PRAVASTATIN SODIUM- pravastatin sodium tablet
Northwind Pharmaceuticals, LLC

Pravastatin Sodium 40 MG

Indications and Usage

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 hypercholesterolemia. Drug 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.

Prevention of Cardiovascular Disease

In hypercholesterolemic patients without clinically evident coronary heart disease (CHD), pravastatin sodium tablets are indicated to:

reduce the risk of myocardial infarction (MI).
reduce the risk of undergoing myocardial revascularization procedures.
reduce the risk of cardiovascular mortality with no increase in death from non-cardiovascular causes.

Hyperlipidemia

Pravastatin sodium tablets are indicated:

as an adjunct to diet to reduce elevated total cholesterol (Total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (ApoB), and triglyceride (TG) levels and to increase high-density lipoprotein cholesterol (HDL-C) in patients with primary hypercholesterolemia and mixed dyslipidemia (Fredrickson Types IIa and IIb).1
as an adjunct to diet for the treatment of patients with elevated serum TG levels (Fredrickson Type IV).
for the treatment of patients with primary dysbetalipoproteinemia (Fredrickson Type III) who do not respond adequately to diet.
as an adjunct to diet and lifestyle modification for treatment of heterozygous familial hypercholesterolemia (HeFH) in children and adolescent patients ages 8 years and older if after an adequate trial of diet the following findings are present:

a. LDL-C remains ≥ 190 mg/dL or

b. LDL-C remains ≥ 160 mg/dL and:

there is a positive family history of premature cardiovascular disease (CVD) or two or more other CVD risk factors are present in the patient.

Limitations of Use

Pravastatin sodium has not been studied in conditions where the major lipoprotein abnormality is elevation of chylomicrons (Fredrickson Types I and V).

Dosage and administration

General Dosing Information

The patient should be placed on a standard cholesterol-lowering diet before receiving pravastatin sodium tablets and should continue on this diet during treatment with pravastatin sodium tablets [see NCEP Treatment Guidelines for details on dietary therapy].

Adult Patients

The recommended starting dose is 40 mg once daily. If a daily dose of 40 mg does not achieve desired cholesterol levels, 80 mg once daily is recommended. In patients with significant renal impairment, a starting dose of 10 mg daily is recommended. Pravastatin sodium tablets can be administered orally as a single dose at any time of the day, with or without food. Since the maximal effect of a given dose is seen within 4 weeks, periodic lipid determinations should be performed at this time and dosage adjusted according to the patient's response to therapy and established treatment guidelines.

Pediatric Patients

Children (Ages 8 to 13 Years, Inclusive)

The recommended dose is 20 mg once daily in children 8 to 13 years of age. Doses greater than 20 mg have not been studied in this patient population.

Adolescents (Ages 14 to 18 Years)

The recommended starting dose is 40 mg once daily in adolescents 14 to 18 years of age. Doses greater than 40 mg have not been studied in this patient population.

Children and adolescents treated with pravastatin should be reevaluated in adulthood and appropriate changes made to their cholesterol-lowering regimen to achieve adult goals for LDL-C [see Indications and Usage (1.2)].

Concomitant Lipid-Altering Therapy

Pravastatin sodium tablets may be used with bile acid resins. When administering a bile-acid-binding resin (e.g., cholestyramine, colestipol) and pravastatin, pravastatin sodium tablets should be given either 1 hour or more before or at least 4 hours following the resin. [See Clinical Pharmacology (12.3).]

Dosage in Patients Taking Cyclosporine

In patients taking immunosuppressive drugs such as cyclosporine concomitantly with pravastatin, therapy should begin with 10 mg of pravastatin sodium once-a-day at bedtime and titration to higher doses should be done with caution. Most patients treated with this combination received a maximum pravastatin sodium dose of 20 mg/day. In patients taking cyclosporine, therapy should be limited to 20 mg of pravastatin sodium once daily [see Warnings and Precautions (5.1) and Drug Interactions (7.1)].

Dosage in Patients Taking Clarithromycin

In patients taking clarithromycin, therapy should be limited to 40 mg of pravastatin sodium once daily [see Drug Interactions (7.2)].

Contraindications

Hypersensitivity

Hypersensitivity to any component of this medication.

Liver

Active liver disease or unexplained, persistent elevations of serum transaminases [see Warnings and Precautions (5.2)].

