Dyslipidemia Management in Adults

NATIONAL GUIDELINE SUMMARY

The following evidence-based guideline was developed to assist Primary Care physicians and other health care professionals in the management of dyslipidemia for primary and secondary prevention of atherosclerotic disease.

Definitions

| Primary Prevention | Refers to people without established coronary artery disease (CAD) |
| Secondary Prevention | Refers to people with established CAD |
| CAD Risk Equivalents | Refers to any of the following: |
| | • Ischemic stroke/TIA, carotid artery stenosis (≥50%), peripheral artery disease (PAD), abdominal aortic aneurysm (AAA) |
| | • Diabetes mellitus (DM) age 40 or older |
| | • 10-year risk of coronary events >20%* |
| | • Chronic kidney disease (CKD) stages 4 or 5 |

Chronic Kidney Disease (CKD) Stages 4 and 5 National Kidney Foundation (NKF) Stages 4 and 5 are defined as a Glomerular Filtration Rate (GFR) <30 mL/min/1.73 m² for at least 3 months

Detection and Evaluation

1 CAD RISK FACTORS

- Age: Male 45 or older; Female 55 or older
- Dyslipidemia: Total cholesterol (TC) ≥200 mg/dL or low-density lipoprotein cholesterol (LDL-C) ≥100 mg/dL in secondary prevention or CAD risk equivalent population; or TC ≥240 mg/dL or LDL-C ≥130 mg/dL in primary prevention; or high-density lipoprotein cholesterol (HDL-C) <40 mg/dL; or triglycerides (TG) ≥150 mg/dL.
- Diabetes Mellitus (DM)
- Hypertension: Blood pressure (BP) ≥140/90 mmHg or on antihypertensive medication
- Current cigarette smoking
- Family history (FHx) of premature CAD: Clinical CAD or sudden death in a first-degree relative age 54 or younger for men or age 64 or younger for women

2 LIPID SCREENING, TESTING AND MONITORING

- See Table 1 for recommendations
- Rule out and, if present, correct any secondary causes of dyslipidemia such as poor glycemic control, hypothyroidism, renal and liver disease, or medications.

Detection and Evaluation (continued)

3 USING 10-YEAR CAD RISK TABLES TO DETERMINE TREATMENT INITIATION PLAN

The need for and intensity of treatment for dyslipidemia in primary prevention depends on a person’s overall risk for CAD. For primary prevention, use the “Recommendations for Dyslipidemia Drug Treatment, Coronary Artery Disease Risk Assessment Tool” tables to determine 10-Year CAD risk status (online at: http://cl.kp.org/pkc/scal/cpg/cpg/html/dyslipid_rx_cad_risk_assess_tool.pdf).

The “Recommendations for Dyslipidemia Drug Treatment, Coronary Artery Disease Risk Assessment Tool” tables, based on the ATP III version of the Framingham risk model, estimate an individual’s risk of a primary cardiac event. The number in each cell is the person’s estimated risk (%) of a CAD event in the next 10 years. Risk status is based on use of tobacco products (“No Tobacco [TBCO]” or “TBCO”), use of blood pressure medications (“No blood pressure (BP) Meds” or “BP Meds”), age, sex, systolic blood pressure (SBP) levels, TC and HDL-C levels, and nonlipid CAD risk factors. The “Recommendations for Dyslipidemia Drug Treatment, Coronary Artery Disease Risk Assessment Tool” tables recommend pharmacologic treatment for three different levels of risk, as indicated by color:

- **Red**: Treatment STRONGLY RECOMMENDED when 10-year CAD risk >20%, if baseline LDL-C ≥100 mg/dL.
- **Orange**: Treatment RECOMMENDED if baseline LDL-C ≥130 mg/dL.
- **Yellow**: Treatment RECOMMENDED IF positive FHx of premature CAD AND baseline LDL-C ≥130 mg/dL.
- **White**: Drug Treatment NOT RECOMMENDED

For men age 50 or older and women age 60 or older, it is OPTIONAL to measure hsCRP, and if hsCRP ≥2 mg/L on 2 tests, treat with simvastatin 40 mg daily. The absolute benefit or cost-effectiveness of using hsCRP to select patients for lipid-lowering treatment is not known. (See Table 2 and Section 4 below for recommendations on the appropriate use of the hsCRP test.)

Table 1: Recommendations for Lipid Screening, Testing and Monitoring

<table>
<thead>
<tr>
<th>Test</th>
<th>Age to Initiate Screening</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CAD Risk Factors</td>
<td>TC + HDL-C* or Fasting Lipid Panel</td>
<td>Age 20 or first KP visit</td>
</tr>
<tr>
<td>One or more CAD Risk Factors or Known CAD or CAD Risk Equivalents</td>
<td>Fasting Lipid Panel</td>
<td>When CAD, CAD Risk Equivalency or CAD Risk Factor is identified</td>
</tr>
</tbody>
</table>

NOTE: A fasting lipid panel should be done anytime a new risk factor is identified and approximately 6 weeks after medication initiation or adjustment.

*TC + HDL-C can be nonfasting.

