Hospital accreditation pounds another 'nail' in the 'smoking' coffin

As regular readers of the *JAOA* will recall, we have consistently called for a smokeless society. We have encouraged the American Osteopathic Association (AOA), the colleges of osteopathic medicine, the osteopathic hospitals, and individual osteopathic physicians to join the cause against smoking by leading the way through example.

We have had the pleasure of reporting the progress made in the establishment of "smoke-free" campuses at many of the colleges of osteopathic medicine. We have told you of the numerous osteopathic hospitals that have restricted or have prohibited smoking in their facilities. Even the central offices of the AOA became "smoke-free" more than 1 year ago. Yet, we can and must do much more in the battle against the number 1 cause of cardiovascular and pulmonary disease and cancer among Americans.

An example of this added effort occurred at the annual convention, held this year in New Orleans. The AOA Board of Trustees approved the recent revision of the Accreditation Standards of the AOA Committee on Hospital Accreditation. The previous policy issued by the committee required that hospitals establish a smoking policy that permitted smoking in designated areas only. The new policy limits patient smoking to strict circumstances. Furthermore, the new policy reads as follows:

The hospital must have, disseminate, and enforce a hospital-wide no-smoking policy.

A. The policy shall prohibit smoking and the use of tobacco products by hospital patients, medical staff, hospital employees, visitors, and volunteers within the hospital buildings.

B. Hospitals may develop medical exceptions to their policy, but only for patients currently under treatment at the facility where abrupt cessation of smoking would be detrimental to the patient.

1. The policy shall prohibit smoking by patients

unless authorized to smoke by the attending physician.

2. The hospital will segregate, where practical, patients authorized to smoke from nonsmoking patients.

This strengthened accreditation standard represents another "nail" in the "smoking" coffin.

THOMAS WESLEY ALLEN, DO
Editor in Chief

Changing of the guard at the AOA

"To remain young one must change," wrote Alexander Chase in *Perspectives*. As the American Osteopathic Association prepares to celebrate a centennial of service to America, change is taking place at our helm. John P. Perrin, executive director since 1982, has assumed the duties of president of the University of Health Sciences College of Osteopathic Medicine (UHS-COM) in Kansas City, Mo.

As the search committee seeks an appropriate replacement for Mr Perrin, AOA President Gilbert S Bucholz, has assumed the duties of acting executive director.

During Mr Perrin's tenure as executive director, the profession has grown substantially in number and in strength. Although this growth was the result of a concerted effort by many, it was Mr Perrin's leadership that provided the catalyst for our advancement.

As the first non-DO executive director, Mr Perrin helped to improve the unity of the profession by promoting open dialogue among the divisional societies and the practice affiliates. With the augmentation of the internal public relations department, Mr Perrin played a vital role in enhancing the public's understanding—and acceptance—of osteopathic medicine.

This public awareness has reached new heights with the ongoing Care-A-Van project.

Administratively, the purchase of the AOA central headquarters building during Mr Perrin's tenure has provided the association and its members with a long-term facility to accommodate further growth. The building, located just off Chicago's Magnificent Mile, has enhanced the profession's image as well.

More than just improving our image, Mr Perrin worked to improve membership services. Under his direction, a new professionalism emerged among the AOA staff. A director of membership services was hired and the finance department was reorganized. Computerized membership services and the addition of electronic publishing equipment are just two

examples of the upgraded facilities that streamline day-to-day operations.

Certainly, Mr Perrin has done much more during his almost-quarter-century association with osteopathic medicine than can be enumerated here. In fact, as president of UHSCOM, Mr Perrin will continue to have a hand in shaping the profession's future.

As we await the arrival of a new executive director who will lead osteopathic medicine into its second century as well as the 21st century, we look back on the past decade with pride and gratitude to Mr Perrin for his outstanding leadership and continued commitment to the profession.

THOMAS WESLEY ALLEN, DO
Editor in Chief

Accepting applications for

Executive Director of the American Osteopathic Association, Chicago, Ill.