Pregnancy

Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since statins decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they are contraindicated during pregnancy and in nursing mothers. PRAVASTATIN SHOULD BE

ADMINISTERED TO WOMEN OF CHILDBEARING AGE ONLY WHEN SUCH PATIENTS ARE HIGHLY UNLIKELY TO CONCEIVE AND HAVE BEEN INFORMED OF THE POTENTIAL HAZARDS. If the patient becomes pregnant while taking this class of drug, therapy should be discontinued immediately and the patient apprised of the potential hazard to the fetus [see Use in Specific Populations (8.1)].

Nursing Mothers

A small amount of pravastatin is excreted in human breastmilk. Because statins have the potential for serious adverse reactions in nursing infants, women who require pravastatin sodium treatment should not breastfeed their infants [see Use in Specific Populations (8.3)].

Warnings and Precautions

Skeletal Muscle

Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with pravastatin and other drugs in this class. A history of renal impairment may be a risk factor for the development of rhabdomyolysis. Such patients merit closer monitoring for skeletal muscle effects.

Uncomplicated myalgia has also been reported in pravastatin-treated patients [see Adverse Reactions (6)]. Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal (ULN), was rare (< 0.1%) in pravastatin clinical trials. Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Predisposing factors include advanced age (> 65), uncontrolled hypothyroidism, and renal impairment. Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.

The risk of myopathy during treatment with statins is increased with concurrent therapy with either erythromycin, cyclosporine, niacin, or fibrates. However, neither myopathy nor significant increases in CPK levels have been observed in 3 reports involving a total of 100 post-transplant patients (24 renal and 76 cardiac) treated for up to 2 years concurrently with pravastatin 10 to 40 mg and cyclosporine. Some of these patients also received other concomitant immunosuppressive therapies. Further, in clinical trials involving small numbers of patients who were treated concurrently with pravastatin and niacin, there were no reports of myopathy. Also, myopathy was not reported in a trial of combination pravastatin (40 mg/day) and gemfibrozil (1200 mg/day), although 4 of 75 patients on the combination showed marked CPK elevations versus 1 of 73 patients receiving placebo. There was a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. The use of fibrates alone may occasionally be associated with myopathy. The benefit of further alterations in lipid levels by the combined use of pravastatin sodium with fibrates should be carefully weighed against the potential risks of this combination.

Cases of myopathy, including rhabdomyolysis, have been reported with pravastatin coadministered with colchicine, and caution should be exercised when prescribing pravastatin with colchicine [see Drug Interactions (7.3)].

Liver

Statins, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. In 3 long-term (4.8 to 5.9 years), placebo-controlled clinical trials (WOS, LIPID, CARE), 19,592 subjects (19,768 randomized) were exposed to pravastatin or placebo [see Clinical

Studies (14)]. In an analysis of serum transaminase values (ALT, AST), incidences of marked abnormalities were compared between the pravastatin and placebo treatment groups; a marked abnormality was defined as a post-treatment test value greater than 3 times the upper limit of normal for subjects with pretreatment values less than or equal to the upper limit of normal, or 4 times the pretreatment value for subjects with pretreatment values greater than the upper limit of normal but less than 1.5 times the upper limit of normal. Marked abnormalities of ALT or AST occurred with similar low frequency (≤ 1.2%) in both treatment groups. Overall, clinical trial experience showed that liver function test abnormalities observed during pravastatin therapy were usually asymptomatic, not associated with cholestasis, and did not appear to be related to treatment duration. In a 320-patient placebo-controlled clinical trial, subjects with chronic (> 6 months) stable liver disease, due primarily to hepatitis C or non-alcoholic fatty liver disease, were treated with 80 mg pravastatin or placebo for up to 9 months. The primary safety endpoint was the proportion of subjects with at least one ALT ≥ 2 times the upper limit of normal for those with normal ALT (≤ the upper limit of normal) at baseline or a doubling of the baseline ALT for those with elevated ALT (> the upper limit of normal) at baseline. By Week 36, 12 out of 160 (7.5%) subjects treated with pravastatin met the prespecified safety ALT endpoint compared to 20 out of 160 (12.5%) subjects receiving placebo. Conclusions regarding liver safety are limited since the study was not large enough to establish similarity between groups (with 95% confidence) in the rates of ALT elevation.

It is recommended that liver function tests be performed prior to the initiation of therapy and when clinically indicated.