**There is insufficient evidence to recommend for or against follow-up lipid screening in men age 20-34 or in women 20-44 with normal baseline lipid levels.
<table>
<thead>
<tr>
<th>People with:</th>
<th>Baseline LDL-C (mg/dL)</th>
<th>Lifestyle Modifications are Recommended in ALL Patients Initiate Treatment with a Daily Evening Dose of:</th>
<th>Target LDL-C (mg/dL)</th>
<th>See Corresponding Number in Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Coronary Syndrome</td>
<td>Any</td>
<td>Atorvastatin 80 mg 1/2 tab</td>
<td>&lt;100 OPTIONAL &lt;70</td>
<td>7 8 9</td>
</tr>
</tbody>
</table>
| • CAD or Ischemic Stroke/TIA  
  • Diabetes Mellitus (DM) age ≥40  
  • AAA or PAD  
  • Carotid artery stenosis (>50%) | ≥160 | Atorvastatin 80 mg 1/2 tab | <100 OPTIONAL <70 | 7 8 10C |
| <160 | Simvastatin 40 mg | 4 7 8 10D |
| • Framingham 10-year risk² >20%  
  • DM age <40 WITH ≥1 risk factor⁴ | ≥160 | Atorvastatin 80 mg 1/2 tab | <100 | 10E |
| 100 - 159 | Simvastatin 40 mg | 3 4 6 8 |
| <100 | Simvastatin 40 mg | 3 4 6 8 |
| DM age <40 WITHOUT risk factors⁴ | ≥160 | Atorvastatin 80 mg 1/2 tab | <100 | 7 8 10D |
| 130-159 | Simvastatin 40 mg | 7 8 10D |
| <130 | Simvastatin 40 mg OPTIONAL | 7 8 10D |
| CKD Stage 4 or 5  
  (GFR <30 mL/min/1.73 m²) | ≥100 | Simvastatin 20 mg | <100 | 10E |
| <100 | Simvastatin 20 mg OPTIONAL | 7 8 10D |
| Framingham 10-year risk² 10-20% | ≥220 | Atorvastatin 80 mg 1/2 tab | <130 | 3 4 6 8 |
| 130-219 | Simvastatin 40 mg | 3 4 6 8 |
| <130 | hsCRP³ OPTIONAL | 3 4 6 8 |
| Framingham 10-year risk² <10% | ≥220 | Atorvastatin 80 mg 1/2 tab | <130 | 3 4 6 8 |
| 190-219 | Simvastatin 40 mg | 3 4 6 8 |
| 160-189 WITH FHx of premature CAD² and Framingham 10-year risk² 5-9% | Simvastatin 40 mg | 3 4 6 8 |
| • WITH FHx of premature CAD² and Framingham 10-year risk² <5% or  
  • WITHOUT FHx of premature CAD² | Simvastatin 40 mg OPTIONAL or hsCRP³ OPTIONAL | 3 4 6 8 |
| 130-159 WITH FHx of premature CAD² and Framingham 10-year risk² 5-9% | Simvastatin 40 mg | 3 4 6 8 |
| • WITH FHx of premature CAD² and Framingham 10-year risk² <5% or  
  • WITHOUT FHx of premature CAD² | hsCRP³ OPTIONAL | 3 4 6 8 |
| <130 | hsCRP³ OPTIONAL | 3 4 6 8 |

1. Based on the balance of benefits versus costs and harms, the LDL-C goal of <70 mg/dL is OPTIONAL.
3. FHx of premature CAD = Family history of premature CAD = Clinical CAD or sudden death in a first-degree relative aged < 55 (men) or < 65 (women).
4. Risk factors are: Duration of DM ≥ 10 years, HTN, HDL-C < 40, FHx of premature CAD, or currently smoking.
5. hsCRP = It is OPTIONAL to measure hsCRP in men ≥ 50 and women ≥ 60 years old, and if hsCRP ≥2 mg/L on two tests, treat with simvastatin 40 mg. The absolute benefit or cost effectiveness of using hsCRP to select patients for lipid-lowering treatment is not known.

### Additional Treatment Recommendations

- Do not use hsCRP to monitor or adjust lipid-lowering therapy.
- Because of the increased potential for myopathy, reduced initial doses of statins, fibrates and niacin should be considered in adults with GFR < 30 mL/min/1.73 m², in those with medical complications, the very elderly, and people taking interacting drugs or using combination lipid-modifying therapy. Statin doses can be cautiously increased, even up to maximal doses, if benefit exceeds risk. (See CKD Section and Statin section of Table 3 for additional information.)
- In patients who are on a high-dose, high-potency statin (e.g., simvastatin 40 mg or equivalent) but who are not at LDL-C goal after 6-8 weeks, clinicians should increase statin intensity (e.g., titrate as needed to a higher-dose, higher-potency statin, such as atorvastatin 80 mg ½ tab). (Strong recommendation)
- In patients who are already on a higher-dose, higher-potency statin (e.g., atorvastatin 80 mg ½ tab) but who are not at LDL-C goal after 6-8 weeks, clinicians may (Weak recommendation):
  - Increase statin intensity (e.g., change to atorvastatin 80 mg)
  - Add niacin (e.g., niacin sustained release)
  - Continue higher-dose, higher-potency statin (e.g., atorvastatin 80 mg ½ tab) and maximize lifestyle modification approaches
  - Add ezetimibe
  - Add a bile acid sequestrant (e.g., colestid)
- In patients who are on a statin, clinicians should not prescribe a fibrate for cardiovascular risk reduction. (Strong recommendation)
- After achievement of LDL-C goal, repeat lipid panel annually to ensure that the patient remains at goal. (It is optional to retest in 3-6 months.)

© 2011 Kaiser Permanente Medical Care Program
For use within Kaiser Permanente only.
 Detection and Evaluation (continued)

4 USE OF HSFRP TEST

• The hsCRP test has no role and should not be ordered in people for whom statin therapy is already recommended. (See Table 2 for recommendations on use of the hsCRP test.)
• The hsCRP test should not be used to monitor or adjust lipid-lowering therapy for primary or secondary prevention.
• In men aged 50 or older and women aged 60 or older who are not selected for treatment based on the “Recommendations for Dyslipidemia Drug Treatment, Coronary Artery Disease Risk Assessment Tool” tables, it is OPTIONAL to measure hsCRP and, if hsCRP is ≥2 mg/L on two tests, to initiate simvastatin 40 mg daily.
• The hsCRP test should only be ordered if the result will prompt a therapeutic decision and the clinician and patient have agreed to initiate statin therapy if the result is high, and to forgo statin therapy if the result is low.

While elevated hsCRP is considered an emerging risk factor for CAD, there is conflicting evidence as to whether the addition of hsCRP testing significantly improves the ability of Framingham risk equations to predict CVD risk for primary prevention patients. The GDT’s decision to support optional use of hsCRP testing in some patients is not based on the improvements that hsCRP adds to Framingham, but rather on the direct evidence from the JUPITER trial which showed that hsCRP results can be used to identify lower risk primary prevention men aged ≥50 and women aged ≥60 who would benefit from statin therapy.

Ordering and Interpretation of hsCRP Test:
• The standard CRP test is not useful for cardiac risk assessment and should not be ordered for this purpose. The correct test is the high-sensitivity CRP, sometimes called the “cardio CRP” or “wide-range CRP.”
• hsCRP should be ordered only in metabolically stable patients who are free of active infection, systemic inflammation*, recent trauma and are not on estrogens therapy, immunosuppressants or glucocorticoids.
• If hsCRP is ≥2 mg/L, repeat hsCRP two weeks later. Statin therapy contingent on hsCRP is only recommended if two hsCRP tests are both ≥2 mg/L.
• If hsCRP is >10 mg/L, the patient should be evaluated for sources of infection or inflammation and the test repeated. *Examples of inflammatory conditions that could invalidate the test results are rheumatoid arthritis, lupus and inflammatory bowel disease. Patients with osteoarthritis should not be excluded.

