



INSTITUTE FOR CLINICAL  
SYSTEMS IMPROVEMENT

---

# Health Care Guideline for Patients and Families

---

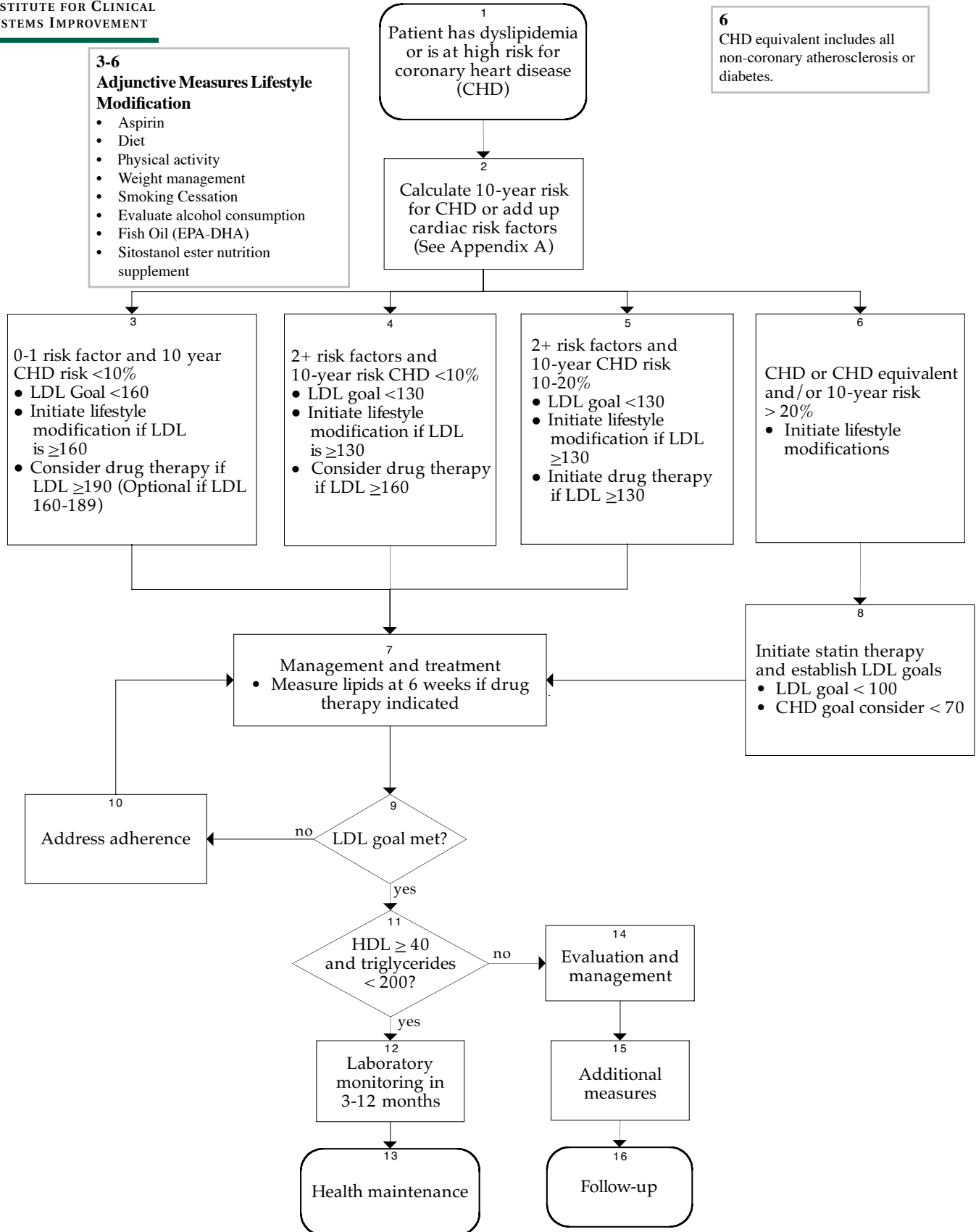
The information contained in this document is a translation of an ICSI health care guideline from medical terminology to commonly used and easily understood English. It is intended for patients, their families and/or caregivers, and other individuals who have little or no health care training. The medical terms used in this document are followed by italicized statements in parentheses that explain the meaning of the term.

The *Lipid Management in Adults for Patients and Families* should not be construed as medical advice or medical opinion related to any specific facts or circumstances. If you are seeking medical advice, you are urged to consult a health care professional regarding your own situation and any specific medical questions you may have. In addition, you should seek assistance from a health care professional in interpreting any *ICSI Health Care Guideline for Patients and Families* and applying it in your individual case.

This translation is available to view and download as a portable document file (PDF). Adobe Acrobat Reader is required. The document can be copied for individual use, and physicians and other direct providers of care may distribute copies to their patients.

All other copyright rights are reserved by the Institute for Clinical Systems Improvement, Inc. (ICSI). ICSI assumes no liability for any adaptations or revisions or modifications made to this *Health Care Guideline for Patients and Families*.

The next scheduled revision will occur within 24 months.



## Table of Contents

<b>Algorithm</b> .....	1
<b>Foreword</b> .....	3
<b>Flow Chart Notes</b> .....	4-10
Introduction .....	4
Patient has Dyslipidemia ( <i>Abnormal Lipid Levels</i> ) or is at High Risk for Coronary Heart Disease (CHD) .....	4
Calculate 10-Year Risk for CHD or Add Up Cardiac Risk Factors .....	4-5
Lifestyle Modification/Drug Therapy/Additional Measures .....	5-6
Management and Treatment .....	6-7
Statin Therapy.....	7-8
LDL Goal Met?.....	8-9
Address Adherence .....	9
HDL is 40 or More and Triglyceride is Less Than 200? .....	9
Laboratory Monitoring in 3-12 Months .....	10
Health Maintenance.....	10
Evaluation and Management .....	10
Additional Measures.....	10
Follow-Up.....	10
<b>Appendix A – Lipid Management in Adults – Risk Calculator</b> .....	11
<b>Appendix B – Omega-3 Fatty Acids</b> .....	12-13
<b>Appendix C – Secondary Causes and Conditions Associated with Hyperlipidemia</b> .....	14
<b>Appendix D – Drug Companion Document</b> .....	15-27
Overview .....	15
Treatment Options for Dyslipidemia ( <i>Abnormal Lipid Levels</i> ).....	16-18
Statins .....	19-20
Fibric Acids .....	21
Niacin .....	22-23
Ethyl Esters of Omega-3 Fatty Acids .....	24
Selective Cholesterol Absorption Inhibitor .....	25
Bile Acid Sequestrants.....	26-27
<b>Appendix E – NCEP Recommendations on Strategies to Improve Adherence</b> .....	28

## Foreword

### What Is an ICSI Health Care Guideline For Patients and Families?

This document is a summary of an ICSI health care guideline that has been "translated" from medical terminology to commonly used and easily understood English. It is intended for patients, their families and/or caregivers, and other individuals who have little or no health care training. The guideline is designed to help you understand the diagnostic and treatment options recommended for a particular condition. Being better informed should help you during discussions with your physician or other health care professional.