Active liver disease or unexplained persistent transaminase elevations are contraindications to the use of pravastatin [see Contraindications (4.2)]. Caution should be exercised when pravastatin is administered to patients who have a recent (< 6 months) history of liver disease, have signs that may suggest liver disease (e.g., unexplained aminotransferase elevations, jaundice), or are heavy users of alcohol.

There have been rare postmarketing reports of fatal and non-fatal hepatic failure in patients taking statins, including pravastatin. If serious liver injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs during treatment with pravastatin sodium, promptly interrupt therapy. If an alternate etiology is not found do not restart pravastatin sodium.

Endocrine Function

Statins interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced ($p < 0.004$) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a ≥ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of statins on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if a statin or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

In a placebo-controlled study of 214 pediatric patients with HeFH, of which 106 were treated with pravastatin (20 mg in the children aged 8 to 13 years and 40 mg in the adolescents aged 14 to 18 years) for 2 years, there were no detectable differences seen in any of the endocrine parameters (ACTH, cortisol, DHEAS, FSH, LH, TSH, estradiol [girls] or testosterone [boys]) relative to placebo. There were no detectable differences seen in height and weight changes, testicular volume changes, or Tanner score relative to placebo.

Adverse Reactions

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4 month-long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant.

For Adverse Clinical Events

Please review the manufacturer's complete FDA submission at: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=a453647b-16de-4795-a550-4f52eac10a26

Laboratory Test Abnormalities

Increases in ALT, AST values and CPK have been observed [see Warnings and Precautions (5.1, 5.2)].

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with statins.

Pediatric Patients

In a 2 year, doubleblind, placebo-controlled study involving 100 boys and 114 girls with HeFH (n=214; age range 8 to 18.5 years, 53% female, 95% Caucasians, < 1% Blacks, 3% Asians, 1% Other), the safety and tolerability profile of pravastatin was generally similar to that of placebo. [See Warnings and Precautions (5.3), Use in Specific Populations (8.4), and Clinical Pharmacology (12.3).]

Drug interactions

For the concurrent therapy of either cyclosporine, fibrates, niacin (nicotinic acid), or erythromycin, the risk of myopathy increases [see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)].

Cyclosporine

The risk of myopathy/rhabdomyolysis is increased with concomitant administration of cyclosporine. Limit pravastatin to 20 mg once daily for concomitant use with cyclosporine [see Dosage and Administration (2.5), Warnings and Precautions (5.1), and Clinical Pharmacology (12.3)].

Clarithromycin

The risk of myopathy/rhabdomyolysis is increased with concomitant administration of clarithromycin. Limit pravastatin to 40 mg once daily for concomitant use with clarithromycin [see Dosage and Administration (2.6), Warnings and Precautions (5.1), and Clinical Pharmacology (12.3)].

Colchicine

The risk of myopathy/rhabdomyolysis is increased with concomitant administration of colchicine [see Warnings and Precautions (5.1)].

Gemfibrozil

Due to an increased risk of myopathy/rhabdomyolysis when HMG-CoA reductase inhibitors are coadministered with gemfibrozil, concomitant administration of pravastatin sodium with gemfibrozil should be avoided [see Warnings and Precautions (5.1)].

Other Fibrates

Because it is known that the risk of myopathy during treatment with HMG-CoA reductase inhibitors is increased with concurrent administration of other fibrates, pravastatin sodium should be administered with caution when used concomitantly with other fibrates [see Warnings and Precautions (5.1)].

Niacin

The risk of skeletal muscle effects may be enhanced when pravastatin is used in combination with niacin; a reduction in pravastatin sodium dosage should be considered in this setting [see Warnings and

Precautions (5.1)].

Use in specific populations

Pregnancy

Pregnancy Category X

[See Contraindications (4.3).]

Safety in pregnant women has not been established. Available data in women inadvertently taking pravastatin while pregnant do not suggest any adverse clinical events. However, there are no adequate and well-controlled studies in pregnant women. Therefore, it is not known whether pravastatin can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Pravastatin should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus and patients have been informed of the potential hazards.