Management

5 LIFESTYLE MODIFICATIONS (continued)

• There is insufficient evidence to recommend for or against low-carbohydrate diets for atherosclerosis prevention.
• Promoting alcohol consumption in people with or without atherosclerotic disease is NOT recommended because of the risk of developing alcohol-related problems.

Evidence from observational studies has shown that smoking cessation, a moderate-to-high level of physical activity (e.g., 30 minutes of brisk walking five times per week), and a low-fat diet can reduce the risk of CAD. A Mediterranean diet emphasizes more bread, pasta, potatoes, fruit, vegetables, and fish, less red meat, and replacement of butter and cream with olive or canola oil. Based on evidence obtained from secondary prevention studies, it is reasonable to assume that Mediterranean or diets regularly containing fish with high-omega-3 content are also effective for primary prevention of atherosclerosis. In addition to replacing saturated fats from red meat, high-omega-3 fish diets are also a source of high-quality protein, vitamins and minerals. (See the “Fish Oil Supplements” section for more information.)

For people who already drink alcohol, advise men to limit intake to two drinks a day, and women to one drink a day. (A drink is defined as 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of liquor.)

6 LIPID TREATMENT GOALS FOR PRIMARY PREVENTION

• An LDL-C treatment goal of <130 mg/dL is recommended for primary prevention in adults who are at sufficient risk to warrant statin treatment.

The evidence from randomized controlled trials (RCTs) seems to indicate a linear relationship between achieved LDL-C and risk of CAD events. However, there is no direct evidence from RCTs comparing different LDL-C targets in primary prevention. The JUPITER trial did not evaluate LDL-C treatment thresholds or targets and should not be used to infer optimal thresholds and targets. Based on consensus, an LDL-C <130 mg/dL is appropriate for primary prevention.

Only after LDL-C is at goal should attention be turned to managing triglycerides (TGs) and HDL-C, except when TGs are ≥500 mg/dL (see “High TG Level” in section 11). After LDL-C is at goal, a non-HDL cholesterol goal of <160 mg/dL is recommended (non-HDL cholesterol is total cholesterol minus HDL-C).

• For primary prevention in adults with non-coronary atherosclerotic disease, 10-year CAD Risk >20%, NKF CKD Stage 4 or 5, ischemic stroke/TIA, and diabetes mellitus, an LDL-C treatment goal of <100 mg/dL is recommended. A non-HDL cholesterol goal of <130 mg/dL is recommended after LDL-C is at goal. If the target LDL-C is difficult to obtain, use clinical judgment to weigh benefits and risks of intensifying drug therapy.

7 LIPID TREATMENT GOALS FOR SECONDARY PREVENTION

• An LDL-C treatment goal of <100 mg/dL is recommended for reducing rates of coronary events in patients with established atherosclerotic disease.

Reducing LDL-C is the primary focus of treatment. Only after the LDL-C is at goal should attention be turned to managing triglycerides (TGs) and HDL-C, except when TGs are ≥500 mg/dL (see “High TG Level” in section 11).
Management (continued)

7 LIPID TREATMENT GOALS FOR SECONDARY PREVENTION (continued)

• A more aggressive LDL-C goal of <70 mg/dL is an option.
With increasing use of more potent statins, there are now many RCTs where the treatment group has attained LDL-C levels substantially below 100 mg/dL. Several have obtained levels below 70 mg/dL. In all cases, the lower LDL-C group had significantly fewer atherosclerotic events. Most of these trials, however, were not designed to evaluate the LDL-C level obtained and it is unknown whether the benefit was from the LDL-C reduction, statin potency, other factors, or a combination of these. The Guideline Team recommends the goal of LDL-C <70 as an option. Many authorities, however, now recommend the <70 mg/dL goal, especially in patients at very high risk.

When LDL-C <100 mg/dL, intensifying treatment should be a shared decision with the patient, taking into consideration factors such as overall CVD risk, TG status, HDL-C, non-HDL cholesterol, medication tolerance, cost and patient preference.

8 CHOICE OF DRUG—PRIMARY AND SECONDARY PREVENTION

Before initiating drug treatment, rule out and, if present, correct any secondary causes of dyslipidemia such as poor glycemic control, hypothyroidism, renal or liver disease, or medications.

Comparisons of individual lipid lowering therapies (statins, resins, fibrates and niacin) vs. placebo, have shown that statins are the most effective for reducing CVD events. Given that all statins appear to be efficacious at lowering LDL-C, the choice of statins should be based on both cost and evidence of direct benefit on important health outcomes (e.g., CVD morbidity and mortality). See Table 3 for dosing and safety recommendations for the use of lipid modifying drugs.

9 LIPID MANAGEMENT IN ACUTE CORONARY SYNDROMES

In patients with acute coronary syndrome:

• Statins are recommended regardless of baseline LDL-C.

• If baseline lipid values are desired, a 12-hour fasting lipid panel is recommended as soon as possible, but definitely within 48 hours after hospital admission.

• If a fasting lipid panel is not possible a non-fasting lipid panel is recommended as soon as possible after hospital admission.

• Repeat the lipid panel two months after hospital discharge.

The stress of acute events can lower LDL-C levels for up to 2 to 3 months. Evidence suggests that people with ACS should receive immediate aggressive statin lipid-lowering treatment. Emphasize the importance of lifestyle modifications and adherence to lipid-lowering medications.

Management (continued)

10 SPECIAL POPULATIONS

A. Metabolic Syndrome. People with metabolic syndrome, are at increased risk for CAD. According to a definition adapted from NCEP ATP III, metabolic syndrome is defined by the presence of three or more of the following:

• Abdominal Obesity – defined as:
  • waist circumference >40 inches (102 cm) in men, and >35 inches (88 cm) in women (waist circumference is the ATP III criterion), or
  • BMI ≥30 kg/m² (BMI is the World Health Organization criterion)

• Triglycerides ≥150mg/dL

• HDL-C <40 mg/dL for men or <50 mg/dL for women

• Blood Pressure ≥130/85 mmHg

• Fasting Plasma Glucose 100-125 mg/dL

(Noe: above-normal FPG may imply insulin resistance; the American Diabetes Association has adopted normal FPG <100 mg/dL, ATP III uses FPG <110 mg/dL.)

