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) <60 ml/min/1.73 m² for at least 3 months |

*Refer to the “Recommendations for Dyslipidemia Drug Treatment, Coronary Artery Disease Risk Assessment Tool” tables for 10-year risk.

Detection and Evaluation (continued)

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


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:

<table>
<thead>
<tr>
<th>Color</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red</td>
<td>STRONGLY RECOMMENDED when 10-year CAD risk &gt;20%, if baseline LDL-C ≥100 mg/dL.</td>
</tr>
<tr>
<td>Orange</td>
<td>RECOMMENDED if baseline LDL-C ≥130 mg/dL.</td>
</tr>
<tr>
<td>Yellow</td>
<td>IF positive FHx of premature CAD AND baseline LDL-C ≥130 mg/dL</td>
</tr>
<tr>
<td>White</td>
<td>NOT RECOMMENDED</td>
</tr>
</tbody>
</table>

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 2. LDL-C Treatment Recommendations

<table>
<thead>
<tr>
<th>People with:</th>
<th>Baseline LDL-C (mg/dL)</th>
<th>Lifestyle Modifications are Recommended in ALL Patients</th>
<th>Target LDL-C (mg/dL)</th>
<th>See Corresponding Number in Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Coronary Syndrome or Acute Ischemic Stroke/TIA</td>
<td>Any</td>
<td>Atorvastatin 40mg-80 mg</td>
<td>&lt;100 OPTIONAL</td>
<td>7 8 9</td>
</tr>
<tr>
<td>• CAD or History of Ischemic Stroke/TIA</td>
<td>≥160</td>
<td>Atorvastatin 40 mg</td>
<td>&lt;100 OPTIONAL</td>
<td>7 8 10C</td>
</tr>
<tr>
<td>• Diabetes Mellitus (DM) age ≥40</td>
<td>&lt;160</td>
<td>Simvastatin 40 mg</td>
<td>&lt;100</td>
<td>4 7 8 10D</td>
</tr>
<tr>
<td>• AAA or PAD</td>
<td>≥100 - 159</td>
<td>Simvastatin 40 mg</td>
<td>OPTIONAL</td>
<td>4 7 8 10D</td>
</tr>
<tr>
<td>• Carotid artery stenosis (&gt;50%)</td>
<td>&lt;100</td>
<td>Simvastatin 40 mg</td>
<td>OPTIONAL</td>
<td>4 7 8 10D</td>
</tr>
<tr>
<td>• Framingham 10-year risk² &gt;20%, DM age &lt;40 WITH ≥1 risk factors²</td>
<td>≥160</td>
<td>Atorvastatin 40 mg</td>
<td>&lt;100</td>
<td>4 7 8 10D</td>
</tr>
<tr>
<td>DM age &lt;40 WITHOUT risk factors⁴</td>
<td>≤160</td>
<td>Atorvastatin 40 mg</td>
<td>&lt;100</td>
<td>4 7 8 10D</td>
</tr>
<tr>
<td>CKD Stage 4 or 5 (GFR &lt;30 mL/min/1.73 m²)</td>
<td>≥100</td>
<td>Simvastatin 20 mg</td>
<td>&lt;100</td>
<td>10E</td>
</tr>
<tr>
<td>Framingham 10-year risk² 10-20%</td>
<td>&lt;220</td>
<td>Atorvastatin 40 mg</td>
<td>&lt;130</td>
<td>3 4 6 8</td>
</tr>
<tr>
<td>Framingham 10-year risk² &lt;10%</td>
<td>≤220</td>
<td>Atorvastatin 40 mg</td>
<td>&lt;130</td>
<td>3 4 6 8</td>
</tr>
</tbody>
</table>

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 40 mg) (Strong recommendation)
- In patients who are already on a higher-dose, higher-potency statin (e.g., atorvastatin 40 mg) 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 40 mg) 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.)
Detection and Evaluation (continued)

4 USE OF hsCRP 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 CVR 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 estrogen 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

- Strongly encourage tobacco cessation, increased physical activity, and a diet that is low in saturated fat, Mediterranean and regularly contains fish with high omega-3 content (e.g., two servings per week of salmon, herring, tuna, sardines and mackerel [except king mackerel which may have excessive mercury content]).

(See the KP National CAD Guideline for more information on lifestyle modifications for secondary prevention.)

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 (TG’s), except when TGs are ≥500 mg/dL. Consider treatment at TG 500-999; treat at TG >/= 1000 (see “High TG Level” in section 11).

- 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.

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 (TG’s), 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

(Note: 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. See “Specific Dyslipidemias” section, Table 2 and Figure 1 for specific goals and treatment for high triglycerides.