Send narrative letter on why you feel qualified for this position, plus current résumé or CV.

Qualified DOs and non-DOs may apply.

Send application, in confidence, to Frank J. McDevitt, DO, chairman, AOA Search Committee, 18593 Jamestown Road, Northville, MI 48167-1832.

The EXCEL Study:

48 weeks, 8,245 patients,
362 medical centers,
in the largest-ever U.S.
randomized, double-blind,
placebo-controlled
trial of patients with primary
hypercholesterolemia

*the results
are in...*

For a Brief Summary of Prescribing Information,
please see the last page of this advertisement.

Bradford, R.H. et al.: Expanded clinical evaluation of lovastatin (EXCEL) study results: I. Efficacy in modifying plasma lipoproteins and adverse event profile in 8,245 patients with moderate hypercholesterolemia, *Archives of Internal Medicine*, January 1991.

Lovastatin lowered
Lovastatin lowered
Lovastatin lowered
Lovastatin raised

MEVACOR® (Lovastatin, MSD) is contraindicated in patients who are hypersensitive to any component of the medication; in patients with active liver disease or unexplained persistent transaminase elevations; in pregnant or lactating patients; and in women of childbearing age, except when such patients are highly unlikely to conceive.

For complete details on MEVACOR, including cautionary information regarding myopathy, drug interactions, and liver enzyme monitoring, please refer to the Prescribing Information.

For a Brief Summary of Prescribing Information, please see the last page of this advertisement.

*Mean percent changes from baseline (n=6,582)

**Triglyceride values are median changes.

Dosage ranged from 20 mg q.p.m. to 40 mg b.i.d.

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LDL cholesterol* 24-40%
total cholesterol* 17-29%
triglycerides** 10-19%
LDL cholesterol* 6.6-9.5%

For many patients with primary hypercholesterolemia
(Types IIa and IIb), when diet and other nondrug
therapies are inadequate

MEVACOR[®]
(LOVASTATIN | MSD)

TABLETS, 10 mg 20 mg 40 mg

MSD
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MEVACOR® (LOVASTATIN | MSD)

CONTRAINDICATIONS: Hypersensitivity to any component of this medication.

Active liver disease or unexplained persistent elevations of serum transaminases.

Pregnancy and lactation.

Atherosclerosis is a chronic process and the discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Moreover, cholesterol and other products of the cholesterol biosynthesis pathway are essential components for fetal development, including synthesis of steroids and cell membranes. Because of the ability of inhibitors of HMG-CoA reductase such as MEVACOR® (lovastatin, MSD) to decrease the synthesis of cholesterol and possibly other products of the cholesterol biosynthesis pathway, MEVACOR may cause fetal harm when administered to a pregnant woman. Therefore, lovastatin is contraindicated during pregnancy. Lovastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive. If the patient becomes pregnant while taking this drug, lovastatin should be discontinued and the patient should be apprised of the potential hazard to the fetus.

WARNINGS: Liver Dysfunction: Marked persistent increases (to more than 3 times the upper limit of normal) in serum transaminases occurred in 1.9% of adult patients who received lovastatin for at least one year in clinical trials (see ADVERSE REACTIONS). When the drug was interrupted or discontinued in these patients, the transaminase levels usually fell slowly to pretreatment levels. The increases usually appeared 3 to 12 months after the start of therapy with lovastatin and were not associated with jaundice or other clinical signs or symptoms. There was no evidence of hypersensitivity.

It is recommended that liver function tests be performed during therapy with lovastatin. Serum transaminases, including ALT (SGPT), should be monitored before treatment begins, every 6 weeks for the first 3 months, every 8 weeks during the remainder of 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 the upper limit of normal and are persistent, the drug should be discontinued. Liver biopsy should be considered if elevations are persistent beyond the discontinuation of the drug.

The drug should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease. Active liver disease or unexplained transaminase elevations are contraindications to the use of lovastatin.

