lipid parameters shown.

Pooled results for major lipids from these three placebo-controlled studies are shown below (Table 5).

Table 5. Selected Lipid Response to Niacin Extended-Release Tablets in Placebo-Controlled Clinical Studies*

Mean Baseline and Median Percent Change from Baseline (25^{th}, 75^{th} Percentiles)				
Niacin Extended-Release Tablets Dose	**n**	**LDL-C**	**HDL-C**	**TG**
1000 mg at bedtime	104			
Baseline (mg/dL)		218	45	172
Percent Change		-7 (-15, 0)	+14 (+7, +23)	-16 (-34, +3)
1500 mg at bedtime	120			
Baseline (mg/dL)		212	46	171
Percent Change		-13 (-21, -4)	+19 (+9, +31)	-25 (-45, -2)
2000 mg at bedtime	85			
Baseline (mg/dL)		220	44	160
Percent Change		-16 (-26, -7)	+22 (+15, +34)	-38 (-52, -14)

* Represents pooled analyses of results; minimum duration on therapy at each dose was 4 weeks.

Gender Effect: Combined data from the three placebo-controlled niacin extended-release tablet studies in patients with primary hyperlipidemia and mixed dyslipidemia suggest that, at each niacin extended-release tablet dose level studied, changes in lipid concentrations are greater for women than for men (Table 6).

Table 6. Effect of Gender on Niacin Extended-Release Tablets Dose Response

		Mean Percent Change from Baseline							
Niacin Extended-Release Tablets Dose	**n** (M/F)	**LDL-C** M	**LDL-C** F	**HDL-C** M	**HDL-C** F	**TG** M	**TG** F	**Apo B** M	**Apo B** F
500 mg at bedtime	50/37	-2	-5	+11	+8	-3	-9	-1	-5
1000 mg at bedtime	76/52	-6*	-11*	+14	+20	-10	-20	-5*	-10*
1500 mg at bedtime	104/59	-12	-16	+19	+24	-17	-28	-13	-15
2000 mg at bedtime	75/53	-15	-18	+23	+26	-30	-36	-16	-16

n = number of male/female patients enrolled.
* Percent change significantly different between genders ($p < 0.05$).

Other Patient Populations: In a double-blind, multi-center, 19-week study the lipid-altering effects of niacin extended-release tablets (forced titration to 2000 mg at bedtime) were compared to baseline in patients whose primary lipid abnormality was a low level of HDL-C (HDL-C ≤40 mg/dL, TG ≤400 mg/dL, and LDL-C ≤160, or <130 mg/dL in the presence of CHD). Results are shown below (Table 7).

Table 7. Lipid Response to Niacin Extended-Release Tablets in Patients with Low HDL-C

		Mean Baseline and Mean Percent Change from Baseline*				
	n	**TC**	**LDL-C**	**HDL-C**	**TG**	**Apo B†**
Baseline (mg/dL)	88	190	120	31	194	106
Week 19 (% Change)	71	-3	0	+26	-30	-9

n = number of patients
* Mean percent change from baseline was significantly different ($p < 0.05$) for all lipid parameters shown except LDL-C.
† n = 72 at baseline and 69 at week 19.

At niacin extended-release tablets 2000 mg/day, median changes from baseline (25^{th}, 75^{th} percentiles) for LDL-C, HDL-C, and TG were - 3% (-14, +12%), +27% (+13, +38%), and -33% (-50, -19%), respectively.

16 HOW SUPPLIED/STORAGE AND HANDLING

Niacin Extended-Release Tablets USP are supplied as follows:

Niacin Extended-Release Tablets USP, 500 mg are white to off-white, film-coated, capsule shaped biconvex tablets debossed with ‘T’ on one side and ‘65’ on other side.