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.
Management (continued)

**10 SPECIAL POPULATIONS (continued)**

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 is <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.

**11 SPECIFIC DYSLIPIDEMIAS**

A. High HDL-C. An HDL-C level of ≥60 mg/dL is considered by the NCEP ATP III to be a “negative risk factor” that may counterbalance a positive risk factor. A high HDL-C level, however, is not always protective. The function of HDL-C, which is currently not readily measurable, may contribute to HDL-C’s benefit, or lack of benefit, and is likely as important as the total amount. A high HDL-C level does not eliminate risk and therefore should not remove the focus from treating high LDL-C levels regardless of the HDL-C level.

B. Very High LDL-C. People with LDL-C ≥190 mg/dL are at high risk for CAD and treatment is recommended, regardless of other risk factors, unless there are compelling reasons against it. Treatment that lowers LDL-C is especially indicated in the presence of other risk factors, particularly a family history of premature CAD.

Management (continued)

**11 SPECIFIC DYSLIPIDEMIAS (continued)**

C. Low HDL-C. HDL-C <40 mg/dL is strongly associated with increased risk of CAD. The preponderance of evidence, however, continues to support LDL-C management as the first priority. If HDL-C remains low after LDL-C has been brought to goal, consider attempts to raise HDL-C. Options include tobacco cessation, increased physical activity, and medication. Niacin is the most potent HDL-C-raising agent, but fibrates and statins also modestly increase HDL-C.

D. High TG Level. 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 expert opinion that a desirable TG level is <150 mg/dL, but there are no studies to support the benefit of obtaining this level. Treatment decisions should be influenced by a person's other lipid levels and nonlipid CAD risk factors. Although there is no direct evidence, there is consensus that TG ≥1000 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 the 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.
Assess for and address secondary causes of hypertriglyceridemia: hyperglycemia, hypothyroidism, renal disease, excessive alcohol intake, obesity and medications (e.g., oral estrogens and oral retinoids).

Consider adding DHA/EPA ≥ 2-4 g daily**

Consider switching to atorvastatin†

Note: **Medical treatment of people with a TG ≥ 1000 is recommended within 2-4 weeks to reduce the risk of pancreatitis.

Medical treatment of people with TG 500-999 is an option to reduce the risk of pancreatitis (No clinical trials have prospectively evaluated the pharmacologic treatment of hypertriglyceridemia and demonstrated reduction in the incidence of pancreatitis, however observational data suggest that the risk of pancreatitis is related to the degree of hypertriglyceridemia)

†For patients on lower potency or dose statins, with a TG≥500, consider switching to high dose atorvastatin 40-80 mg.

‡For example, if adherence to DHA/EPA is likely to be problematic, if severe elevation of TGs over 5000, if history of pancreatitis, etc.
Table 3. Lipid-Lowering Medications: Efficacy, Safety, Cost and Comments

### Bile Acid Sequestrants

<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>
<th>SAFETY COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>COLESTIPOL (COLESTIPOL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$ - $3000*</td>
</tr>
<tr>
<td>Powder for suspension (scoop) or 1 gram tablets</td>
<td>16%↓</td>
<td>0%±-5%↑</td>
<td>0%-20%↑</td>
<td>$ - $3000*</td>
<td>Side effects: constipation, dyspepsia, abdominal pain, bloating, belching, diarrhea, and nausea. Drug Interactions: Bile acid sequestrants may interfere with the absorption of other oral medications (e.g., digoxin, ezetimibe, levethoxine, statins, vitamin K, warfarin); therefore, other medications should be taken one hour before or four hours after resins. Contraindications: Complete biliary obstruction, bowel obstruction, or hypertriglyceridemia.</td>
</tr>
<tr>
<td>CHOLESTYRAMINE (QUESTRA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$ - $3000*</td>
</tr>
<tr>
<td>Powder for suspension (scoop)</td>
<td>1 scoop (= 4 tablets) per day</td>
<td>16%↓</td>
<td>0%±-5%↑</td>
<td>0%-20%↑</td>
<td>$ - $3000*</td>
</tr>
<tr>
<td>2 scoops (= 8 tablets) per day</td>
<td>23%↓</td>
<td>0%±-5%↑</td>
<td>0%-20%↑</td>
<td>$ - $3000*</td>
<td></td>
</tr>
<tr>
<td>3 scoops (= 12 tablets) per day</td>
<td>26%↓</td>
<td>0%±-5%↑</td>
<td>0%-20%↑</td>
<td>$ - $3000*</td>
<td></td>
</tr>
<tr>
<td>6 scoops (max dose) per day</td>
<td>33%↓</td>
<td>0%±-5%↑</td>
<td>0%-20%↑</td>
<td>$ - $3000*</td>
<td></td>
</tr>
</tbody>
</table>