As with other lipid-lowering agents, moderate (less than 3 times the upper limit of normal) elevations of serum transaminases have been reported following therapy with MEVACOR (see ADVERSE REACTIONS). These changes appeared soon after initiation of therapy with MEVACOR, were often transient, were not accompanied by any symptoms, and interruption of treatment was not required.

Skeletal Muscle: Rhabdomyolysis has been associated with lovastatin therapy alone, when combined with immunosuppressive therapy including cyclosporine in cardiac transplant patients, and when combined in non-transplant patients with either gemfibrozil or lipid-lowering doses (≥ 1 g/day) of nicotinic acid. Some of the affected patients had preexisting renal insufficiency, usually as a consequence of long-standing diabetes. Acute renal failure from rhabdomyolysis has been seen more commonly with the lovastatin-gemfibrozil combination and has also been reported in transplant patients receiving lovastatin plus cyclosporine.

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with lovastatin. Therefore, patients receiving concomitant lovastatin and erythromycin should be carefully monitored.

Fulminant rhabdomyolysis has been seen as early as 3 weeks after initiation of combined therapy with gemfibrozil and lovastatin but may be seen after several months. For these reasons, it is felt that, in most subjects who have had an unsatisfactory lipid response to either drug alone, the possible benefits of combined therapy with lovastatin and gemfibrozil do not outweigh the risks of severe myopathy, rhabdomyolysis, and acute renal failure. While it is not known whether this interaction occurs with fibrates other than gemfibrozil, myopathy and rhabdomyolysis have occasionally been associated with the use of other fibrates alone, including clofibrate. Therefore, the combined use of lovastatin with other fibrates should generally be avoided.

Physicians contemplating combined therapy with lovastatin and lipid-lowering doses of nicotinic acid or with immunosuppressive drugs should carefully weigh the potential benefits and risks and should carefully 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 of either drug. Periodic CPK determinations may be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy. The monitoring of lovastatin drug and metabolite levels may be considered in transplant patients who are treated with immunosuppressives and lovastatin.

Lovastatin therapy should be temporarily withheld or discontinued in any patient with an acute, serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis, including severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine, and electrolyte disorders, and uncontrolled seizures.

Myalgia has been associated with lovastatin therapy. Transient, mildly elevated creatine phosphokinase levels are commonly seen in lovastatin-treated patients. However, in clinical trials, approximately 0.5% of patients developed a myopathy, i.e., myalgia or muscle weakness associated with markedly elevated CPK levels. Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness, or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. Lovastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.

Most of the patients who have developed myopathy (including rhabdomyolysis) while taking lovastatin were receiving concomitant therapy with immunosuppressive drugs, gemfibrozil, or lipid-lowering doses of nicotinic acid. In clinical trials, about 30% of patients on concomitant immunosuppressive therapy including cyclosporine developed myopathy; the corresponding percentages for gemfibrozil and niacin were approximately 5% and 2%, respectively.

In 6 patients with cardiac transplants taking immunosuppressive therapy including cyclosporine concomitantly with lovastatin 20 mg/day, the average plasma level of active metabolites derived from lovastatin was elevated to approximately 4 times the expected levels. Because of an apparent relationship between increased plasma levels of active metabolites derived from lovastatin and myopathy, the daily dosage in patients taking immunosuppressants should not exceed 20 mg/day (see DOSAGE AND ADMINISTRATION). Even at this dosage, the benefits and risks of using lovastatin in patients taking immunosuppressants should be carefully considered.

PRECAUTIONS: General: Before instituting therapy with MEVACOR, an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, weight reduction in obese patients, and to treat other underlying medical problems (see INDICATIONS AND USAGE).

Lovastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with lovastatin.

Homozygous Familial Hypercholesterolemia: MEVACOR® (lovastatin, MSD) is less effective in patients with the rare homozygous familial hypercholesterolemia, possibly because these patients have no functional LDL receptors. MEVACOR appears to be more likely to raise serum transaminases (see ADVERSE REACTIONS) in these homozygous patients.