Rare reports of congenital anomalies have been received following intrauterine exposure to other statins. In a review2 of approximately 100 prospectively followed pregnancies in women exposed to simvastatin or lovastatin, the incidences of congenital anomalies, spontaneous abortions, and fetal deaths/stillbirths did not exceed what would be expected in the general population. The number of cases is adequate to exclude a ≥ 3- to 4-fold increase in congenital anomalies over the background incidence. In 89% of the prospectively followed pregnancies, drug treatment was initiated prior to pregnancy and was discontinued at some point in the first trimester when pregnancy was identified. As safety in pregnant women has not been established and there is no apparent benefit to therapy with pravastatin sodium during pregnancy [see Contraindications (4.3)], treatment should be immediately discontinued as soon as pregnancy is recognized. Pravastatin sodium should be administered to women of childbearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards.

Pravastatin was neither embryolethal nor teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 10 times (rabbit) or 120 times (rat) the human exposure at 80 mg/day maximum recommended human dose (MRHD) based on surface area (mg/m2).

In pregnant rats given oral gavage doses of 4, 20, 100, 500, and 1000 mg/kg/day from gestation days 7 through 17 (organogenesis) increased mortality of offspring and skeletal anomalies were observed at 100 mg/kg/day systemic exposure, 10 times the human exposure at 80 mg/day MRHD based on body surface area (mg/m2).

In pregnant rats given oral gavage doses of 10, 100, and 1000 mg/kg/day from gestation day 17 through lactation day 21 (weaning) increased mortality of offspring and developmental delays were observed at 100 mg/kg/day systemic exposure, 12 times the human exposure at 80 mg/day MRHD based on body surface area (mg/m2).

Nursing Mothers

A small amount of pravastatin is excreted in human breastmilk. Because of the potential for serious adverse reactions in nursing infants, women taking pravastatin sodium should not nurse [see Contraindications (4.4)].

Pravastatin crosses the placenta and is found in fetal tissue at 30% maternal plasma levels following a single 20 mg/kg dose given to pregnant rats on gestation day 18. Similar studies in lactating rats indicate secretion of pravastatin into breastmilk at 0.2 to 6.5 times higher levels than maternal plasma at exposures equivalent to 2 times human exposure at the MRHD.

Pediatric Use

The safety and effectiveness of pravastatin sodium in children and adolescents from 8 to 18 years of age have been evaluated in a placebo-controlled study of 2 years duration. Patients treated with

pravastatin had an adverse experience profile generally similar to that of patients treated with placebo with influenza and headache commonly reported in both treatment groups. [See Adverse Reactions (6.4).] Doses greater than 40 mg have not been studied in this population. Children and adolescent females of childbearing potential should be counseled on appropriate contraceptive methods while on pravastatin therapy [see Contraindications (4.3) and Use in Specific Populations (8.1)]. For dosing information [see Dosage and Administration (2.3).]

Doubleblind, placebo-controlled pravastatin studies in children less than 8 years of age have not been conducted.

Geriatric Use

The beneficial effect of pravastatin in elderly subjects in reducing cardiovascular events and in modifying lipid profiles was similar to that seen in younger subjects. The adverse event profile in the elderly was similar to that in the overall population. Other reported clinical experience has not identified differences in responses to pravastatin between elderly and younger patients.

Mean pravastatin AUCs are slightly (25% to 50%) higher in elderly subjects than in healthy young subjects, but mean maximum plasma concentration (Cmax), time to maximum plasma concentration (Tmax), and half-life (t½) values are similar in both age groups and substantial accumulation of pravastatin would not be expected in the elderly [see Clinical Pharmacology (12.3)].

Since advanced age (≥ 65 years) is a predisposing factor for myopathy, pravastatin sodium should be prescribed with caution in the elderly [see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)].

Homozygous Familial Hypercholesterolemia

Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that statins are less effective because the patients lack functional LDL receptors.

Overdosage

To date, there has been limited experience with overdosage of pravastatin. If an overdose occurs, it should be treated symptomatically with laboratory monitoring and supportive measures should be instituted as required.

Description

Pravastatin sodium is one of a class of lipid-lowering compounds, the statins, which reduce cholesterol biosynthesis. These agents are competitive inhibitors of HMG-CoA reductase, the enzyme catalyzing the early rate-limiting step in cholesterol biosynthesis, conversion of HMG-CoA to mevalonate.

Pravastatin sodium is designated chemically as 1-Naphthalene-heptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ,6-trihydroxy-2-methyl-8-(2-methyl-1-oxobutoxy)-, monosodium salt, [1S-[1α(βS*,δS*),2α,6α,8β(R*),8aα]]-.