### 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 NSAID (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 glucose and HbA1c that are amenable to slight adjustments of oral antidiabetic drugs or insulin. Improved cardiovascular outcomes with niacin treatment have been demonstrated in people both with and without diabetes. Sustained-release niacin is generally better tolerated than immediate-release preparations, and has been safely used in clinical trials at doses of up to 2000 mg daily (e.g., OTC Slo-Niacin in HATS). Maximum dose for sustained-release (OTC Slo-Niacin) and extended-release (NF-Niaspan) is 2000 mg daily; if more niacin desirable effects, switch to an immediate-release preparation and titrate to a maximum of 3000 to 4500 mg daily in divided doses. Instruct patients to report symptoms of muscle injury (generalized muscle aches and/or weakness) or symptoms suggestive of liver toxicity (fatigue, nausea, anorexia). Monitor serum aminotransferase levels, fasting blood sugar and uric acid levels at baseline and periodically.

### Fibric Acid Derivatives (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-C 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 it, particularly if baseline TGs are high. 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 products, principally at high doses (>2,000 mg) without medical supervision or when patients were converted from immediate-release to sustained-release niacin products. Statin doses may decrease if patients are 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. 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 NSAID (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 glucose and HbA1c that are amenable to slight adjustments of oral antidiabetic drugs or insulin. Improved cardiovascular outcomes with niacin treatment have been demonstrated in people both with and without diabetes. Sustained-release niacin is generally better tolerated than immediate-release preparations, and has been safely used in clinical trials at doses of up to 2000 mg daily (e.g., OTC Slo-Niacin in HATS). Maximum dose for sustained-release (OTC Slo-Niacin) and extended-release (NF-Niaspan) is 2000 mg daily; if more niacin desirable effects, switch to an immediate-release preparation and titrate to a maximum of 3000 to 4500 mg daily in divided doses. Instruct patients to report symptoms of muscle injury (generalized muscle aches and/or weakness) or symptoms suggestive of liver toxicity (fatigue, nausea, anorexia). Monitor serum aminotransferase levels, fasting blood sugar and uric acid levels at baseline and periodically.

### Niacin Dosing

- **IMMEDIATE-RELEASE NIACIN**
  - Initial dose: 50-100 mg/day - Titrate slowly to 1000-3000 mg/d (divide doses)
  - 5-25%↓
  - 15-35%↑
  - 20-50%↓
  - $ -

- **SUSTAINED-RELEASE NIACIN (SLO-NIAKIN OTC)**
  - 500-2000 mg qHS or 500-1000 mg BID
  - 5-25%↓
  - 15-35%↑
  - 20-50%↓
  - $-$$

- **EXTENDED-RELEASE NIACIN (NF—NIASPAN)-B**
  - 500-2000 mg qHS
  - 5-25%↓
  - 15-35%↑
  - 20-50%↓
  - $$$-

### Fibrate Dosing

<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>
<th>SAFETY COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEMFIBROZIL (LOPID)</td>
<td></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>$ -</td>
<td>Side effects: dyspepsia, rash, abnormal liver function, gallstones, and rarely, with decreasing frequency, hepatitis, myopathy, and rhabdomyolysis. 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).</td>
</tr>
<tr>
<td>FENOFIBRATE (generic TRICOR, LOFIBRA)</td>
<td>Microcoated Tablets 54, 160 mg</td>
<td>No change ↑ or ↓</td>
<td>10-35%↑</td>
<td>20-50%↓</td>
<td>$ -</td>
</tr>
<tr>
<td>Usual initial dose: 160 mg daily with meal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**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 (12/12) or OTC for niacin; patient costs against caps will be higher.
**SAFETY COMMENTS**

- **7-30%**
- **Side effects:** flatulence (<5%), constipation (<5%), headache (<4%).
- Do not start new patients on simvastatin 80 mg or increase simvastatin 7-30%.
- **CKD Stage 4 or 5:** In people with GFR <30 mL/min/1.73 m², liver safety.

**Recommended statin.** Based on evidence of efficacy, safety and cost, atorvastatin and simvastatin are the preferred Formulary statins. 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 low, and 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.