Bottles of 90 NDC 59651-018-90

Bottles of 180	NDC 59651-018-18
Bottles of 500	NDC 59651-018-05

Niacin Extended-Release Tablets USP, 750 mg are white to off-white, film-coated, capsule shaped biconvex tablets debossed with ‘T’ on one side and ‘66’ on other side.

Bottles of 90	NDC 59651-019-90
Bottles of 180	NDC 59651-019-18
Bottles of 500	NDC 59651-019-05

Niacin Extended-Release Tablets USP, 1000 mg are white to off-white, film-coated, oval shaped biconvex tablets debossed with ‘T’ on one side and ‘67’ on other side.

Bottles of 90	NDC 59651-020-90
Bottles of 180	NDC 59651-020-18
Bottles of 500	NDC 59651-020-05

Storage: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Dispense in a tight container with a child-resistant closure.

17 PATIENT COUNSELING INFORMATION

17.1 Patient Counseling

Patients should be advised to adhere to their National Cholesterol Education Program (NCEP) recommended diet, a regular exercise program, and periodic testing of a fasting lipid panel.

Patients should be advised to inform other healthcare professionals prescribing a new medication that they are taking niacin extended-release tablets.

The patient should be informed of the following:

Dosing Time

Niacin extended-release tablets should be taken at bedtime, after a low-fat snack. Administration on an empty stomach is not recommended.

Tablet Integrity

Niacin extended-release tablets should not be broken, crushed or chewed, but should be swallowed whole.

Dosing Interruption

If dosing is interrupted for any length of time, their physician should be contacted prior to restarting therapy; re-titration is recommended.

Muscle Pain

Notify their physician of any unexplained muscle pain, tenderness, or weakness promptly. They should discuss all medication, both prescription and over the counter, with their physician.

Flushing

Flushing (warmth, redness, itching and/or tingling of the skin) is a common side effect of niacin therapy that may subside after several weeks of consistent niacin extended-release tablets use. Flushing may vary in severity and is more likely to occur with initiation of therapy, or during dose increases. By dosing at bedtime, flushing will most likely occur during sleep. However, if awakened by flushing at night, the patient should get up slowly, especially if feeling dizzy, feeling faint, or taking blood pressure medications. Advise patients of the symptoms of flushing and how they differ from the symptoms of a myocardial infarction.

Use of Aspirin Medication

Taking aspirin (up to the recommended dose of 325 mg) approximately 30 minutes before dosing can minimize flushing.

Diet

Avoid ingestion of alcohol, hot beverages and spicy foods around the time of taking niacin extended-release tablets to minimize flushing.

Supplements

Notify their physician if they are taking vitamins or other nutritional supplements containing niacin or nicotinamide.

Dizziness

Notify their physician if symptoms of dizziness occur.

Diabetics

If diabetic, to notify their physician of changes in blood glucose.

Pregnancy

Discuss future pregnancy plans with your patients, and discuss when to stop niacin extended-release tablets if they are trying to conceive. Patients should be advised that if they become pregnant, they should stop taking niacin extended-release tablets and call their healthcare professional.

Breastfeeding

Women who are breastfeeding should be advised to not use niacin extended-release tablets. Patients, who have a lipid disorder and are breastfeeding, should be advised to discuss the options with their healthcare professional.

PATIENT INFORMATION
Niacin Extended-Release Tablets USP

(nye' a sin)

Read this information carefully before you start taking niacin extended-release tablets and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What are niacin extended-release tablets?

Niacin extended-release tablets are a prescription medicine used with diet and exercise to increase the good cholesterol (HDL) and lower the bad cholesterol (LDL) and fats (triglycerides) in your blood.

- Niacin extended-release tablets are also used to lower the risk of heart attack in people who have had a heart attack and have high cholesterol.
- In people with coronary artery disease and high cholesterol, niacin extended-release tablets, when used with a bile acid-binding resin (another cholesterol medicine) can slow down or lessen the build-up of plaque (fatty deposits) in your arteries.
- In people with heart problems and well-controlled cholesterol, taking niacin extended-release tablets with another cholesterol-lowering medicine (simvastatin) does not reduce heart attacks or strokes more than taking simvastatin alone.