However, an ICSI Health Care Guideline for Patients and Families should not be construed as medical advice or medical opinion related to any specific facts or circumstances. If you are seeking medical advice, please consult a health care professional regarding your particular situation, any specific medical questions you may have, and the application of the guideline to your individual case.

This translation can be viewed and downloaded as a portable document file (PDF) on <http://www.icsi.org>. Adobe Acrobat Reader is required. The document may be copied for individual use, and health care professionals may distribute copies to patients. Instructions for accessing these guidelines are listed below:

- <http://www.icsi.org>
- click on "For Patients" at the top
- select the category you are interested in

You will find the healthcare guideline for Patients and Families as well as links to other resources for that topic.

All other copyright rights are reserved by ICSI. ICSI assumes no liability for any adaptations or revisions or modifications made to this guideline.

### How are ICSI Health Care Guidelines Developed?

ICSI, the Institute for Clinical Systems Improvement, is an independent, non-profit organization dedicated to helping identify best clinical practices for health care professionals. A significant part of ICSI's mission is to create and maintain clinical guidelines to help health care professionals evaluate and treat patients with a particular condition. A team of experts develops each ICSI guideline, using the most current information about a particular condition. This information is carefully evaluated, reviewed, and compiled before it is published.

Each guideline recommends a strategy for making decisions, but it is not intended to replace a physician's judgment or establish a protocol (strict plan) for all patients. One set of recommendations is rarely the only approach to a problem.

### How Do I use the Flowchart?

The flowchart represents the major steps in the process of evaluating and treating a patient with a particular condition. Numbers within the flowchart correspond with a flowchart note. Some flowchart boxes will not have a corresponding note.

# Flowchart Notes

## Introduction

Fats in the blood are called lipids, but many people are more familiar with the terms "cholesterol" and "triglycerides." Abnormal lipid levels can contribute to coronary heart disease, peripheral vascular (*blood vessel*) disease, stroke, and other health problems. Managing abnormal lipid levels (dyslipidemia) is therefore an important health care goal.

Recommended lipid levels for adults are shown in the table below.

	Total Cholesterol (mg/dL)	Triclycerides (mg/dL)	HDL ("good" cholesterol) (mg/dL)	LDL ("bad" cholesterol) (mg/dL)
Ideal	Less than 200	Less than 150	More than 40	Less than 100

This guideline describes the treatment of adults between the ages of 20 and older who are dyslipidemic (*having abnormal lipid levels*).

### 1. Patient Has Dyslipidemia (*Abnormal Lipid Levels*) or is at High Risk for Coronary Heart Disease (CHD)

Other medical conditions that cause abnormal lipid levels should be considered and treated when appropriate. Diet and exercise are the cornerstones of treatment for patients who have dyslipidemia (*abnormal lipid levels*) and no symptoms. Patients with an elevated LDL-cholesterol level should begin the American Heart Association (AHA) Step I diet and an individualized program of regular aerobic exercise. A diet low in fat, especially saturated fat, and high in soluble fiber is recommended. Overweight patients should be advised to reduce their calorie intake to achieve weight loss. Patients should follow the diet and exercise program for a reasonable amount of time to determine whether their LDL-cholesterol level is lowered to the target range. For many patients without symptoms, a diet and exercise program is sufficient.

Patients with a history of non-coronary atherosclerosis (*hardening of the blood vessels in the body not associated with the heart*) including carotid occlusive disease (*narrowing of blood vessels in the neck*), abdominal aneurysm (*an abnormal ballooning in the wall of the blood vessel*), or peripheral vascular disease (*blood vessels in the arms and legs*) or who have diabetes are at high-risk for CHD and are considered CHD-equivalent.

### 2. Calculate 10-Year Risk for CHD or Add Up Cardiac Risk Factors

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) defines high risk as a net of two or more CHD risk factors, which warrants more aggressive intervention. Identified risk factors are:

- Age 45 years or older for men; age 55 years or older, or premature menopause without hormone therapy for women. CHD rates are higher in the elderly than in the young, and higher in men more than in women of the same age.
- A family history of premature CHD, defined as definite myocardial infarction (MI; *heart attack*) or sudden death before age 55 in the father or a male primary relative (*sibling or parent*), or before age 65 in the mother or a female primary relative.

- Currently smoking.
- Hypertension (*high blood pressure*), defined as blood pressure greater than 140/90 mmHg (confirmed by measurement on several occasions) or current use of any anti-hypertensive medication.
- Low HDL-cholesterol level (less than 40 mg/dL).
- Nontraditional risk factors such as C-Reactive protein (CRP - *a protein that can indicate inflammation*) and total homocysteine (*amino acid that can irritate blood vessels*) have been shown to have some predictive values in screening for vascular disease. The value of screening for these risk factors has not yet been proven.

See Appendix A, "Lipid Management in Adults – Risk Calculator."

Obesity and physical inactivity are not listed as risk factors, but should be considered as targets for intervention. Obesity operates through other risk factors (hypertension [*high blood pressure*], hyperlipidemia [*high lipid levels*], decreased HDL-cholesterol, and diabetes mellitus).

If HDL-cholesterol is 60 mg/dL or higher, one risk factor may be subtracted because high HDL-cholesterol levels decrease CHD risk. For example, if a patient has three risk factors but his or her HDL-cholesterol level is 60 mg/dL or higher, one risk factor is subtracted, leaving a total of two risk factors.

Please refer to Appendix B, "Omega-3 Fatty Acids," and Appendix C, "Secondary Causes and Conditions Associated with Hyperlipidemia," for more information.

### 3-6. Lifestyle Modification/Drug Therapy/Additional Measures

Changes in lifestyle include diet, aerobic exercise, weight management, aspirin, evaluation of alcohol consumption, fish oil (EPA-DHA), smoking cessation, and nutritional supplements containing sitostanol ester (*a substance from a plant seed used in margarine and salad dressings to help lower cholesterol*). To avoid unintended toxic effects from vitamins, patients should be cautioned not to exceed recommended doses.

Vitamin E supplements should not be used. Studies have shown no benefit in preventing clinical outcomes and smaller studies suggest a decrease in the beneficial effects of statin medications and cause a progression of CHD.

The decision to begin drug therapy must be based on a clinical discussion with the patient in which the evidence-based outcome data, possible side effects, and costs are weighed.

Please refer to Appendix B, "Omega-3 Fatty Acids," and Appendix D, "Drug Companion Document," for additional information.

Patients with risk factors for CHD but no history of disease who receive lipid-lowering therapy are likely to experience a decreased risk of CHD. This, however, has no effect on all-cause mortality (*death due to all causes*).

In patients with a history of CHD (including unstable angina [*chest pain caused by CHD*] and acute MI [*heart attack*]), treatment with statins (*medication that lowers lipids*) has consistently shown a decreased risk of death from CHD.

#### Occlusive Vascular Disease (OVD)

OVD is defined as a diagnosis of carotid occlusive vascular disease (*narrowing of blood vessels in the neck*), peripheral vascular disease (*blood vessels in the arms and legs*), or both. Patients with OVD are at increased risk for CHD, even without clinical symptoms of CHD. Physicians should help such patients decide whether aggressive lipid lowering is indicated. (Patients who need aggressive lipid lowering can

be managed according to the "Patients with Known CHD" flowchart in this guideline.) For patients with a history of stroke or cerebrovascular (*blood vessels in the brain*) atherosclerosis (*fatty deposits in the arteries*), aggressive treatment with a statin-based regimen (*medication that lowers lipids*) may be advisable.