Drug Interactions: Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS, Skeletal Muscle.

Coumarin Anticoagulants: In a clinical trial in warfarin-treated patients designed specifically to observe a potential effect of lovastatin on the prothrombin time, lovastatin in dosages up to 40 mg b.i.d. did not produce any consistent alteration of the anticoagulant action of warfarin. However, since the drug was marketed, clinically evident bleeding and/or increased prothrombin time have been reported in a few patients taking coumarin anticoagulants concomitantly with lovastatin. The causal relationship to lovastatin is unclear. Nevertheless, it is recommended that in patients taking anticoagulants, prothrombin time be determined before starting lovastatin and frequently enough during early therapy to insure that no significant alteration of prothrombin time occurs. Once a stable prothrombin time has been documented, prothrombin times can be monitored at the intervals usually recommended for patients on coumarin anticoagulants. If the dose of lovastatin is changed, the same procedure should be repeated. Lovastatin therapy has not been associated with bleeding or with changes in prothrombin time in patients not taking anticoagulants.

Antipyrine: Antipyrine is a model for drugs metabolized by the microsomal hepatic enzyme system (cytochrome P450 system). Because lovastatin had no effect on the pharmacokinetics of antipyrine, interactions with other drugs metabolized via this mechanism are not expected.

Propranolol: In normal volunteers, there was no clinically significant pharmacokinetic or pharmacodynamic interaction with concomitant administration of single doses of lovastatin and propranolol.

Digoxin: In patients with hypercholesterolemia, concomitant administration of lovastatin and digoxin resulted in no effect on digoxin plasma concentrations.

Other Concomitant Therapy: Although specific interaction studies were not performed, in clinical studies, lovastatin was used concomitantly with beta blockers, calcium channel blockers, diuretics, and nonsteroidal anti-inflammatory drugs (NSAIDs) without evidence of clinically significant adverse interactions.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 21-month carcinogenic study in mice, a statistically significant ($p < 0.05$) increase in the incidence of hepatocellular carcinomas and adenomas was observed at doses of 500 mg/kg/day (312 times the maximum recommended human dose) of lovastatin. These changes were not seen in mice given doses of 20 and 100 mg/kg/day (12.5 and 62.5 times the maximum recommended human dose).

A statistically significant increase ($p = 0.05$) in the incidence of pulmonary adenomas was seen in female mice receiving 500 mg/kg/day (312 times the maximum recommended human dose); no similar changes were seen in males at any dose or in females receiving 20 or 100 mg/kg/day (12.5 or 62.5 times the maximum recommended human dose). Because the incidence of pulmonary tumors was within the range of untreated animals in studies of similar duration, the relationship of this latter change to treatment is not known.

In addition, an increase in the incidence of papilloma in the non-glandular mucosa of the stomach was observed in mice receiving 100 and 500 mg/kg/day (62.5 and 312 times the maximum recommended human dose); no increase was seen at a dosage of 20 mg/kg/day (12.5 times the maximum recommended human dose). The glandular mucosa was not affected. The human stomach contains only glandular mucosa. Importantly, there is a strong association between this change and hyperplasia of the squamous epithelium (acanthosis) in this region; acanthosis is a characteristic change observed in the non-glandular mucosa of rodents treated with HMG-CoA reductase inhibitors and is most probably a result of inhibition of the reductase in this tissue.

Similar squamous epithelium is found in the esophagus and anorectal junction of the mouse and rat; however, no evidence of a similar drug-induced hyperplastic response was observed in these tissues in studies of up to 21 months in the mouse given up to 500 mg/kg/day (312 times the maximum recommended human dose), or in a study of 24 months in the rat given 180 mg/kg/day (112 times the maximum recommended human dose).

In a 24-month carcinogenicity study in rats, there was a positive dose response relationship for hepatocellular carcinogenicity in males (unadjusted $p = 0.025$). However, because the incidence of hepatocellular carcinogenicity observed in male rats in this study is similar to that observed spontaneously in this strain of rat, the implications of this finding are unclear.

Drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration and giant cell formation were seen in dogs starting at 20 mg/kg/day (12.5 times the maximum recommended human dose). The clinical significance of these findings is unclear.

No evidence of mutagenicity was observed in a microbial mutagen test using mutant strains of *Salmonella typhimurium* with or without rat or mouse liver metabolic activation. In addition, no evidence of damage to genetic material was noted in an *in vitro* alkaline elution assay using rat or mouse hepatocytes, a V-79 mammalian cell forward mutation study, an *in vitro* chromosome aberration study in CHO cells, or an *in vivo* chromosomal aberration assay in mouse bone marrow.

No drug-related effects on fertility were found in studies with rats.

Pregnancy: Pregnancy Category X: See CONTRAINDICATIONS.

Lovastatin has been shown to produce skeletal malformations in the rat fetus at doses of 800 mg/kg/day (500 times the maximum recommended human dose). At similar doses in mice, an increase in skeletal malformations was observed. These individual changes are within the range of those observed spontaneously in this strain of mouse. No drug-induced changes were seen in either species at doses of up to 80 mg/kg/day (50 times the maximum recommended human dose). No skeletal malformations were noted in rabbits at up to 15 mg/kg/day (highest tolerated dose—about 9 times the maximum recommended human dose). There are no data in pregnant women.

Nursing Mothers: Studies in rats have shown that lovastatin is excreted in the milk. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from MEVACOR, women taking lovastatin should not nurse their infants (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in children have not been established. Because children are not likely to benefit from cholesterol lowering for at least a decade and because experience with this drug is limited (no studies in subjects below the age of 20 years), treatment of children with lovastatin is not recommended at this time.

ADVERSE REACTIONS: MEVACOR is generally well tolerated; adverse reactions usually have been mild and transient. Less than 1% of patients were discontinued from controlled clinical studies due to adverse experiences attributable to MEVACOR; about one-third of these patients were discontinued due to increases in serum transaminases.

Clinical Adverse Experiences: Adverse experiences reported in patients treated with MEVACOR® (lovastatin, MSD) in controlled clinical studies are shown in the table below:

	MEVACOR (N = 613)	Placebo (N = 82)	Cholestyramine (N = 88)	Pro (N = 10)
Gastrointestinal				
Constipation	4.9	—	34.1	—
Diarrhea	5.5	4.9	8.0	—
Dyspepsia	3.9	—	13.6	—
Flatulence	6.4	2.4	21.6	—
Abdominal pain/cramps	5.7	2.4	5.7	—
Heartburn	1.6	—	8.0	—
Nausea	4.7	3.7	9.1	—
Musculoskeletal				
Muscle cramps	1.1	—	1.1	—
Myalgia	2.4	1.2	—	—
Nervous System/Psychiatric				
Dizziness	2.0	1.2	—	—
Headache	9.3	4.9	4.5	—
Skin				
Rash/pruritus	5.2	—	4.5	—
Special Senses				
Blurred vision	1.5	—	1.1	—
Dysgeusia	0.8	—	1.1	—

Laboratory Tests: Marked persistent increases of serum transaminase have been noted (see WARNINGS).

About 11% of patients had elevations of creatine phosphokinase (levels of at least twice the normal value on one or more occasions) corresponding values for the control agents were cholestyramine, 9%; probucol, 2%. This was attributable to the noncardiac fraction of CPK. Large increases in CPK have sometimes been reported (see WARNINGS, Skeletal Muscle).

Concomitant Therapy: In controlled clinical studies in which lovastatin was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with lovastatin or cholestyramine. Other lipid-lowering agents were not administered concomitantly with lovastatin during controlled clinical studies. In uncontrolled clinical studies, most of the patients who have developed myopathy were receiving concomitant therapy with immunosuppressive drugs, gemfibrozil, or niacin (nicotinic acid) (see WARNINGS, Skeletal Muscle).