Pravastatin sodium, USP is white to yellowish white powder or crystalline powder, hygroscopic in nature. It is a relatively polar hydrophilic compound with a partition coefficient (octanol/water) of 0.59 at a pH of 7. It is freely soluble in water and in methanol. Soluble in ethanol.

Each pravastatin sodium tablet intended for oral administration contains 10 mg or 20 mg or 40 mg or 80 mg of pravastatin sodium. In addition, each tablet contains the following inactive ingredients: croscarmellose sodium, lactose anhydrous, magnesium stearate, microcrystalline cellulose, polyoxyl 35 castor oil and sodium carbonate anhydrous.

Clinical Pharmacology

Mechanism of Action

Pravastatin is a reversible inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme that catalyzes the conversion of HMG-CoA to mevalonate, an early and rate limiting step in the biosynthetic pathway for cholesterol. In addition, pravastatin reduces VLDL and TG and increases HDL-C.

Pharmacokinetics

General

Absorption

Pravastatin sodium is administered orally in the active form. In studies in man, peak plasma pravastatin concentrations occurred 1 to 1.5 hours upon oral administration. Based on urinary recovery of total radiolabeled drug, the average oral absorption of pravastatin is 34% and absolute bioavailability is 17%. While the presence of food in the gastrointestinal tract reduces systemic bioavailability, the lipid-lowering effects of the drug are similar whether taken with or 1 hour prior to meals.

Pravastatin plasma concentrations, including area under the concentration-time curve (AUC), Cmax, and steady-state minimum (Cmin), are directly proportional to administered dose. Systemic bioavailability of pravastatin administered following a bedtime dose was decreased 60% compared to that following an AM dose. Despite this decrease in systemic bioavailability, the efficacy of pravastatin administered once daily in the evening, although not statistically significant, was marginally more effective than that after a morning dose.

The coefficient of variation (CV), based on between-subject variability, was 50% to 60% for AUC. The geometric means of pravastatin Cmax and AUC following a 20 mg dose in the fasted state were 26.5 ng/mL and 59.8 ng*hr/mL, respectively.

Steady-state AUCs, Cmax, and Cmin plasma concentrations showed no evidence of pravastatin accumulation following once or twice daily administration of pravastatin sodium tablets.

Distribution

Approximately 50% of the circulating drug is bound to plasma proteins.

Metabolism

The major biotransformation pathways for pravastatin are: (a) isomerization to 6-epi pravastatin and the 3α-hydroxyisomer of pravastatin (SQ 31,906) and (b) enzymatic ring hydroxylation to SQ 31,945. The 3α-hydroxyisomeric metabolite (SQ 31,906) has 1/10 to 1/40 the HMG-CoA reductase inhibitory activity of the parent compound. Pravastatin undergoes extensive first-pass extraction in the liver (extraction ratio 0.66).

Excretion

Approximately 20% of a radiolabeled oral dose is excreted in urine and 70% in the feces. After intravenous administration of radiolabeled pravastatin to normal volunteers, approximately 47% of total body clearance was via renal excretion and 53% by non-renal routes (i.e., biliary excretion and biotransformation).

Following single dose oral administration of 14C-pravastatin, the radioactive elimination t½ for pravastatin is 1.8 hours in humans.

Specific Populations

Renal Impairment

A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3α-hydroxy isomeric metabolite (SQ 31,906). Compared to healthy subjects with normal renal function, patients with severe renal impairment had 69% and 37% higher mean AUC and

Cmax values, respectively, and a 0.61 hour shorter t½ for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945).

Hepatic Impairment

In a study comparing the kinetics of pravastatin in patients with biopsy confirmed cirrhosis (N=7) and normal subjects (N=7), the mean AUC varied 18-fold in cirrhotic patients and 5-fold in healthy subjects. Similarly, the peak pravastatin values varied 47-fold for cirrhotic patients compared to 6-fold for healthy subjects. [See Warnings and Precautions (5.2).]

Geriatric

In a single oral dose study using pravastatin 20 mg, the mean AUC for pravastatin was approximately 27% greater and the mean cumulative urinary excretion (CUE) approximately 19% lower in elderly men (65 to 75 years old) compared with younger men (19 to 31 years old). In a similar study conducted in women, the mean AUC for pravastatin was approximately 46% higher and the mean CUE approximately 18% lower in elderly women (65 to 78 years old) compared with younger women (18 to 38 years old). In both studies, Cmax, Tmax, and t½ values were similar in older and younger subjects. [See Use in Specific Populations (8.5).]