### Metabolic Syndrome

Specific recommendations for the management of lipid disorders in people with metabolic syndrome have been described in recent national guidelines. The recommendations emphasize lifestyle management (weight loss, physical activity, dietary fat restriction). However, the risk of OVD is increased in these individuals, making lipid treatment complex. Specific treatment targets and recommendations have not been fully clarified. Further data will be required before more specific recommendations regarding the diagnosis and treatment of lipid disorders in this syndrome can be developed. These issues will be addressed in detail in future revisions of the guideline as more definitive data become available.

#### Other management strategies (therapeutic lifestyle changes):

- Diet
- Aerobic exercise
- Weight management
- Smoking Cessation
- Aspirin
- Sterol and stanol ester if taken as directed. Stanol ester is more effective and maintains efficacy longer.
- Fish oil (EPA-DHA)

## 7. Management and Treatment

The patient should receive dietary instruction through a class or individually from a registered dietitian or trained professional. Additional measures (see Note #15, "Additional Measures") should be reinforced. Other health issues should be considered. Lipid levels should be checked again in 6 weeks. Use of medication is based on risk level and patient preference. Referral to a lipid clinic should be considered.

No primary prevention studies have addressed the use of lipid-lowering drugs in persons at low risk for CHD, and there is no evidence to support drug treatment in this population. The incidence of CHD in men under 40 and premenopausal women is very low, and drug treatment in these groups is discouraged.

Primary prevention studies of lipid-lowering drugs have not shown a decrease in mortality, although most studies have shown about a 30 percent reduction in CHD events. Study populations have consisted predominately of middle-aged men, some with other risk factors. Similar benefit in higher-risk women can be assumed but has not been demonstrated. The major primary prevention studies have been 4-6 year studies.

The decision to begin and continue lipid-lowering drugs should be made together by the patient and the physician.

Please refer to Appendix D, "Drug Companion Document" for additional information.

**Table 4: Primary Prevention for CHD**

Therapy	Population
Statin	Men > 45
Statin	Men > 45 and HTN
Statin	Men > 45 and FHx
Statin	Men > 45 / Women > 55 with HDL-cholesterol < 50, LDL-cholesterol > 130
Aspirin	Men > 50
Estrogen	Pmenop Women > 50

Abbreviations:

Statin – medication that lowers lipids

HTN – hypertension (*high blood pressure*)

FHx – family history of CHD (*heart disease*)

Pmenop – post menopausal

## 8. Statin Therapy

Recent studies indicate that for patients with coronary artery disease or coronary artery disease equivalents, statin treatment (*medication that lowers lipids*) significantly reduces cardiovascular (*heart*) mortality (*death*) and major CV (Cardiovascular Disease - *heart disease*) events regardless of baseline LDL levels. These data support the use of statins in such high-risk patients regardless of LDL level.

Specific statin (*medication that lowers lipids*) and dose should be selected based on cost and amount of lipid lowering required.

Thus, for care of patients with established CHD (Coronary Heart Disease) or CHD equivalent (which include occlusive carotid (*narrowing of blood vessels in the neck*) disease, peripheral vascular disease (*blood vessels in the arms and legs*), abdominal aortic (*a weakening of the artery wall in one of the body's main blood vessels*) aneurysm, or diabetes), the use of statin therapy is recommended.

Bedtime or evening dose of statin is more effective (higher cholesterol synthesis).

To maximize absorption, Lovastatin needs to be taken with food but lovastatin SR should be taken on an empty stomach.

Dosage adjustments should not be made more often than every 4 weeks after a fasting lipid panel.

### Patients Unable to Use Statin Therapy

If patients are intolerant to a statin, clinicians are encouraged to have the patient try the other statins in reduced doses before ruling out all statins. If patients are unable to take a statin, then fibric acids, niacin, and ezetimibe and bile-acid sequestrants are available.

### Safety Considerations in Prescribing Statins in Primary Care Settings

#### DO

- Check baseline renal (*kidney*) function and thyroid function (TSH) prior to initiating statin therapy.
- Check ALT or AST (*enzymes found in the blood from the heart, liver, and muscles*) levels prior to prescribing a statin and after any planned increase in statin dose.

- Consider the potential for drug-drug interactions when prescribing statins. Vitamin E intake may reduce the benefit of statins.
- Be alert for patient characteristics that may increase the risk for myopathy (*disorder of the muscles*) during statin therapy, such as advanced age (particularly elderly women), renal (*kidney*) or liver impairment, diabetes with evidence of hepatic (*liver*) fatty changes, hypothyroidism (*under active thyroid*), drugs of abuse (amphetamines, phencyclidine, heroin, cocaine), surgery, trauma, ischemia-reperfusion (*restoring blood flow to heart tissue*), debilitated status, excessive alcohol intake, heavy exercise.
- Provide patient education regarding recognition and reporting of symptoms of myopathy (*disorder of the muscles*) during statin therapy.
- Counsel patients to discontinue statin therapy during a short course of a macrolide or ketolide antibiotic (eg, azithromycin, clarithromycin, erythromycin, or telithromycin).
- Suspect myopathy (*disorder of the muscles*) when a statin-treated patient complains of unexplained, generalized muscle pain, tenderness, or weakness. Joint pain, nocturnal (*night*) leg cramps, or localized pain are not symptoms of myopathy.
- Check CK (*enzyme found in the blood from the heart, liver, and muscles*) levels when a patient reports symptoms of myopathy.
- If CK levels are less than 5 times upper limit of normal, repeat measurement in 1 week.
- If CK levels are elevated to 5 times upper limit of normal or greater, discontinue statin therapy and monitor serum CK levels.
- Assess for signs of dehydration or renal compromise in patients with myopathy.
- Consider referral for patients requiring combination lipid-lowering therapy or document the need for this therapy, such as lack of response to monotherapy (*single drug therapy*) in a high-risk patient.
- When adding a statin to the regimen of a patient already receiving a fibrate, initiate at the lowest starting dose of statin.
- Consider the differences in pharmacokinetic (*the interaction of drugs with the body*) profiles among statins, particularly in patients requiring long-term therapy with drugs that are CYP3A4 substrates, inhibitors (*enzyme used in drug metabolism that either increases or decreases drug effectiveness*), or both.

**DON'T**

- Prescribe statin-fibrate combination therapy in patients with the following conditions: impaired liver or renal (*kidney*) function (creatinine level greater than 2.0mg/dL), cyclosporine or tacrolimus therapy, long-term macrolide antibiotic therapy or azole antifungal therapy, advanced age (greater than 70 years), skeletal muscle conditions.
- Prescribe high-dose statin therapy for elderly patients and patients with renal insufficiency, or in combination with fibrates or cyclosporine.
- Vitamin E may reduce the benefit of statins or of statin-niacin combination therapy. Vitamin E does not appear to reduce the risk of major cardiovascular events.