It is not known if niacin extended-release tablets are safe and effective in children 16 years of age and under.

Who should not take niacin extended-release tablets?

Do not take niacin extended-release tablets if you have:

- liver problems
- a stomach ulcer
- bleeding problems
- an allergy to niacin or any of the ingredients in niacin extended-release tablets. See the end of this leaflet for a complete list of ingredients in niacin extended-release tablets.

What should I tell my doctor before taking niacin extended-release tablets?

Before you take niacin extended-release tablets, tell your doctor, if you:

- have diabetes. Tell your doctor if your blood sugar levels change after you take niacin extended-release tablets.
- have gout
- have kidney problems
- are pregnant or plan to become pregnant. It is not known if niacin extended-release tablets will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant while taking niacin extended-release tablets.
- are breastfeeding or plan to breastfeed. Niacin can pass into your breast milk. You and your doctor should decide if you will take niacin extended-release tablets or breastfeed. You should not do both. Talk to your doctor about the best way to feed your baby if you take niacin extended-release tablets.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, herbal supplements or other nutritional supplements containing niacin or nicotinamide. Niacin extended-release tablets and other medicines may affect each other causing side effects. Niacin extended-release tablets may affect the way other medicines work, and other medicines may affect how niacin extended-release tablets work.

Especially tell your doctor if you take:

- other medicines to lower cholesterol or triglycerides
- aspirin
- blood pressure medicines
- blood thinner medicines

- large amounts of alcohol

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take niacin extended-release tablets?

- Take niacin extended-release tablets exactly as your doctor tells you to take them.
- Take niacin extended-release tablets whole. Do not break, crush or chew niacin extended-release tablets before swallowing.
- Take niacin extended-release tablets 1 time a day at bedtime after a low-fat snack. Niacin extended-release tablets should not be taken on an empty stomach.
- All forms of niacin are not the same as niacin extended-release tablets. Do not switch between forms of niacin without first talking to your doctor as severe liver damage can occur.
- Do not change your dose or stop taking niacin extended-release tablets unless your doctor tells you to.
- If you need to stop taking niacin extended-release tablets, call your doctor before you start taking niacin extended-release tablets again. Your doctor may need to lower your dose of niacin extended-release tablets.
- If you forget to take a dose of niacin extended-release tablets, take it as soon as you remember.
- If you take too much Niacin, call your doctor right away.
- Medicines used to lower your cholesterol called bile acid resins, such as colestipol and cholestyramine, should not be taken at the same time of day as niacin extended-release tablets. You should take niacin extended-release tablets and the bile acid resin medicine at least 4 to 6 hours apart.
- Your doctor may do blood tests before you start taking niacin extended-release tablets and during your treatment. You should see your doctor regularly to check your cholesterol and triglyceride levels and to check for side effects.

What are the possible side effects of niacin extended-release tablets?

Niacin extended-release tablets may cause serious side effects, including:

- **severe liver problems. Signs of liver problems include:**
  - increased tiredness
  - dark colored urine (tea-colored)
  - loss of appetite
  - light colored stools
  - nausea
  - right upper stomach (abdomen) pain
  - yellowing of your skin or whites of your eye
  - itchy skin

- **unexplained muscle pain, tenderness or weakness**
- **high blood sugar level (glucose)**

Call your doctor right away if you have any of the side effects listed above.

The most common side effects of niacin extended-release tablets include:

- flushing
- diarrhea

- nausea
- vomiting
- increased cough
- rash

Flushing is the most common side effect of niacin extended-release tablets. Flushing happens when tiny blood vessels near the surface of the skin (especially on the face, neck, chest and/or back) open wider. Symptoms of flushing may include any or all of the following:

- warmth
- redness
- itching
- tingling of the skin

Flushing does not always happen. If it does, it is usually within 2 to 4 hours after taking a dose of niacin extended-release tablets. Flushing may last for a few hours. Flushing is more likely to happen when you first start taking niacin extended-release tablets or when your dose of niacin extended-release tablets is increased. Flushing may get better after several weeks.