There is indirect evidence that the metabolic syndrome is associated with increased risk of CAD, but no data exist to quantify that risk beyond that calculated with the traditional risk factors. Similarly, there is no direct evidence informing whether people with metabolic syndrome should have lipid goals different from those determined by the traditional risk factors.

It is beyond the scope of this dyslipidemia guideline to recommend treatment for all the components of the metabolic syndrome. The treatment recommendations in this guideline focus on management of the lipid abnormalities associated with the metabolic syndrome. Reducing LDL-C is the primary treatment goal for all people with metabolic syndrome. After the LDL-C goal is achieved, non-HDL cholesterol can be targeted. Many of these people may require combination therapy to achieve both LDL-C and non-HDL cholesterol goals. See “Specific Dyslipidemias” section, Table 2 and Figure 1 for specific goals and treatment.

ATP III suggests that the presence of the metabolic syndrome in people with known CAD defines a “very high risk” and is a reason to consider the optional LDL-C treatment goal of <70 mg/dL and the optional non-HDL cholesterol goal of <100 mg/dL.

Note: In people with diabetes mellitus, improving blood glucose control via therapeutic lifestyle changes and the appropriate use of glucose-lowering medications may make achieving non-HDL cholesterol targets easier.

B. Elderly (age 65 or older). Evidence from randomized controlled trials indicates that people between age 65 and 85 benefit from lipid lowering. The effectiveness and benefits of drug therapy seen in this population are essentially the same as seen in people under age 65. The decision to treat should be based on a person’s lipid and nonlipid CAD risk factors and physiologic rather than chronologic age. Very elderly people may have an increased risk for side effects from some lipid-lowering medications and reduced initial doses may be appropriate (see Table 3).

C. Diabetes Mellitus Age 40 or Older. Both the Heart Protection Study and the Collaborative Atorvastatin Diabetes Study (CARDs) showed that people with diabetes and without established CAD are at high risk and derive a large benefit from statin treatment, regardless of baseline LDL-C. Based on these data, statin therapy is recommended, regardless of baseline LDL-C. As in CAD, these trials were not designed to determine the optimal target LDL-C. An LDL-C goal of <100 mg/dL, with an optional goal of <70 mg/dL, is recommended for all people with diabetes aged 40 or older.
D. Diabetes Mellitus Age 39 or Under. There are no studies that examine the effects of lipid-lowering on CAD outcomes in this population. Furthermore, the "Recommendations for Dyslipidemia Drug Treatment, Coronary Artery Disease Risk Assessment Tool" tables (derived from the ATP III Framingham risk calculator) do not estimate risk for people with diabetes. However, it is well-recognized that people with diabetes are at much higher risk for CAD than those without diabetes. The Guideline Team considered the contribution of other risk factors in this population and made the following recommendations:

Age 39 or younger with diabetes AND ≥1 risk factor*:

- Statin therapy is RECOMMENDED when LDL-C ≥100 mg/dL.
- Statin therapy is OPTIONAL when LDL-C <100 mg/dL.

Age 39 or younger with diabetes and NO risk factors*:

- Statin therapy is RECOMMENDED when LDL-C ≥130 mg/dL.
- Statin therapy is OPTIONAL when LDL-C <130 mg/dL.

*Risk factors include: duration of diabetes ≥10 years, HDL-C <40 mg/dL, current smoker or family history of premature CAD (Clinical CAD or sudden death in a first-degree relative aged <55 [men] and <65 [women]).

E. Chronic Kidney Disease. People with CKD, including NKF Stages 1, 2 and 3, are at increased risk for CVD morbidity and mortality. Because people with CKD frequently have other comorbidities, it is difficult to quantify the amount of CAD risk associated with CKD in the absence of comorbidities. There are emerging data that suggest a GFR 30-44 imparts a significantly increased risk for CVD, but not equivalent to the risk of people with established CAD.

Therefore our current recommendations for people with NKF stages 1, 2 and 3 remains unchanged: there is insufficient evidence that people with CKD stages 1, 2 or 3 should be treated differently on the basis of their CKD status alone. There is evidence that people with CKD stages 4 or 5 are at sufficiently high risk to be considered CAD Risk Equivalents. Therefore, treatment is RECOMMENDED in people with CKD Stages 4 or 5 if baseline LDL-C ≥100 and treatment is OPTIONAL if LDL-C <100 mg/dL. The goal LDL-C is <100 mg/dL.

See Tables 2 and 3 for dosing and safety recommendations for the use of lipid modifying drugs in CKD patients.

F. Low HDL-C.

- An HDL-C level of ≥60 mg/dL is considered to be within the normal range.
- An HDL-C level of <40 mg/dL is considered to be low and is associated with increased risk for CAD.

If HDL-C remains low after LDL-C has been brought to goal, treatment to attain this goal includes those agents that lower LDL-C. Weight reduction and physical activity are recommended; drug therapy to attain this goal includes those agents that lower either LDL-C or TG's.

G. High TG Level.

- There is expert opinion that a desirable TG level is <150 mg/dL, but there are no studies to demonstrate that reducing TG levels will reduce CAD events.
- Neither the threshold for initiation of therapy, nor the goal of therapy, is known. Although there is direct evidence that lowering LDL-C reduces the risk of CAD events, there are no clinical trials to demonstrate that reducing TG levels will reduce CAD events.
- There is evidence that elevated TG is independently associated with increased risk of atherosclerosis. However, not all people with high TGs are at increased risk, and neither the threshold for initiation of therapy, nor the goal of therapy, is known.
- Although there is direct evidence that lowering LDL-C reduces the risk of CAD events, there are no clinical trials to demonstrate that reducing TG levels will reduce CAD events.
- There is no direct evidence, there is consensus that TG ≥500 mg/dL warrants treatment to prevent pancreatitis. Specific recommendations for treating high TG level are presented in Figure 1 below.

Adjunctive Therapy

FISH OIL SUPPLEMENTS

Fish oils have important effects on TGs and LDL-C. See Table 3 for information regarding the effects of fish oils on TG.

- Fish oil supplements (~1 g/day of eicosapentaenoic acid/docosahexaenoic acid [EPA/DHA]) are optional for post-MI patients for the purpose of reducing CAD events.
- There is insufficient evidence to recommend for or against fish oil supplements for the purpose of reducing CAD events in people who have not had an MI.