**9. LDL Goal Met?**

Patients with coronary heart disease (CHD) have an LDL goal less than 70 mg/dL. A recent trial provides evidence that intensive statin therapy to reduce LDL-cholesterol levels below 100 mg/dL showed substantial clinical benefit in patients with stable CAD.

If lipid goals are not met, it is important to intensify therapy until goals are reached. Intensifying lipid treatment within four months of an abnormal LDL value occurs less than 20% of the time. This problem, referred to as "clinical inertia," is a major obstacle to improved lipid management.

Clinical inertia is defined as failure to intensify therapy at an office visit when the patient is above their evidence-based goal. Studies at HPRF (Health Partners Research Foundation) suggest that in high-risk patients such as those with diabetes or heart disease, clinical inertia may be found at over half the office visits.

Organized efforts to use decision support tools with or without electronic medical records may help reduce the problem of clinical inertia.

## 10. Address Adherence

Asking non-threatening, open-ended questions during patient interviews can be a useful method of assessing adherence with drug therapy. The interview should include probing for factors that contribute to non-adherence, including adverse reactions, misunderstandings of asymptomatic (*showing no symptoms*) or chronic disease treatment, depression, cognitive impairment (*inability to understand intellectually*), complex dosing regimens, and financial constraints.

- A. Assess the patient's knowledge of his/her medication and medical condition:

"Can you explain why you are taking this medication?"

"How do you take your medication (with food or on an empty stomach; in the morning or the evening)?"

- B. Assess the patient's medication administration process:

"Many patients have difficulty remembering to take their medication. From what you recall, have you ever had trouble remembering to take your medication?"

"How do you remember to take your medication each day? Do you use a reminder device such as a pill box or alarm?"

- C. Assess the patient's barriers to compliance:

"What is the most difficult task for you in reaching your cholesterol goal?"

"Are you comfortable with your ability to follow the treatment plan that we have designed for you?"

"Are you experiencing any unusual symptoms that you fear may be due to your medication?"

"Is the cost of your medication interfering with your treatment?"

For more information on adherence, please refer to Appendix E, "NCEP (National Cholesterol Education Program) Recommendations on Strategies to Improve Compliance."

## 11. HDL is 40 or More and Triglyceride is Less Than 200?

If the triglyceride level exceeds 400 mg/dL, the LDL-cholesterol level cannot be calculated according to the Friedewald formula (*used to determine LDL-cholesterol*). In such cases, a direct measurement of LDL-cholesterol, where available, can be used.

Non-HDL cholesterol becomes a secondary target when triglycerides are 200-499. The non-HDL target is 30 mg/dL higher than the LDL target. Non-HDL cholesterol is calculated by the formula: non-HDL cholesterol = Total cholesterol – HDL-cholesterol.

## 12. Laboratory Monitoring in 3-12 Months

Refer to Appendix D, "Drug Companion Document."

## 13. Health Maintenance

Health maintenance includes periodic monitoring, risk factor modification, and reinforcement of additional measures (see Note #15, "Additional Measures.")

## 14. Evaluation and Management

Evaluation of elevated triglycerides includes screening for diabetes and hypothyroidism (*underactive thyroid*), and considering other health problems. If triglycerides are greater than 500, triglyceride-lowering drugs become the first-line therapy. The clinician may wish to consider the use of fibric acid and niacin or statin therapy.

Uncontrolled glucose levels in patients with diabetes contribute to hypertriglyceridemia (*high triglyceride levels*). Glucose levels in patients with diabetes should be under control to bring triglyceride levels under control.

Please refer to Appendix B, "Omega-3 Fatty Acids," Appendix C, "Secondary Causes and Conditions Associated with Hyperlipidemia," and Appendix D, "Drug Companion Document."

## 15. Additional Measures

Evidence suggests that adults with elevated lipid levels should follow the Therapeutic Lifestyle Changes or something more aggressive. Nutritional assessment and evaluation should be carried out by a registered dietitian whenever possible. Please refer to Notes #3-6, "Lifestyle Modification/Drug Therapy/Additional Measures" for more information.

## 16. Follow-Up

A lipid profile should be obtained at least annually.

## Appendix A – Lipid Management in Adults - Risk Calculator

Table 1.

Age	Points				
	20-39	40-49	50-59	60-69	70-79
Nonsmoker	0	0	0	0	0
Smoker-Male	8	5	3	1	1
Smoker-Female	9	7	4	2	1

Table 2.

Systolic BP	Points			
	Untreated		Treated	
	Male	Female	Male	Female
<120	0	0	0	0
120-129	0	1	1	3
130-139	1	2	2	4
140-159	1	3	2	5
≥160	2	4	3	6

Table 3.

HDL	Points
≥ 60	-1
50-59	0
40-49	1
< 40	2

Table 6.

Table 1+2+3+4+5 Point Total	10-Year Risk %	
	Male	Female
< 0	< 1	< 1
0	1	< 1
1	1	< 1
2	1	< 1
3	1	< 1
4	1	< 1
5	2	< 1
6	2	< 1
7	3	< 1
8	4	< 1
9	5	1
10	6	1
11	8	1
12	10	1
13	12	2
14	16	2
15	20	3
16	25	4
17	> 30	5
18	> 30	6
19	> 30	8
20	> 30	11
21	> 30	14
22	> 30	17
23	> 30	22
24	> 30	27
> 25	> 30	> 30

Table 4.

Age	Points	
	Male	Female
20-34	-9	-7
35-39	-4	-3
40-44	0	0
45-49	3	3
50-54	6	6
55-59	8	8
60-64	10	10
65-69	11	12
70-74	12	14
75-79	13	16

Table 5.

Age	Points									
	20-39		40-49		50-59		60-69		70-79	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
<160	0	0	0	0	0	0	0	0	0	0
160-199	4	4	3	3	2	2	1	1	0	1
200-239	7	8	5	6	3	4	1	2	0	1
240-279	9	11	6	8	4	5	2	3	1	2
>280	11	13	8	10	5	7	3	4	1	2

There is an "on-line" and a palm format downloadable CV risk calculator that is used in assessing 10-year risk of CV disease used in the ATP III report and this guideline on lipid management. The links are:

On-line calculator: <http://hin.nhlbi.nih.gov/atpiii/calculator.asp?usertype=prof>

Palm format (downloadable): <http://hin.nhlbi.nih.gov/atpiii/riskcalc.htm>

## Appendix B – Omega-3 Fatty Acids

### Omega-3 Fatty Acids

Omega-3 fatty acids are found in fish oil and in some vegetable oils, nuts, seeds and soy. You can get omega-3 fatty acids from some foods or from over-the-counter and prescription supplements. Fish oil contains two important omega-3 fatty acids: EPA (eicosapentanoic acid) and DHA (docosahexanoic acid). Plant sources provide ALA (alpha-linolenic acid). Studies of EPA and DHA, suggest that:

- Doses of up to 1 gram per day reduce risk of heart attacks in high-risk patients.
- Doses of up to 3 grams per day lower serum triglyceride levels.