If you wake up at night because of flushing, get up slowly, especially if you:

- feel dizzy or faint
- take blood pressure medicines

To lower your chance of flushing:

- Ask your doctor if you can take aspirin to help lower the flushing side effect from niacin extended-release tablets. You can take aspirin (up to the recommended dose of 325 mg) about 30 minutes before you take niacin extended-release tablets to help lower the flushing side effect.
- Do not drink hot beverages (including coffee), alcohol, or eat spicy foods around the time you take niacin extended-release tablets.
- Take niacin extended-release tablets with a low-fat snack to lessen upset stomach.

People with high cholesterol and heart disease are at risk for a heart attack. Symptoms of a heart attack may be different from a flushing reaction from niacin extended-release tablets. **The following may be symptoms of a heart attack due to heart disease and not a flushing reaction:**

- chest pain
- pain in other areas of your upper body such as one or both arms, back, neck, jaw or stomach
- shortness of breath
- sweating
- nausea
- lightheadedness

The chest pain you have with a heart attack may feel like uncomfortable pressure, squeezing, fullness or pain that lasts more than a few minutes, or that goes away and comes back. Heart attacks may be sudden and intense, but often start slowly, with mild pain or discomfort.

Call your doctor right away if you have any symptoms of a heart attack.

Tell your doctor if you have any side effect that bothers you or does not go away.

These are not all the possible side effects of niacin extended-release tablets. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store niacin extended-release tablets?

- Store niacin extended-release tablets at 68°F to 77°F (20°C to 25°C).

Keep niacin extended-release tablets and all medicines out of the reach of children.

General information about the safe and effective use of niacin extended-release tablets.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use niacin extended-release tablets for a condition for which it was not prescribed. Do not give niacin extended-release tablets to other people, even if they have the same symptoms that you have. They may harm them.

This leaflet summarizes the most important information about niacin extended-release tablets. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about niacin extended-release tablets that is written for health professionals.

For more information call Aurobindo Pharma USA, Inc. at 1-866-850-2876.

What are the ingredients in niacin extended-release tablets?

Active ingredient: niacin

Inactive Ingredients: colloidal silicon dioxide, hydrogenated castor oil, hypromellose, lactose monohydrate, magnesium stearate, polyethylene glycol, titanium dioxide.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Distributed by:
Aurobindo Pharma USA, Inc.
279 Princeton-Hightstown Road
East Windsor, NJ 08520

Manufactured by:
Aurobindo Pharma Limited
Hyderabad–500 038, India
Revised: 09/2018