For existing CAD, there are conflicting RCT data on the effectiveness of fish oil supplements for reducing mortality and CAD events. While one large RCT (GISSI-P) has shown that a fish oil supplement can reduce total and cardiac mortality in post-MI patients, it is uncertain from meta-analyses of secondary prevention trials whether high fish oil consumption has a significant effect on risk of CAD events. The composition of the prescription omega-3 product used in GISSI-P differs substantially from its presently marketed FDA-approved formulation. Additionally, OTC fish oil supplements—not regulated by the FDA—contain widely varying omega-3 fatty acid content with different EPA/DHA ratios. As a result of these factors, the GDT consensus is that the use of fish oil supplements in post-MI patients is optional.
Adjunctive Therapy (continued)

ASPIRIN TREATMENT

Use of Aspirin for Primary CVD Prophylaxis:

- In the absence of known CAD, stroke or DM—
  - When the CAD risk is high*, low-dose aspirin (81 mg daily) is recommended.
  - For intermediate risk* of CAD, discuss low-dose aspirin (81 mg daily) as adjunctive therapy. Use of aspirin should be based on each individual’s benefit/risk** status. When CAD risk is low*, the benefits of aspirin are unlikely to outweigh the risks.

- Uncontrolled hypertension is a relative contraindication to aspirin primary prophylaxis.

- Consider underlying risk for coronary heart disease, as well as the relative values patients attach to the main outcomes, when discussing aspirin with potential candidates.

Continuing research has validated the recommendation regarding the use of aspirin as concomitant therapy for patients with controlled hypertension. Based on the information and evidence presented, the GDT concluded that among people with controlled hypertension, the use of aspirin therapy for primary CVD prophylaxis should be based on individual CAD risk levels.

*According to Kaiser Permanente “Recommendations for Dyslipidemia Drug Treatment, Coronary Artery Disease Risk Assessment Tool” tables: low risk is <10%, intermediate risk is 10-20%, and high risk is >20%.

**The benefit for men is primarily reduction in nonfatal MI; benefit for women is stroke reduction. Low-dose aspirin increases the risk for GI bleeding and hemorrhagic stroke, and risk for hemorrhagic stroke may increase with uncontrolled hypertension, particularly stage 2. NNTs to prevent one adverse CV outcome vs. NNHs (usually GI bleed requiring transfusion) for men and women on low-dose aspirin for primary CV prophylaxis for 6.4 years are: men - NNT 270 and NNH 303; women - NNT 333 and NNH 400. For 1,000 patients at high CAD risk, aspirin would prevent 6-20 nonfatal MIs, but would cause 0-2 hemorrhagic strokes and 2-4 major GI bleeds. For patients at low CAD risk, aspirin would prevent 1-4 MIs but would cause 0-2 hemorrhagic strokes and 2-4 major GI bleeds.

Figure 1: Triglyceride (TG) Treatment Recommendations

Caveats:

- All people with CAD and people with diabetes mellitus age 40 or older should be on a statin.1,2
- Secondary causes of hypertriglyceridemia should be investigated, and if present, addressed: hyperglycemia, hypothyroidism, renal disease, excessive alcohol intake, medications,3 and obesity.

<table>
<thead>
<tr>
<th>TG ≥1,000 mg/dL</th>
<th>TG 500–999 mg/dL</th>
<th>TG 200–499 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recheck and intensify therapy every 2 weeks until &lt;1,000 mg/dL</td>
<td>Recheck and intensify therapy every 2-4 weeks until &lt;500 mg/dL</td>
<td>Recheck and intensify therapy every 6-8 weeks until non-HDL-C ≤30 mg/dL above LDL-C goal</td>
</tr>
</tbody>
</table>

- Intensify diet and exercise
   AND
   - Fibrates2,4 – OR –
   - Omega-3 fatty acids2,5
   THEN
   - Niacin2,6 – OR –
   - Initiate or intensify statin therapy1,2 – OR –
   - Combinations of above2,4
   - If unable to reach goals, or other problems or questions arise, consult a lipid specialist.

Footnotes:

1. A minimum dose of simvastatin 40 mg is recommended if GFR ≥ 30 ml/min (see Table 2).
2. See Table 3 for more information on specific drugs and drug combinations.
3. Beta-blockers, bile acid sequestrants, estrogens, etretinate, immunosuppressants, isotretinoin, prednisone, protease inhibitors and thiazide diuretics can raise TG.
4. Caution is advised for statin-niacin and statin-fibrate combinations (i.e., begin with reduced statin dose, and carefully titrate, if warranted). Use fenofibrate if patient is on a statin, use gemfibrozil if not on a statin.
5. Dose for TG-lowering is 2-4 gm/day of DHA-EPA content.
6. Maximum dose for sustained release (SR) niacin monotherapy is 2 gm/day. Slo-Niacin® is the preferred formulary SR niacin agent.
7. Non-HDL-C = Total Cholesterol minus HDL-C.
### Bile Acid Sequestrants

**Indications:** High LDL-C, Bile acid sequestering resins are not systemically absorbed and are therefore safe to use in people with liver disease. They lower LDL-C, have minimal if any effect on HDL-C, and often raise TG. No laboratory monitoring (other than lipid profiles) is necessary.

Bile acid sequestrants are most effectively used in combination with other agents when further LDL-C reduction is required (see "Combination Therapy"), but should not be used when baseline TG ≥ 200 mg/dL because they can increase TG levels significantly (e.g., 20%). Combining a resin with a psyllium seed preparation may reduce GI side effects and further reduce the LDL-C. Colestipol and cholestyramine may be given once daily or in divided doses. Bulk generic cholestyramine powder is the least expensive formulation.

<table>
<thead>
<tr>
<th>BILE ACID SEQUESTRANT DOSING</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>COLESTIPOL (COLESTID)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Powder for suspension (scop) or 1 gram tablets</td>
<td>16%↓</td>
<td>0%–5%↑</td>
<td>0%–20%↑</td>
<td>$ - $99.99</td>
</tr>
<tr>
<td>CHOLESTYRAMINE (QUESTRAN)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Powder for suspension (scoop) 1 scoop (≈ 4 tablets) per day</td>
<td>16%↓</td>
<td>0%–5%↑</td>
<td>0%–20%↑</td>
<td>$ - $99.99</td>
</tr>
<tr>
<td>2 scoops (≈ 8 tablets) per day</td>
<td>23%↓</td>
<td>0%–5%↑</td>
<td>0%–20%↑</td>
<td>$ - $99.99</td>
</tr>
<tr>
<td>3 scoops (≈ 12 tablets) per day</td>
<td>25%↓</td>
<td>0%–5%↑</td>
<td>0%–20%↑</td>
<td>$ - $99.99</td>
</tr>
<tr>
<td>6 scoops (max dose) per day</td>
<td>27%↓</td>
<td>0%–5%↑</td>
<td>0%–20%↑</td>
<td>$ - $99.99</td>
</tr>
</tbody>
</table>

**SAFETY COMMENTS**
- Side effects: constipation, dyspepsia, abdominal pain, bloating, belching, diarrhea, and nausea.
- Drug Interactions: Bile acid sequestrants may interfere with the absorption of other oral medications (e.g., digoxin, ezetimibe, levodopa, statins, vitamin K, warfarin); therefore, other medications should be taken one hour before or four hours after resins.
- Contraindications: Complete biliary obstruction, bowel obstruction, or hypertriglyceridemia.