### Tips for Getting More Omega-3 Fatty Acids

- Use vegetable oils that are high in omega-3 fatty acids. Examples are canola oil, soybean oil, flaxseed oil and walnut oil.
- Select fish from the chart below and eat at least 7 ounces per week. Prepare fish by grilling, baking, broiling or poaching.
- Add walnuts or ground flaxseed to cereals, yogurt and salads. Whole flaxseeds will not work as well – they simply pass through the body undigested.
- Substitute ground flaxseed for fat (butter or oil) in baked products. Try using 3 tablespoons of ground flaxseed instead of 1 tablespoon of oil.
- Snack on edamame (steamed soybeans, sold fresh or frozen).
- Omega-3 fatty acid supplements should be refrigerated and eaten with food. This will reduce the possibility of a mild fishy after taste.

### Fish Sources of Omega-3 Fatty Acids

Serving Size: 3.5 ounces, cooked

**Safety Note:** Pregnant and nursing women and young children should avoid shark, swordfish, king mackerel and tilefish. These contain high levels of mercury. Albacore tuna has more mercury than canned light tuna. Albacore tuna should be limited to no more than 6 ounces per week.

Fish	EPA + DHA content (g/Serving)	Calories/Serving
Farmed salmon	2.15	206
Atlantic herring	2.01	203
Wild salmon	1.84	182
Sardines, canned in tomato sauce	1.35	186
Atlantic mackerel	1.20	262
Farmed rainbow trout	1.15	169
Wild rainbow trout	0.980	150
White tuna, canned in water	0.860	128
Halibut	0.470	140
Shrimp	0.320	99
Fresh yellowfin tuna	0.280	139
Light tuna, canned in water	0.270	116
Atlantic cod	0.160	105

## Plant Sources of Omega-3 Fatty Acids

Food	Amount	Omega-3 fatty acids (g/serving)	Fiber (g/serving)	Calories/Serving
Flaxseed oil	1 tablespoon	7.249	n/a	120
Ground flaxseed	1 tablespoon	1.597	1.9	37
English walnuts	1 tablespoon (7 halves)	1.290	0.9	93
Soy oil	1 tablespoon	0.940	n/a	120
Canola oil,	1 tablespoon	0.862	n/a	120
Tofu, raw, firm	1/2 cup	0.733	2.9	183
Green soybeans, cooked	1/2 cup	0.319	3.8	127
Navy beans, cooked	1 cup	0.213	19.1	255
Wheat germ	1/4 cup	0.208	3.8	104
Avocado, raw	1 cup sliced	0.182	9.8	234
Black walnuts	1 tablespoon (7 halves)	0.155	0.5	48
Kidney Beans, canned	1 cup	0.125	19.1	210
Baked beans, canned	1 cup	0.104	10.4	239

2006 American Dietetic Association Disorders of Lipid Metabolism Tool Kit.

Sources: [www.nal.usda.gov/fnic/foodcomp/search](http://www.nal.usda.gov/fnic/foodcomp/search), [www.nutritiondata.com](http://www.nutritiondata.com), U.S. Food and Drug Administration. *What you need to know about mercury in fish and shellfish*. FDA/CFSAN Consumer Advisory EPA-823-R-04-005. March 2004.

<http://www.cfsan.fda.gov/~dms/admehg3.html>.

## Appendix C – Secondary Causes and Conditions Associated with Hyperlipdemia

		Cholesterol	Triglyceride	HDL-Cholesterol
<b>Drugs</b>				
	Anti-hypertensives:			
	Thiazides	Increase	Increase	
	Loop diuretic			Decrease
	Beta blockers		Increase	Increase/decrease
	Hormones:			
	Glucocorticoids	Increase	Increase	
	Anabolic steroids	Increase		Increase
	Oral contraceptives	Increase/no effect	Increase	Increase/decrease
	Estrogens	Decrease	Increase	Increase
	Progestins	Increase		Decrease
	Growth hormone		Increase	
	Others:			
	Amiodarone	Increase		
	Isotretinoin	Increase	Increase	Decrease
	Cyclosporine	Increase		
<b>Diseases/Conditions</b>				
	Metabolic/Endocrine:			
	Diabetes (esp NIDDM)	Increase	Increase	Decrease
	Hypothyroidism	Increase	Increase	
	Anorexia nervosa	Increase		
	Obesity	Increase	Increase	Decrease
	Pregnancy	Increase	Increase	
	Acromegaly		Increase	
	Hyperuricemia/gout	Increase	Decrease	
	Liver Disorders:			
	Hepatocellular	Increase	Decrease	
	Cholestasis	Increase		Decrease
	Renal Diseases:			
	Nephrotic syndrome	Increase	Increase	Decrease
	Chronic renal failure	Increase/decrease	Increase/decrease	Decrease
	Others:			
	SLE	Increase	Increase	
	Rheumatoid arthritis	Decrease	Decrease	Increase
	Pancreatitis		Increase	
<b>Dietary Factors</b>				
	Alcohol abuse		Increase	Increase
	High fat diet	Increase	Increase	
	Low fat diet	Decrease	Decrease	Decrease
	High cholesterol diet	Increase		
	Weight gain		Increase	
	Very high fiber diet	Decrease		

Sources: McKenney JM, Hawkins DW. "Management of lipid disorders." In Handbook on the Management of Lipid Disorders, 2nd edition. Richmond, VA: National Pharmacy Cholesterol Council, 2001. (Class R)

Stone NJ. "Secondary causes of hyperlipidemia." Med Clin North Am 78:117-41, 1994. (Class R)

## **Appendix D – Drug Companion Document: Overview**

This document may provide assistance to the clinician who initiates and provides ongoing drug therapy for patients with dyslipidemia patient (*abnormal lipid levels*). It includes the following information:

- Treatment options for dyslipidemia (abnormal lipid levels)
- Drug discussions on the following medications (in order of discussion):
  - Statins
  - Fibrates
  - Niacin
  - Ethyl Esters of Omega-3 Fatty Acids
  - Selective cholesterol absorption inhibitor
  - Bile acid sequestrants

Please note: The information is not all-inclusive, and providers should consult manufacturers' product labeling inserts, the *Physician's Desk Reference*, etc., for full prescribing information.

## Appendix D – Drug Companion Document: Treatment Options for Dyslipidemia (Abnormal Lipid Levels)

Type of Dyslipidemia	Lipid Subfractions	Primary Therapy	Secondary Therapy
High LDL-Cholesterol and Triglycerides	LDL ↑    HDL ≥ 40    Trig. > 200	<ul style="list-style-type: none"> <li>Weight loss</li> <li>Physical activity</li> <li>Discontinue smoking</li> <li>No alcohol</li> <li>Improve diabetes mellitus control</li> <li>TLC**</li> </ul>	Statin Niacin* Omega-3 fatty acids
	LDL ↑    HDL < 40    Trig. > 200		Statin Fibric acids Niacin* Omega-3 fatty acids Ezetimide
High LDL-Cholesterol	LDL ↑    HDL ≥ 40	<ul style="list-style-type: none"> <li>Weight loss</li> <li>Physical activity</li> <li>TLC**</li> <li>Discontinue smoking</li> </ul>	Statin Fibric acids Niacin* Ezetimide Bile acid sequestrant
	LDL ↑    HDL < 40		Statin Fibric acids Niacin* Bile acid sequestrant Ezetimide
Isolated Low HDL-Cholesterol	HDL < 40 LDL is normal	<ul style="list-style-type: none"> <li>Physical activity</li> <li>Discontinue smoking</li> </ul>	(drug recommendations for treatment remain controversial except in CHD) Fibric acids*** Statin Niacin*
High Triglycerides		<ul style="list-style-type: none"> <li>Weight loss</li> <li>Discontinue smoking</li> <li>No alcohol</li> <li>Improve diabetes mellitus control</li> <li>TLC**</li> <li>Physical activity</li> </ul>	Fibric acids Niacin* Omega-3 fatty acids

\* Niacin can elevate glucose in patients with diabetes. Review the drug education sheet with the patient when initiating niacin therapy.