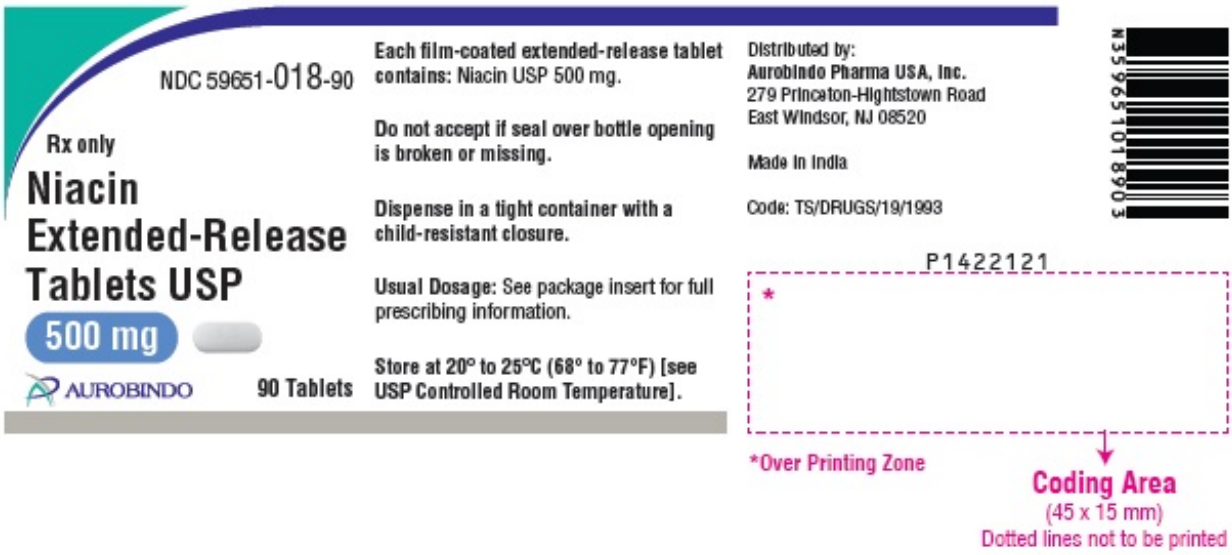
PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 500 mg (90 Tablets Bottle)

NDC 59651-018-90

Rx only
Niacin

Extended-Release
Tablets USP
500 mg

AUROBINDO 90 Tablets

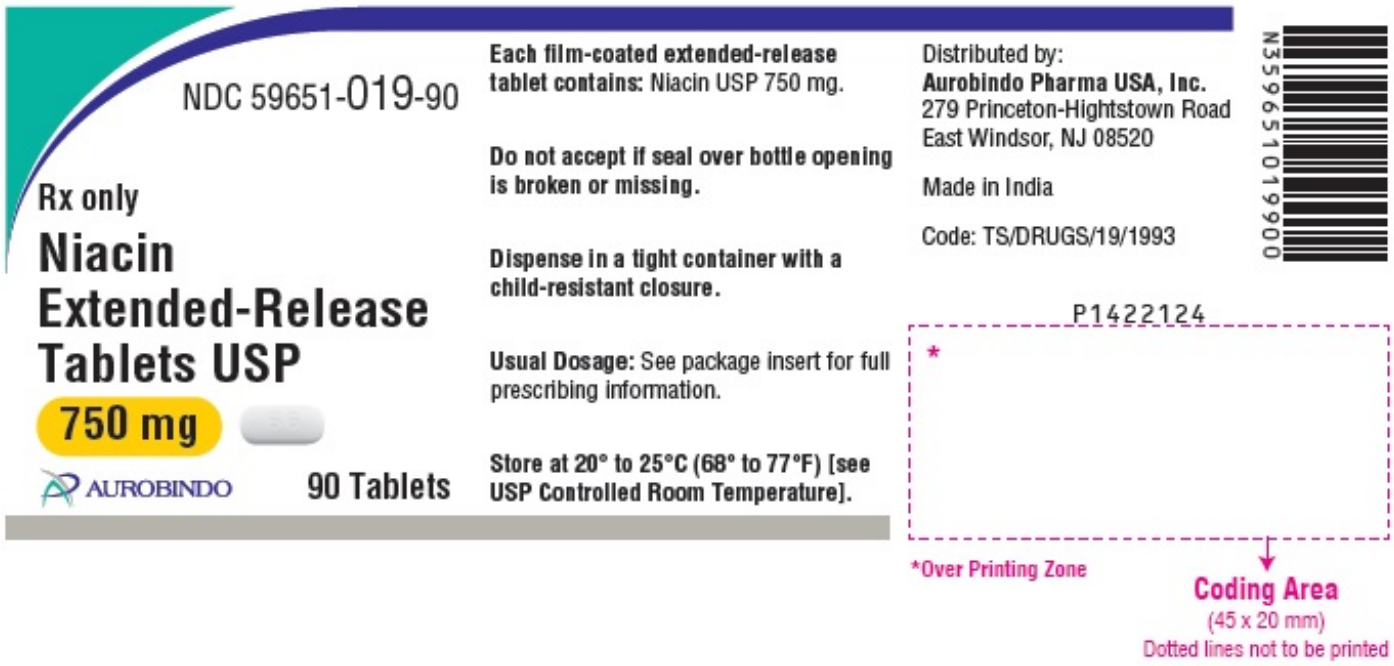


PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 750 mg (90 Tablets Bottle)