Pediatric

After 2 weeks of once-daily 20 mg oral pravastatin administration, the geometric means of AUC were 80.7 (CV 44%) and 44.8 (CV 89%) ng*hr/mL for children (8 to 11 years, N=14) and adolescents (12 to 16 years, N=10), respectively. The corresponding values for Cmax were 42.4 (CV 54%) and 18.6 ng/mL (CV 100%) for children and adolescents, respectively. No conclusion can be made based on these findings due to the small number of samples and large variability. [See Use in Specific Populations .]

For complete Drug-Drug Interactions information and complete drug information please visit the manufacturer's FDA submission at:

http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=a453647b-16de-4795-a550-4f52eac10a26

Patient Medication Information

Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever [see Warnings and Precautions (5.1)].

It is recommended that liver enzyme tests be performed before the initiation of pravastatin sodium, and thereafter when clinically indicated. All patients treated with pravastatin sodium should be advised to promptly report any symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice [see Warnings and Precautions

Label

NDC: 51655-072-52

MFG: 68382-072-05

Pravastatin Sodium 40 MG

30 Tablets

Rx Only

Lot#:

Exp. Date:

Each tablet contains: pravastatin sodium, USP....40mg

Dosage: See prescriber's instructions

Store at 68-77 degrees F.

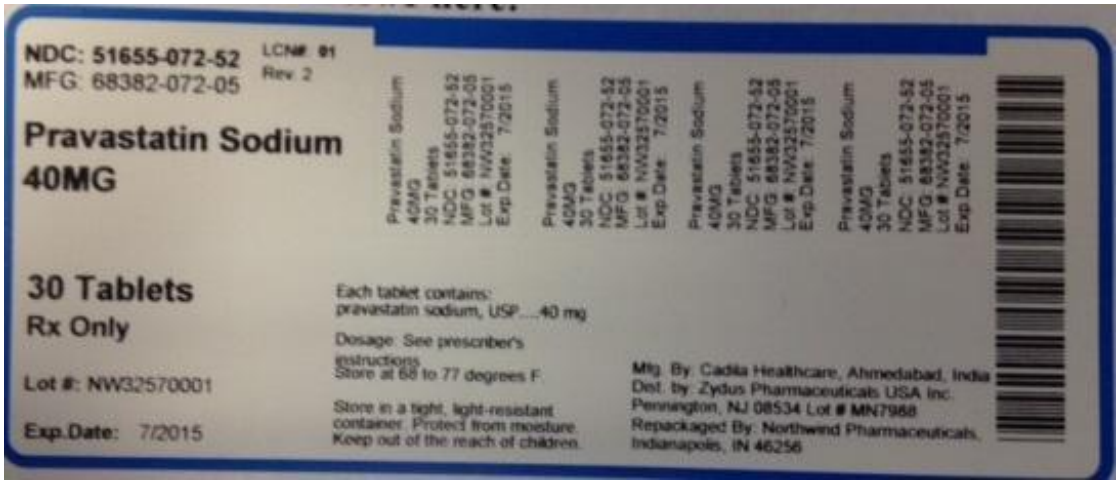
Store in a tight, light-resistant container. Protect from moisture.

Keep out of the reach of children.

Mfg by: Cadila Healthcare, Ahmedabad, India

Dist. by: Zydus Pharmaceuticals USA Inc. Pennignton, NJ 08534 Lot#

Repackaged by: Northwind Pharmaceuticals, Indianapolis, IN 46256



PRAVASTATIN SODIUM

pravastatin sodium tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51655-072(NDC:68382-072)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
PRAVASTATIN SODIUM (UNII: 3M8608UQ61) (PRAVASTATIN - UNII:KXO2KT9N0G)	PRAVASTATIN SODIUM	40 mg

Product Characteristics			
Color	white	**Score**	no score
Shape	OVAL	**Size**	14mm
Flavor		**Imprint Code**	ZC44
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:51655-072-52	30 in 1 BOTTLE, DISPENSING		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA077751	07/10/2014	

Labeler - Northwind Pharmaceuticals, LLC (036986393)

Registrant - Northwind Pharmaceuticals, LLC (036986393)

Establishment

Name	Address	ID/FEI	Business Operations
Northwind Pharmaceuticals, LLC		036986393	repack(51655-072)

Revised: 7/2014 Northwind Pharmaceuticals, LLC