\*\* TLC – Therapeutic Lifestyle Change

\*\*\* Although not FDA-labeled, use of gemfibrozil is supported by the VA-HIT Study.

If considering combination therapy or alternative agents, suggest lipid clinic consultation.

**Treatment Options for Dyslipidemia**

<i>Lipid Disorder</i>	<i>Monotherapy</i>	<i>Combination Therapy</i>
Hypercholesterolemia (high LDL, normal HDL, normal triglycerides)	Statin Ezetimibe Niacin Bile acid sequestrant (BAS)	Statin + ezetimibe Statin + niacin Statin + BAS Statin + niacin + BAS Niacin + BAS
Hyperlipidemia (high LDL, high triglyceride, normal or low HDL)	Statin Fibric acids Niacin	Statin + fibric acids Niacin + statin Niacin + fibric acids Niacin + BAS
Hypertriglyceridemia (high triglycerides)	Statin Fibric acids Niacin	Niacin + fibric acids
Isolated low HDL	Fibric acids Statins Niacin	

Reducing LDL cholesterol levels is the primary approach to lowering risk of coronary heart disease (CHD). In some patients, triglycerides may be elevated along with LDL cholesterol; therefore, reducing triglycerides and increasing HDL cholesterol may also be desirable.

Selection of drug therapy is dependent on several factors, including:

- Lipoprotein (*cholesterol/triglyceride compound*) levels and percent reduction needed to attain goal,
- Concurrent drug therapies that could increase the risk of side effects occurring with specific lipid-lowering drugs, and
- Presence of other medical disorders that may affect drug metabolism, increase risk of side effects, or be adversely affected by a specific lipid-lowering drug.

**Monotherapy (*Therapy with One Drug*)**

**Statins are the drugs of choice for lowering LDL-cholesterol and aggressive treatment with statins should be pursued.** Statins also have a modest effect on reducing triglycerides and increasing HDL-cholesterol. Several studies with clinical endpoints support use of statins in primary and secondary prevention.

If a patient is intolerant to a statin, clinicians are encouraged to have the patient try the other statins before ruling them all out. This is especially important in secondary prevention. In the Heart Protection Study, there was no significant difference between the simvastatin 40 mg and placebo groups, in the number of patients with elevations of serum transaminases or unexplained muscle aches or weakness.

**If patients are unable to take statins then bile acid sequestrants, niacin, fibric acids and ezetimibe can be used.**

- Oral estrogen hormone replacement therapy (HRT) may increase triglyceride levels and should generally not be started in postmenopausal women. It may be continued on a case-by-case basis.

- Patients with triglycerides greater than 500 mg/dL are at increased risk of developing acute pancreatitis (*inflammation of the pancreas*). This risk increases significantly as triglycerides increase to greater than 1000 mg/dL. Fibric acids and niacin are the drugs of choice for this condition. Although triglycerides may not normalize with either drug, the risk of pancreatitis is reduced.

#### **Combination Therapy (*Therapy with Two or More Drugs*)**

Although combination therapy is not supported by outcome-based studies, some high-risk patients will require combination therapy. Most likely, these patients will have CHD. Using low doses of two complimentary agents can often reduce LDL-cholesterol to a greater extent than a higher dose of either agent, such as when a statin is combined with either ezetimibe or a bile acid sequestrant, with fewer side effects and possibly less cost. In very resistant cases, triple therapy may be needed.

In patients with mixed hyperlipidemia (*increased LDL-cholesterol and triglycerides*), the primary goal is decreasing LDL-cholesterol. A high triglyceride (200 mg/dL - 499 mg/dL) with hypercholesterolemia (*high cholesterol alone*) signals a relatively high risk of CHD. These patients often have a low HDL-cholesterol. Combination of a cholesterol lowering drug with a triglyceride lowering drug to achieve the non-HDL-cholesterol goal may be most warranted in patients with established coronary artery disease who are at very high risk of recurrent coronary events. Combining nicotinic acid with a statin is favorable for improving LDL-cholesterol, HDL-cholesterol, and triglycerides. Use of fibric acids leads to effective decrease in triglycerides and increased HDL-cholesterol, but effect on LDL-cholesterol is varied.

An increased incidence of severe myopathy (*related to muscles*) has been reported when a statin was combined with nicotinic acid or fibric acids. Most of these cases involved a high dose of the statin in patients with reduced renal function. When these combinations were evaluated in patients with normal renal and liver function in controlled clinical trials, myopathy rarely occurred (incidence of approximately 0.12%). **In general, these combinations need not be avoided but careful patient selection, monitoring, and patient education are required.** These combinations should generally be avoided in patients with acute or serious chronic illness (especially chronic renal disease), patients undergoing surgery or in patients who are already receiving cyclosporine, macrolide antibiotics, nefazodone, azole antifungal agents, or protease inhibitors.

Renal function should be assessed along with a baseline creatinine kinase (CK). Patients must be asked to report promptly any unexplained muscle aches or weakness, especially if malaise or fever is present, flu-like symptoms (without upper respiratory infection), or brownish urine. If these symptoms occur, repeat the CPK test and rule out other causes, for example, recently increased or unusually vigorous exercise. If CPK is rapidly rising or 10 times the upper limit of normal, both drugs should be discontinued until the symptoms subside and the CPK returns to normal.

## Appendix D – Drug Companion Document: Statins

Atorvastatin (Lipitor®), fluvastatin (Lescol®), lovastatin (Mevacor®), lovastatin sustained release (Altacor), pravastatin (Pravachol®), and simvastatin (Zocor®)

### Efficacy

In various studies, statins have been shown to reduce:

- LDL cholesterol levels
- Trygliceride levels
- Major coronary and vascular events
- Mortality

Results vary depending on factors such as baseline lipid levels, medications, dosages, level of coronary heart disease (CHD) risk, and other factors.

### Contraindications

Statins should not be prescribed in the presence of:

- Active liver disease
- Pregnancy
- Lactation

### Potential side effects

The use of statins may result in the following adverse events:

- Mild gastrointestinal complaints, headache, insomnia
- Hepatotoxicity (*injury to the liver*)
- Asymptomatic increases in serum transaminases (*a type of amino acid*).
- Special caution should be used when prescribing statins for patients who abuse alcohol, impaired renal (*kidney*) insufficiency, complex medical problems, a multiple-drug regimen, or advanced age.
- Myopathy (*muscular tissue disease*). Regardless of statin used, patients must be told to report promptly any unexplained muscle aches or weakness, malaise or fever, flu-like symptoms (without upper respiratory infection), or brown urine.