### Niacin (Nicotinic Acid)

**Indications:** High LDL-C, Low HDL-C, and/or High TG. Niacin lowers LDL-C and TG and is the most potent agent available for raising HDL-C. It has been shown to reduce CAD events, especially in combination with a statin in people with high CVD risk and low HDL-C.

Careful dosage titration is required to promote tolerance and adherence to therapy. Flushing and pruritus can be minimized by slow up-titration, taking with meals, and taking aspirin (162-325 mg) or an NSAI (e.g., ibuprofen 200 mg) 30 minutes before each niacin dose. Niacin doses less than 2 grams/day generally include minimal and transient increases in acid levels at baseline and periodically.

<table>
<thead>
<tr>
<th>NIACIN DOSING</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMMEDIATE-RELEASE NIACIN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial dose: 50-100 mg/day - Titrate slowly to 1000-3000 mg/d (divide doses)</td>
<td>5-25%↓</td>
<td>15-35%↑</td>
<td>20-50%↓</td>
<td>$100–300</td>
</tr>
<tr>
<td>SUSTAINED-RELEASE NIACIN (SLO-NIACIN OTC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>500-2000 mg qhs or 500-1000 mg BID</td>
<td>5-25%↓</td>
<td>15-35%↑</td>
<td>20-50%↓</td>
<td>$101–300</td>
</tr>
<tr>
<td>EXTENDED-RELEASE NIACIN (NF—NIASPAN)-B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>500-2000 mg qhs</td>
<td>5-25%↓</td>
<td>15-35%↑</td>
<td>20-50%↓</td>
<td>$301–600</td>
</tr>
</tbody>
</table>

**SAFETY COMMENTS**
- Side Effects: Flushing, itching, tingling, headache, pruritus, and dyspepsia are common side effects that may limit adherence. Additional adverse effects include hepatotoxicity, loss of glycemic control, stomach ulcers, and increased uric acid.
- Hepatotoxicity and fatal hepatic necrosis have been reported with the OTC sustained-release niacin products, principally at high doses (>2,000 mg) without medical supervision or when patients were converted from immediate-release to sustained-release niacin on a mg:mg basis.
- Drug Interactions: statins
- Contraindications: Acute liver disease, active peptic ulcer disease, poorly controlled diabetes, and gout.

### Fibrates (Fibrates)

**Indications:** High TG and/or Low HDL-C. Fibrates are effective at lowering TGs and modestly raising HDL-C. Fibrates have variable effects on LDL-C and sometimes increase it, particularly if baseline TGs are high.

Clinical evidence from the VA-HIT study suggests that gemfibrozil provides benefit for secondary prevention people with a low HDL-C and without an elevated LDL-C. Because of the preponderance of statin clinical trial data, statins are the first-line drug choice for CVD prevention, even in people with a low HDL-C and without an elevated LDL-C. If TG ≥500 mg/dL in people with CAD, ischemic stroke/TIA, AAA, PAD, significant carotid artery stenosis (>50%), or age 40 or older with DM, combination statin (to prevent CVD events) and TG-lowering therapy (to prevent pancreatitis) is recommended. Compared with gemfibrozil, fenofibrate provides an additional 8-11% LDL reduction in Type IIa and IIb dyslipidemias; marked increases in LDL-C (up to 45%) may result when either fibrate is used to treat patients with very high TGs (>500 mg/dL). The clinical significance of the TG lowering and LDL-C increase is not known.

<table>
<thead>
<tr>
<th>FIBRATE DOSING</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEMFIBROZIL (LOPID)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>600 mg BID AC</td>
<td>No change or ↓</td>
<td>10-35%↑</td>
<td>20-50%↓</td>
<td>$101–300</td>
</tr>
<tr>
<td>FENOFIBRATE (generic TRICOR, LOFIBRA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microcrated Tablets 54, 160 mg</td>
<td>No change or ↓</td>
<td>10-35%↑</td>
<td>20-50%↓</td>
<td>$101–300</td>
</tr>
</tbody>
</table>

**SAFETY COMMENTS**
- Side Effects: Rhabdomyolysis, myopathy, and risk of myopathy. Rhabdomyolysis has been reported with both gemfibrozil and fenofibrate monotherapy.
- Drug Interactions: More data needed to define efficacy/safety of fibrate/statin combination therapy. If combination therapy required, an initial lower statin dose is recommended due to increased myopathy and rhabdomyolysis risk. Statin doses may be cautiously increased, up to maximal doses, if benefit exceeds risk. Fenofibrate is less likely to interact with statins than gemfibrozil and is preferred when combination therapy with statins is indicated. Both fenofibrate and gemfibrozil may increase the response to warfarin effects (monitor INR).
- CKD stages 4 and 5: Use lower fibrate doses if GFR <30 mL/min/1.73 m². Reversible elevation of serum creatinine levels has been reported with both agents (higher with fenofibrate), but the clinical significance of this phenomenon is unclear.
- Contraindications: Pre-existing gallbladder disease, hepatic or severe renal dysfunction.

Legend:
- **NF** Non-Formulary
- **B** Brand copayment, no generic available
- **OTC** nonprescription, over-the-counter.