NDC 59651-019-90

Rx only
Niacin
Extended-Release
Tablets USP
750 mg

AUROBINDO 90 Tablets

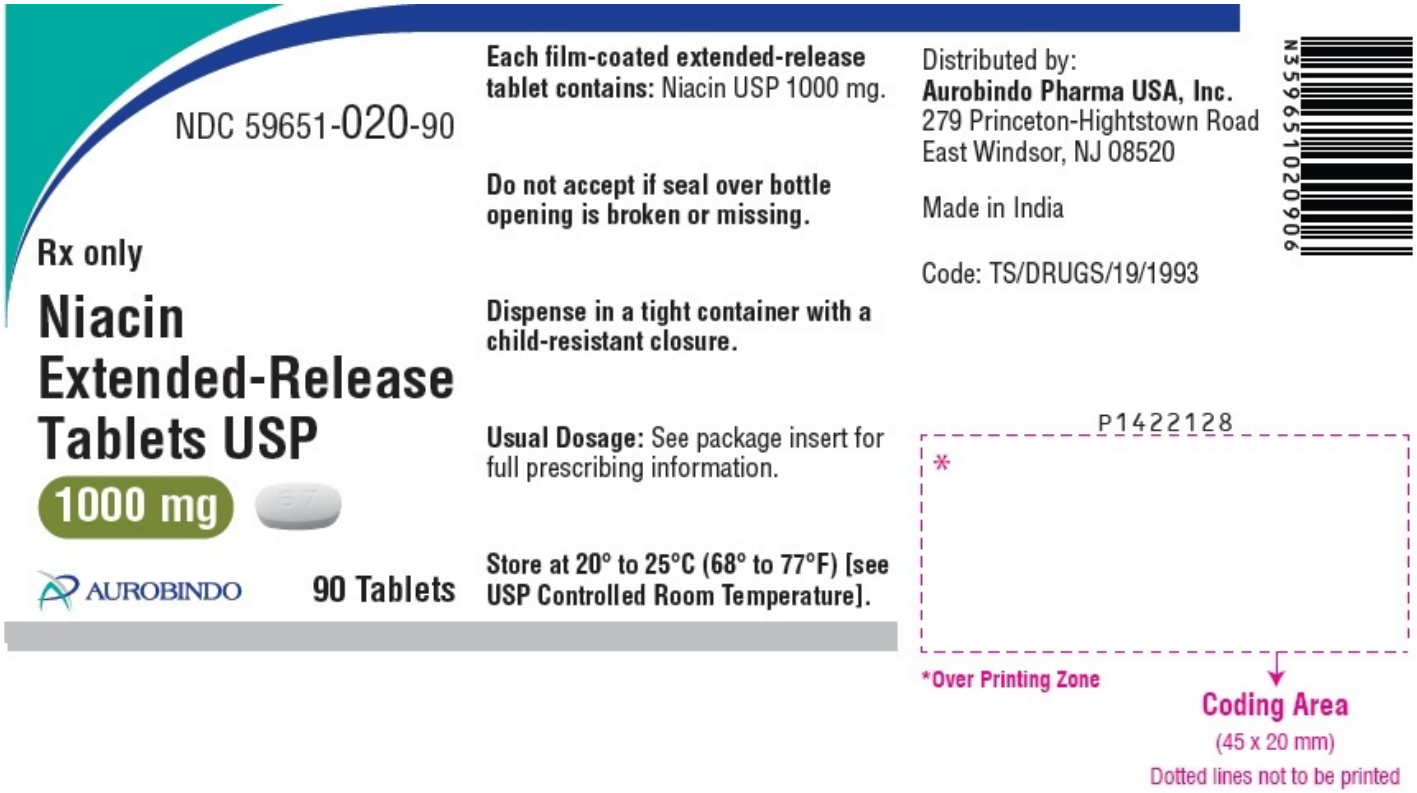


PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 1000 mg (90 Tablets Bottle)

NDC 59651-020-90

Rx only
Niacin
Extended-Release
Tablets USP
1000 mg

AUROBINDO 90 Tablets



NIACIN

niacin tablet, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:59651-018
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NIACIN (UNII: 2679MF687A) (NIACIN - UNII:2679MF687A)	NIACIN	500 mg

Inactive Ingredients	
Ingredient Name	**Strength**
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
HYDROGENATED CASTOR OIL (UNII: ZF94AP8MEY)	
HYPROMELLOSE 2910 (50 MPA.S) (UNII: 1IVH67816N)	
HYPROMELLOSE 2208 (100000 MPA.S) (UNII: VM7F0B23ZI)	
HYPROMELLOSE 2910 (6 MPA.S) (UNII: 0WZ8WG20P6)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	WHITE (White to off-white)	**Score**	no score
Shape	CAPSULE (Capsule shaped biconvex)	**Size**	17mm
Flavor		**Imprint Code**	T;65
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:59651-018-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	
2	NDC:59651-018-18	180 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	
3	NDC:59651-018-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209236	02/01/2018	

NIACIN

niacin tablet, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:59651-019
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NIACIN (UNII: 2679MF687A) (NIACIN - UNII:2679MF687A)	NIACIN	750 mg

Inactive Ingredients	
Ingredient Name	**Strength**
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
HYDROGENATED CASTOR OIL (UNII: ZF94AP8MEY)	
HYPROMELLOSE 2910 (50 MPA.S) (UNII: 1IVH67816N)	
HYPROMELLOSE 2208 (100000 MPA.S) (UNII: VM7F0B23ZI)	