### Combining a statin with a fibric acid

Some key safety points for combining a statin and a fibric acid include:

- Ensure that the patient has normal renal function.
- Ensure that there is no other potential drug interaction that could increase the blood level of the statin or fibric acid.
- Limit the initial statin dose to the starting or intermediate dose. The dose of statin can then be increased cautiously if needed.

- If at all possible, macrolide antibiotics should be avoided in patients on a statin, especially if the patient has renal (*kidney*) insufficiency or is already on another drug or other drugs known to increase the risk of myopathy (*muscular tissue disease*). If a macrolide antibiotic cannot be avoided, consideration should be given to temporarily discontinuing or reducing the dose of the statin. If long-term therapy with the macrolide is needed, change to pravastatin or fluvastatin.
- Patients taking statins that are metabolized by the 3A 4 isoenzyme should be advised to limit consumption of grapefruit to no more than 8 ounces of juice or one-half fruit per day.
- If a patient is on diltiazem or verapamil (*heart disorder medications*), the statin should be initiated with the recommended starting dose, and increased only if warranted. Alternatively, pravastatin or fluvastatin could be used.
- Major surgery is a known risk factor for rhabdomyolysis (*destruction of muscle*). Consider temporarily stopping the statin until the patient is home and ambulatory.

**Dosing considerations**

- Bedtime or evening dose of statin is more effective.
- To maximize absorption, lovastatin needs to be taken with food, but lovastatin SR should be taken on an empty stomach.
- Dose adjustments should not be made more often than every 4 weeks after a fasting lipid panel (*a test that measures cholesterol, triglycerides, HDL and LDL*).

## Appendix D – Drug Companion Document: Fibric Acids

Gemfibrozil (Lopid®), fenofibrate (Tricor®) and fenofibrate micronized (Lofibra®)

### Efficacy

Fibric acids have been shown to:

- Reduce triglycerides
- Increase HDL cholesterol
- Reduce total cholesterol in patients without elevated triglycerides
- Fenofibrate may lower LDL cholesterol more than gemfibrozil but it is less effective than statins.
- Reduce CHD death/nonfatal MI in patients with documented CHD and low HDL cholesterol
- Good for severe hypertriglyceridemia (*high triglyceride levels*) in patients at risk for pancreatitis
- Good for prevention of coronary heart disease (*CHD*) when patient has abnormal lipid triad of depressed HDL cholesterol, elevated LDL cholesterol, and elevated triglycerides (not proven for fenofibrate).
- May be particularly useful in diabetics with mixed hyperlipidemia (*high LDL cholesterol and triglyceride*) and for patients with dysbetalipoproteinemia (*high levels of lipoproteins in the blood*).

### Contraindications

Do not prescribe fibric acids in the presence of:

- Severe hepatic or renal impairment, including primary biliary cirrhosis (*disease of the biliary tract*)
- Pre-existing gallbladder disease

### Potential side effects

- Use with caution in patients with a history of liver disease.
- GI complaints, including abdominal pain and diarrhea
- Hematologic (*related to the blood*) adverse reactions are rare.
- Gallstones and atrial fibrillation are rare.

### Drug interactions

- The use of fibric acids with warfarin may increase the anticoagulant effect; closing monitoring of INR (*blood test used to monitor anticoagulant therapy*) is recommended.
- Risk of myopathy (*muscular tissue disease*) and possibly rhabdomyolysis (*destruction of muscle tissue*) appears increased when fibric acid is taken with statins or cyclosporine, but controlled clinical trials have failed to document a substantial risk in patients with normal renal function.

### Dosing considerations

Dose reduction may be necessary in patients with impaired renal function.

## Appendix D – Drug Companion Document: Niacin

Many crystalline (*immediate release*) and SR (*sustained release*) preparations (Nicobid®, Enduracin®) are available over the counter. The ER (extended release) preparation Niaspan® is a prescription drug.

### Efficacy

- Niacin reduces LDL cholesterol and triglycerides and increases HDL cholesterol.
- Useful for mixed hyperlipidemia (*high LDL cholesterol and triglyceride*)

### Contraindications

Do not prescribe niacin in the presence of:

- Active liver disease
- Active peptic ulcer
- Pregnancy/lactation
- Arterial hemorrhage (*uncontrolled bleeding in an artery*)
- Alcohol abuse
- Severe gout (*a form of arthritis*)

### Potential side effects

- Due to side effects, long-term use of niacin is usually reserved for those at highest short-term risk, that is, those with coronary heart disease (CHD), CHD risk equivalents, or 2+ risk factors with 10-year risk of CHD of 10-20 percent. It is not known whether long-term use of niacin for lower-risk patients with isolated low HDL cholesterol is beneficial.
- Flushing and pruritis (*itching*) of face and upper trunk are common. Tolerance usually develops and patients are more accepting if they know what to expect. With crystalline niacin, flush and pruritis (*itching*) usually occur within 30 minutes and are gone in about that time. Flushing is reduced with SR niacin, but it still occurs.
- Liver toxicity may be associated with niacin. Risk appears greater with SR niacin, and appears dose-related (most occurring with 2 or more grams/day or more of SR niacin).
- Gastrointestinal complaints (*nausea, abdominal pain*) are more common with SR niacin and are minimized by taking the drug with meals.
- Uric acid may be slightly increased. Although rarely, this may lead to acute gout (*a form of arthritis*).
- Niacin use in patients with diabetes is safe. Glucose monitoring is critical for the use of niacin in patients with type 2 diabetes or glucose (*blood sugar*) intolerance. Some adjustment in their hypoglycemic therapy may be needed. The presence of insulin resistance syndrome may mitigate the use of niacin.
- Take care in prescribing niacin in patients with renal (*kidney*) dysfunction.

**Drug interactions**

- Combining niacin with a statin may increase the risk of myopathy (*muscular tissue disease*) based on early experience with lovastatin. Subsequent controlled trials of statins with niacin have reported few or no cases.
- Niacin/statin combinations are useful for decreasing triglycerides and LDL cholesterol and increasing HDL cholesterol.
- When also taking cholestyramine or colestipod, separate ingestion of niacin by 4-6 hours or as great a time as possible.
- There is compelling evidence niacin and statin therapy improve outcomes.

Please refer to information in the niacin and statin sections of this appendix for more information on Advicor (*niaspan/mevacor combination product*).

**Dosing considerations**

- Slow dose titration allows patient to develop tolerance to flushing and pruritis (*itching*).
- Avoiding hot beverages and alcohol at time of dosing is recommended to minimize flushing. A single brand should be used to prevent inadvertent switching to an SR form.
- SR niacin should be titrated and may be started with 125-250 mg, twice a day with meals. Further increases should be based on response and tolerance. A single brand should be used because of significant variability in bioavailability.
- Niaspan® should be taken at bedtime with a low-fat snack. Daily dose should not be increased more than 500 mg every 4 weeks to a maximum dose of 2 grams at bedtime. Women may respond to lower doses.
- Advicor® (Niaspan® with lovastatin) should be taken at bedtime with a low-fat snack.
- To reduce flushing, patients may pretreat with an aspirin or other non-steroidal anti-inflammatory drug approximately 30 minutes prior to taking Advicor®, Niaspan, or niacin.