Cost Legend (per year):
- ≤ $100
- $101–300
- $301–600
- $601–1000
- > $1000

*Costs are acquisition price/year (12/08) or OTC for niacin; patient costs against caps will be higher.*

---

© 2011 Kaiser Permanente Medical Care Program
For use within Kaiser Permanente only.
Table 3. Lipid-Lowering Medications: Efficacy, Safety, Cost and Comments (continued)

<table>
<thead>
<tr>
<th>HMG-CoA Reductase Inhibitors (Statins)</th>
</tr>
</thead>
</table>

**Indications:** High LDL-C, CAD, CAD Risk Equivalent, DM age 40 or older. Statins are the most potent agents available for reduction of LDL-C and clinical events. They also moderately lower TG and raise HDL-C. Their effectiveness in lowering LDL-C and reducing clinical events, overall safety, tolerability, and ease of use make them the first-line drugs of choice for the management of dyslipidemia and CVD risk. See Table 2 for initial doses and other treatment considerations. For each doubling of the dose, an additional LDL-C reduction of approximately 6-7% is expected. TG reductions as well as increases in HDL-C vary as a function of statin dose and baseline TG and HDL-C levels. If goals are not reached at maximum statin dose and potency, consider combination therapy (adding niacin, ezetimibe, resins or statins/stereos) or referral to a lipid specialist. (See “Combination Therapy” section below.)

**Recommended statin.** Based on evidence of efficacy, safety and cost, simvastatin is the preferred Formulary statin. For optimal LDL-C reduction, administer daily in the evening.

**Liver safety.** Significantly elevated aminotransferase levels often resolve on rechallenge or with continued therapy. Incidence of statin-induced true hepatotoxicity is small; authorities have questioned whether such an entity exists. Statins may be used in people with fatty liver/nonalcoholic steatohepatitis (NASH) if their serum aminotransferase levels are <3 x ULN and stable.

**Important:** Patients should understand that they are at far greater risk from cardiovascular disease than from statin-induced liver injury. Nonetheless, it is prudent to delay initiation of statins (and many other medications) in people with active liver disease until stability is demonstrated. Obtaining a baseline ALT before starting statin therapy is recommended. To be conservative, rechecking ALT level 6 weeks after treatment initiation and after each dosage increase is also recommended. Stop the statin if the ALT increases to >3 x ULN.

**Muscle symptoms.** Though infrequent, significant generalized muscle aches and/or weakness can occur with statin use in a dose-related fashion. Rarely, this can progress to serious myopathy and rhabdomyolysis. Muscle symptoms and possibly even myopathy can occur in the absence of any elevation of the CK enzyme. Further, CK enzyme elevation can occur in the absence of muscle symptoms or damage and in asymptomatic people not on statins. Therefore, we do not recommend routine monitoring of CK, but rather recommend counseling the patient to report significant generalized muscle symptoms.

**Management recommendations.** If patient has either ALT >3 x ULN or persistent significant generalized muscle aches and/or weakness, the following three possible management strategies are recommended. Choose option based on seriousness of adverse event and individual judgment.

- Discontinue statin until ALT elevation or muscle symptoms resolve and rechallenge with same statin and dose. Patient often tolerates this, implying adverse event is not related to statin.
- Discontinue statin until ALT elevation or muscle symptoms resolve and restart the same statin at lower dose. If tolerated, titrate up as needed.
- Discontinue statin until ALT elevation or muscle symptoms resolve and start a different statin. Use simvastatin and lovastatin initially because of low cost. Pravastatin is an alternative, recommended on the theoretical basis of its hydrophilicity and minimal interactions with CYP 3A4 inhibitors.

**SIDE EFFECTS**

<table>
<thead>
<tr>
<th>STATIN DOING</th>
<th>All 5 statins have good CVD outcome data.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LDL-C EFFECTS</td>
</tr>
<tr>
<td>SIMVASTATIN (ZOCOR)</td>
<td>10 mg daily</td>
</tr>
<tr>
<td></td>
<td>20 mg daily</td>
</tr>
<tr>
<td></td>
<td>40 mg daily</td>
</tr>
<tr>
<td></td>
<td>80 mg daily</td>
</tr>
<tr>
<td>LOVASTATIN (MEVACOR)</td>
<td>10 mg daily</td>
</tr>
<tr>
<td></td>
<td>20 mg daily</td>
</tr>
<tr>
<td></td>
<td>40 mg daily</td>
</tr>
<tr>
<td></td>
<td>80 mg daily (2 x 40 mg tablets)</td>
</tr>
<tr>
<td>PRAVASTATIN (PRAVACHOL)</td>
<td>10 mg daily</td>
</tr>
<tr>
<td></td>
<td>20 mg daily</td>
</tr>
<tr>
<td></td>
<td>40 mg daily</td>
</tr>
<tr>
<td></td>
<td>80 mg daily</td>
</tr>
<tr>
<td>NF-ATORVASTATIN (LIPITOR)-B</td>
<td>10 mg daily (use ½ 20 mg tablet)</td>
</tr>
<tr>
<td></td>
<td>20 mg daily (use ½ 40 mg tablet)</td>
</tr>
<tr>
<td></td>
<td>40 mg daily (use ½ 80 mg tablet)</td>
</tr>
<tr>
<td></td>
<td>80 mg daily</td>
</tr>
<tr>
<td>NF-ROSVASTATIN (CRESTOR)-B</td>
<td>5 mg daily</td>
</tr>
<tr>
<td></td>
<td>10 mg daily</td>
</tr>
<tr>
<td></td>
<td>20 mg daily</td>
</tr>
<tr>
<td></td>
<td>40 mg daily</td>
</tr>
</tbody>
</table>

**SAFETY COMMENTS**

- Do not start new patients on simvastatin 80 mg or increase simvastatin dose to 80 mg.
- Side effects: flatulence (<5%), constipation (<5%), headache (<4%), myalgia (<3%), abdominal pain/cramping (2-3%), weakness (<2%), nausea (<2%), elevated serum aminotransferase (1-2%), and muscle cramps (<1%).
- Myopathy and potentially fatal rhabdomyolysis are rare side effects. The risk is increased in people who are also prescribed interacting drugs, people who are frail or have medical complications, the very elderly, and people with impaired renal function. For these people, consider initiating therapy with reduced doses, and increasing cautiously if benefit exceeds risk.
- Potent inhibitors of CYP 3A4: Because risk of muscle injury is related to statin exposure, the use of erythromycin, clarithromycin, azole antifungals (ketoconazole, itraconazole), nefazodone, protease inhibitors, or regular consumption of >1 quart/day of grapefruit juice is not recommended with lovastatin, simvastatin, and NF-atorvastatin. Pravastatin and NF-rosvastatin have a theoretical advantage for people on chronic therapy with the same medications based on a decreased potential for adverse CYP 3A4-mediated drug interactions.
- Other Drugs: For people taking cyclosporine, verapamil, diltiazem, or amiodarone, consider switching to alternate medications before initiating statins. If those medications need to be continued or for people taking fraboles, or niacin ≥1000 mg daily, initiate statins in lower doses and increase cautiously if benefit exceeds risk.
- Contraindications: Active liver disease or unexplained persistent elevation of serum aminotransferase levels and pregnancy and lactation. For women of child-bearing potential who elect to initiate statin therapy, contraception and/or Plan B should be discussed and prescribed.