HYPROMELLOSE 2910 (6 MPA.S) (UNII: 0WZ8WG20P6)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	WHITE (White to off-white)	**Score**	no score
Shape	CAPSULE (Capsule shaped biconvex)	**Size**	19mm
Flavor		**Imprint Code**	T;66
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:59651-019-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	
2	NDC:59651-019-18	180 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	
3	NDC:59651-019-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209236	02/01/2018	

NIACIN

niacin tablet, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:59651-020
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NIACIN (UNII: 2679MF687A) (NIACIN - UNII:2679MF687A)	NIACIN	1000 mg

Inactive Ingredients	
Ingredient Name	**Strength**
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
HYDROGENATED CASTOR OIL (UNII: ZF94AP8MEY)	
HYPROMELLOSE 2910 (50 MPA.S) (UNII: 1IVH67816N)	
HYPROMELLOSE 2208 (100000 MPA.S) (UNII: VM7F0B23ZI)	
HYPROMELLOSE 2910 (6 MPA.S) (UNII: 0WZ8WG20P6)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	WHITE (White to off-white)	**Score**	no score
Shape	OVAL (Oval shaped biconvex)	**Size**	19mm
Flavor		**Imprint Code**	T;67
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:59651-020-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	
2	NDC:59651-020-18	180 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	
3	NDC:59651-020-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2018	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209236	02/01/2018	

Labeler - Aurobindo Pharma Limited (650082092)

Establishment

Name	Address	ID/FEI	Business Operations
Aurobindo Pharma Limited		918917642	ANALYSIS(59651-018, 59651-019, 59651-020) , MANUFACTURE(59651-018, 59651-019, 59651-020)