## **Appendix D – Drug Companion Document: Ethyl Esters of Omega-3 Fatty Acids; Fish Oil (Omacor®)**

### **Efficacy**

- Indicated for adjunct to diet in adults with very high triglyceride levels (greater than 500 mg/dL).
- Effects on cardiovascular mortality and morbidity in patients with very high triglyceride levels is unknown
- Effects on the risk of pancreatitis in patients with very high triglyceride levels is unknown.
- Mean Triglyceride decrease of 45 percent.
- Mean HDL-cholesterol increase of 13 percent.
- Mean LDL-cholesterol increase of 31 percent.
- The percent reductions and elevations are based on patients receiving Omacor® 4 grams per day for four months.
- Withdraw treatment if inadequate response after two months of therapy.
- Effective in lowering serum triglycerides over one year in patients with CHD and combined hyperlipidaemia, whose triglycerides remained elevated despite simvastatin treatment.
- As effective as gemfibrozil in reducing serum triglyceride levels.

### **Safety**

- Use caution in patients with a history of sensitivity or allergy to fish.
- Pregnancy category C: Use in pregnant women only if the potential benefit justifies the potential risk to the fetus.
- Use caution in breast feeding women, due to lack of human safety information.

### **Dosing**

- The daily dose of Omacor is 4 g per day. The daily dose may be taken as a single 4 g dose or as two 2 g doses (2 grams given twice daily).
- Patients should be placed on a standard cholesterol-lowering diet before receiving omega-3-acid ethyl esters and should continue on this diet during treatment with omega-3-acid ethyl esters.

## Appendix D – Drug Companion Document: Selective Cholesterol Absorption Inhibitor

Ezetimibe (Zetia®)

### Efficacy

- Additive effects on LDL-cholesterol reduction
- Reduces LDL cholesterol levels
- LDL cholesterol reduction enhanced when used in combination with statins
- Long-term effects on cardiovascular morbidity and mortality are unknown

### Contraindications

- Pregnancy, lactation
- Moderate to severe hepatic (*related to the liver*) insufficiency
- Do not use with fibrates until studied in humans

### Potential side effects

- Abdominal pain, diarrhea
- Sinusitis (*infection of the sinuses*), arthralgia (joint pain), and back pain
- Short-term tolerability is similar to placebo. Long-term safety is unknown.
- Not recommended for use in patients with moderate to severe hepatic (*related to the liver*) impairment

### Drug interactions

- Coadministration with fibrates is not recommended until human studies have been conducted.
- Cholestyramine decreases ezetimibe absorption. Patients on cyclosporine and ezetimibe should be monitored carefully.
- The use of ezetimibe and statins together should not be used in patients with active liver disease or unexplained persistent elevations in serum transaminases (*a type of amino acid*).

### Dosing considerations

- 10 mg once daily without regard to meals or time of day
- Ezetimibe may be taken at the same time as a statin
- Ezetimibe should be given 2 hours before or 4 hours after bile acid sequestrants.

## Appendix D – Drug Companion Document: Bile Acid Sequestrants

Cholestyramine powder (Questran®, Questran® Lite, Prevalite®), colestipol powder and tablets (Colestid®), and colesevelam tablets (Welchol®)

### Efficacy

Studies have shown that bile acid sequestrants:

- Reduces risk of fatal and no-fatal MI (*heart attack*)
- Lower LDL cholesterol and are especially useful for patients with moderately elevated LDL cholesterol
- May increase triglycerides
- Good for combination therapy – LDL cholesterol reductions are enhanced with low doses of sequestrant – most potent combination is with a statin

### Contraindications

Bile acid sequestrants should be not prescribed in the presence of:

- Complete biliary or bowel obstruction (*obstruction of the biliary tract or bowel*)
- Triglycerides greater than 400 mg/dl or as a monotherapy if triglycerides are greater than 200 mg/dl.
- Family history of dysbetalipoproteinemia (*high levels of lipoproteins in the blood*)
- While not contraindicated in pregnancy and lactation, consideration must be given to potential adverse effects on the baby because of impaired maternal absorption of nutrients and vitamins.

### Potential side effects

- Not systemically absorbed – side effects limited to gastrointestinal tract, including bloating and belching
- With cholestyramine and colestipol, dosing is limited by patient tolerance of constipation. Constipation may occur less often with colesevelam.
- Patients with phenylketonuria (*inherited metabolic disease – PKU*) should know that Questran® Lite, Prevalite®, and flavored colestipol powder contain aspartame (*artificial sweetener*). Regular Questran® and unflavored colestipol powder and tablets do not.

### Drug interactions

- Drug interactions are minimized by taking other medications 1 hour before the sequestrant or 4 hours after.
- The net effect of combining cholestyramine with warfarin is unpredictable. Colestipol and colesevelam have been reported not to interact with warfarin, and thus may be safer agents. Separating these agents by at least 4 hours from warfarin and close monitoring of INR (*blood test used to monitor anticoagulant therapy*) is recommended.

**Dosing considerations**

- Prior to ingestion, powders must be mixed in liquid or food with high moisture content (for example, gelatin, applesauce, soup [add **only** after heating], nonfat yogurt, etc.). Palatability of the powders may be improved by mixing a day ahead and storing in the refrigerator (unless mixed in something hot).
- Tablets must be taken with a liquid.

## Appendix E – NCEP Recommendations on Strategies to Improve Adherence

The ATP III (Adult Treatment Panel III) guideline, "Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults," includes recommendations on strategies to improve adherence by patients and providers. ATP III recommends the use of state-of-the-art multidisciplinary methods that target the patients, providers, and health delivery systems to achieve maximum adherence to primary and secondary prevention efforts. The following table summarizes the ATP III recommendations regarding adherence.

### Interventions to Improve Adherence

#### Focus on the patient

- Simplify medication regimens.
- Provide explicit patient instruction and use good counseling techniques to teach the patient how to follow the prescribed treatment.
- Encourage the use of prompts to help patients remember treatment regimens.
- Use systems to reinforce adherence and maintain contact with the patient.
- Encourage the support of family and friends.
- Reinforce and reward adherence.
- Increase visits for patients unable to achieve treatment goal.
- Increase convenience and access to care.
- Involve patients in their care through self-monitoring.

#### Focus on the physician and medical office

- Teach physicians to implement lipid treatment guidelines.
- Use reminders to prompt physicians to attend to lipid management.
- Identify a patient advocate in the office to help deliver or prompt care.
- Use patients to prompt preventive care.
- Develop a standardized treatment plan to structure care.
- Use feedback from past performance to foster change in future care.
- Remind patients of appointments and follow up missed appointments.

#### Focus on the health delivery system

- Provide lipid management through a lipid clinic.
- Use case management by nurses.
- Use telemedicine (*interactive, real-time television used to provide health care*).
- Establish collaborative care of pharmacists.
- Execute critical care pathways in hospitals.

This information reproduced from the National Cholesterol Education Program. "Detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III)." National Institutes of Health. 2001. Section IX-11.