Uncontrolled Clinical Studies: The adverse experiences observed in uncontrolled studies were similar to those seen in controlled clinical studies. Abnormal liver function tests were observed at a higher incidence than in the controlled studies (see WARNINGS, Liver Dysfunction). Myalgia (myalgia with marked CPK elevations) was reported in approximately 0.5% of patients (see WARNINGS, Skeletal Muscle).

Causal Relationship Unclear: Nervous System: Peripheral neuropathy has been reported; the relationship to lovastatin is uncertain. Vague, evoked response, nerve conduction measurements, and electromyography in over 30 patients showed no evidence of neurotoxic effects of lovastatin.

Eye: Lens opacities (see CLINICAL PHARMACOLOGY, Clinical Studies).

Post-marketing Experience: Additional adverse experiences occurred since the drug was marketed are listed below:

Clinical Adverse Experiences

Gastrointestinal: Hepatitis, chronic active hepatitis, cholestasis, jaundice, fatty change in liver, and, rarely fulminant hepatic necrosis, rhinitis, and hepatoma; anorexia, vomiting.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus-like syndrome, polymyositis, rheumatism, vasculitis, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, and dyspnea.

Nervous System/Psychiatric: Psychic disturbances, including anxiety, paresthesia.

Skin: Erythema multiforme, including Stevens-Johnson syndrome; toxic epidermal necrolysis.

Causal Relationship Unknown

Eye: Progression of cataracts (lens opacities).

Gastrointestinal: Pancreatitis, stomatitis.

Skin: Alopecia.

Nervous System/Psychiatric: Depression, insomnia.

Metabolic: Edema.

Clinical Laboratory Test Findings

Liver Function Tests: Liver function test abnormalities, including elevated alkaline phosphatase and bilirubin.

Thyroid Function Tests: Rare reports of thyroid function test abnormalities in patients taking concomitant thyroxine.

OVERDOSE: The oral LD₅₀ of MEVACOR in mice is 20 g/kg.

Five healthy human volunteers have received up to 200 mg of lovastatin as a single dose without clinically significant adverse experiences. A few cases of accidental overdose have been reported; no patients had specific symptoms, and all patients recovered without sequelae. The minimum dose taken was 5 to 6 g.

Until further experience is obtained, no specific treatment of overdose with MEVACOR can be recommended.

The diability of lovastatin and its metabolites in man is not known at present.

DOSAGE AND ADMINISTRATION: The patient should be placed on a standard cholesterol-lowering diet before receiving MEVACOR and should continue on this diet during treatment with MEVACOR. MEVACOR should be given with meals.

The recommended starting dose is 20 mg once a day given with evening meal. The recommended dosing range is 20 to 80 mg/day in single or divided doses; the maximum recommended dose is 80 mg/day. Adjustments of dosage should be made at intervals of 4 weeks or more. Doses should be individualized according to the patient's response (Tables I to IV under CLINICAL PHARMACOLOGY, Clinical Studies for dosage response).

For those patients with severely elevated serum cholesterol level (i.e., > 300 mg/dL [7.8 mmol/L] on diet), MEVACOR may be initiated at 40 mg/day.

In patients taking immunosuppressive drugs concomitantly with lovastatin (see WARNINGS, Skeletal Muscle), therapy should begin at 10 mg of MEVACOR and should not exceed 20 mg/day.

Cholesterol levels should be monitored periodically and consideration should be given to reducing the dosage of MEVACOR if cholesterol level falls below the targeted range.

Concomitant Therapy: Preliminary evidence suggests that the cholesterol-lowering effects of lovastatin and the bile acid sequestrant, colestyramine, are additive.

Dosage in Patients with Renal Insufficiency: In patients with severe renal insufficiency (creatinine clearance < 30 mL/min), dosage increases above 20 mg/day should be carefully considered and, if deemed necessary, implemented cautiously (see CLINICAL PHARMACOLOGY and WARNINGS, Skeletal Muscle).

For more detailed information, consult your MSD Representative or Prescribing Information, Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19486. JOMC49R(5)