**Legend:**

- NF: Non-Formulary
- B: Brand copayment, no generic available
- OTC: nonprescription, over-the-counter.

*Costs are acquisition price/year (12/08) or OTC for niacin; patient costs against caps will be higher.

© 2011 Kaiser Permanente Medical Care Program
For use within Kaiser Permanente only.

CMIO81011-2
Last Reviewed/Revised: 11/2011
### Cholesterol Absorption Inhibitors

**Indications:** High LDL-C.

**Ezetimibe.** NF - ezetimibe inhibits dietary and biliary cholesterol absorption at the intestinal wall via its effect on brush border transporter proteins. Used as monotherapy at 10 mg daily, it reduces LDL-C by approximately 18%, though there is wide individual patient variation. It lowers TG slightly and can raise HDL-C minimally. Ezetimibe is well tolerated, with minimal adverse effects.

**Ezetimibe-Simvastatin (Vytorin).** Ezetimibe-simvastatin (Vytorin) is a combination tablet containing ezetimibe 10 mg and simvastatin in doses ranging from 10 to 80 mg. It can provide marked LDL-C lowering (~90%). There are no outcome data to determine whether ezetimibe combined with simvastatin reduces CVD events better than simvastatin alone. At the date, large clinical trials evaluating the role of lipid-lowering therapy have demonstrated that lower LDL-C confers lower cardiovascular risk. Vytorin’s demonstrated robust LDL-C lowering provides the rationale for using it to achieve large LDL-C reductions. Because the richest body of evidence that links lipid-lowering and CVD event reduction is for statin monotherapy, patients should first be titrated to the highest tolerated dose of a formulary statin in order to achieve their LDL-C target. For those who remain above target or cannot tolerate a high enough statin dose, combination ezetimibe-simvastatin is a reasonable treatment option. Vytorin is less expensive to use than separate prescriptions for any statin PLUS NF - ezetimibe.

### Fish Oils, Omega-3-acid ethyl esters

**Indications and Dosage:** Very high triglycerides (≥ 500 mg/dL) – 4 gm (EPA + DHA) per day. History of myocardial infarction or for 2nd Prevention – 1 gm (EPA + DHA) per day.

There is conflicting evidence regarding the use of fish oil supplements for CVD prevention, where a lower dose (1 gm/day) has been shown to reduce sudden death in post-MI patients. See “Fish Oil Supplements” on page 5 for further information. Approximately 90% of the total omega-3 polyunsaturated fatty acid content of prescription-only NF - Lovaza is EPA + DHA as compared to a range of 30% - 65% for OTC fish oil supplements. Thus 1 gm Lovaza ≈ 2 - 3 gm of OTC products in terms of EPA + DHA content. KP does not endorse NF - Lovaza or any of the OTC products; they are listed to illustrate variability of EPA + DHA content among different products as well as the wide range of costs.

### DRUGS AND DOSING

<table>
<thead>
<tr>
<th>For Triglyceride &gt; 500 mg/dL Reduction:</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/ YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NF - Omega-3-acid ethyl esters 1 gm capsule (Lovaza) – B (465 mg EPA + 375 mg DHA per capsule)</strong></td>
<td>4-45%↑</td>
<td>0-3%↑</td>
<td>45%↓</td>
<td>$$$$$</td>
</tr>
<tr>
<td>• 4 caps/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NF - Kirkland Signature™ EC Fish Oil Concentrate 1200 mg Softgels (374 mg EPA + 310 mg DHA per capsule) – OTC</strong></td>
<td>4-45%↑</td>
<td>0-3%↑</td>
<td>45%↓</td>
<td>$$</td>
</tr>
<tr>
<td>• 6 caps/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NF - NVC Omega-3 Fish Oil/Vit E Soft Gels (180 mg EPA + 120 mg DHA + 5 IU Vit E) – OTC</strong></td>
<td>4-45%↑</td>
<td>0-3%↑</td>
<td>45%↓</td>
<td>$$</td>
</tr>
<tr>
<td>• 12 caps/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>For Post-MI or Secondary Prevention:</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/ YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NF - Omega-3-acid ethyl esters 1 gm capsule (Lovaza) – B (465 mg EPA + 375 mg DHA per capsule)</strong></td>
<td>No effect</td>
<td>No effect</td>
<td>No effect</td>
<td>$$</td>
</tr>
<tr>
<td>• 1 cap/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NF - Kirkland Signature™ EC Fish Oil Concentrate 1200 mg Softgels (374 mg EPA + 310 mg DHA per capsule) – OTC</strong></td>
<td>No effect</td>
<td>No effect</td>
<td>No effect</td>
<td>$</td>
</tr>
<tr>
<td>• 2 caps/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NF - NVC Omega-3 Fish Oil/Vit E Soft Gels (180 mg EPA + 120 mg DHA) – KP OTC</strong></td>
<td>No effect</td>
<td>No effect</td>
<td>No effect</td>
<td>$</td>
</tr>
<tr>
<td>• 3 caps/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### FOR UP-TO-DATE INFORMATION:

- **Dosing, Safety, Drug Interactions, and Formulary Changes:** Go to the Drug Information Intranet site at http://pharmacy.kp.org
- **National Clinical Practice Guidelines:** Go to the CMI Intranet site at http://cl.kp.org/portal/site/NCAL and search for “National Guidelines”.

### Intranet Web Site:


**Legend:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Cost Legend (per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NF</td>
<td>Non-Formulary</td>
<td>≤ $100</td>
</tr>
<tr>
<td>B</td>
<td>Brand copayment, no generic available OTC</td>
<td>$101–300</td>
</tr>
<tr>
<td>OTC</td>
<td>nonprescription, over-the-counter</td>
<td>$301–600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$$$: $601–1000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$$$$$: &gt; $1000</td>
</tr>
</tbody>
</table>

*Costs are acquisition price/year (12/08) or OTC for niacin; patient costs against caps will be higher.

© 2011 Kaiser Permanente Medical Care Program
For use within Kaiser Permanente only.

---

CMI081011-2
Last Reviewed/Revised: 11/2011