**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.**

- Obtain a baseline ALT before or early in the course of therapy.
- Routine monitoring of ALT is not recommended. Check ALT only if there is clinical suspicion for hepatotoxicity.
- If a patient has persistent significant generalized muscle aches and/or weakness or ALT >3 x ULN, the following three possible management strategies are recommended.
  - Discontinue statin until muscle symptoms or ALT elevation resolve and restart the same statin at lower dose or less frequent dose. If tolerated, titrate up as needed.
  - Discontinue statin until muscle symptoms or ALT elevation resolve and start a different statin. Pravastatin or Rosuvastatin are alternatives, recommended on the theoretical basis of their hydrophilicity and minimal interactions with CYP 3A4 inhibitors.
  - Discontinue statin until muscle symptoms or ALT elevation resolve and rechallenge with same statin and dose. Patients often tolerate this, implying adverse event is not related to statin.

---

### Table 3. Lipid-Lowering Medications: Efficacy, Safety, Cost and Comments (continued)

<table>
<thead>
<tr>
<th>HMG-CoA Reductase Inhibitors (Statins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>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 stanols/sterols) or referral to a lipid specialist. (See “Combination Therapy” section below.)</td>
</tr>
<tr>
<td><strong>Recommended statin.</strong> Based on evidence of efficacy, safety and cost, atorvastatin and simvastatin are the preferred Formulary statins. For optimal LDL-C reduction, administer daily in the evening.</td>
</tr>
<tr>
<td><strong>Liver safety.</strong> Significantly elevated aminotransferase levels often resolve on rechallenge or with continued therapy. Incidence of statin-induced true hepatotoxicity is low, and 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 &lt;3 x ULN and stable.</td>
</tr>
</tbody>
</table>

**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.

**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.**

- Obtain a baseline ALT before or early in the course of therapy.
- Routine monitoring of ALT is not recommended. Check ALT only if there is clinical suspicion for hepatotoxicity.
- If a patient has persistent significant generalized muscle aches and/or weakness or ALT >3 x ULN, the following three possible management strategies are recommended.
  - Discontinue statin until muscle symptoms or ALT elevation resolve and restart the same statin at lower dose or less frequent dose. If tolerated, titrate up as needed.
  - Discontinue statin until muscle symptoms or ALT elevation resolve and start a different statin. Pravastatin or Rosuvastatin are alternatives, recommended on the theoretical basis of their hydrophilicity and minimal interactions with CYP 3A4 inhibitors.
  - Discontinue statin until muscle symptoms or ALT elevation resolve and rechallenge with same statin and dose. Patients often tolerate this, implying adverse event is not related to statin.

**STATIN DOSING**

**All 5 statins have good CVD outcome data.**

<table>
<thead>
<tr>
<th>ATORVASTATIN (LIPITOR)</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg daily</td>
<td>34% ↓</td>
<td>5-9% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>20 mg daily</td>
<td>41% ↓</td>
<td>5-9% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>40 mg daily</td>
<td>47% ↓</td>
<td>2-5% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>80 mg daily</td>
<td>54% ↓</td>
<td>2-5% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SIMVASTATIN (ZOCOR)</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg daily</td>
<td>27% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>20 mg daily</td>
<td>34% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>40 mg daily</td>
<td>47% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>80 mg daily (2 x 40 mg tablets)</td>
<td>41% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LOVASTATIN (MEVACOR)</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg daily</td>
<td>20% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>20 mg daily</td>
<td>27% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>40 mg daily</td>
<td>34% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>80 mg daily</td>
<td>41% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PRAVASTATIN (PRAVACHOL)</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg daily</td>
<td>20% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>20 mg daily</td>
<td>27% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>40 mg daily</td>
<td>34% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
<tr>
<td>80 mg daily</td>
<td>41% ↓</td>
<td>5-15% ↑</td>
<td>7-30% ↓</td>
<td>$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NF-ROSVASTATIN (CRESTOR)-B</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/YEAR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 mg daily</td>
<td>40% ↓</td>
<td>8-14% ↑</td>
<td>10-35% ↓</td>
<td>$$$$$</td>
</tr>
<tr>
<td>10 mg daily</td>
<td>46% ↓</td>
<td>8-14% ↑</td>
<td>10-35% ↓</td>
<td>$$$$$</td>
</tr>
<tr>
<td>20 mg daily</td>
<td>52% ↓</td>
<td>8-14% ↑</td>
<td>10-35% ↓</td>
<td>$$$$$</td>
</tr>
<tr>
<td>40 mg daily</td>
<td>56% ↓</td>
<td>8-14% ↑</td>
<td>10-35% ↓</td>
<td>$$$$$</td>
</tr>
</tbody>
</table>

**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
- $6001–$1000
- $10001+

*Costs are acquisition price/year (12/12) or OTC for niacin; patient costs against caps will be higher.
Table 3. Lipid-Lowering Medications: Efficacy, Safety, Cost and Comments (continued)

### 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. As with niacin and resins, it may be useful in people who need LDL-C lowering but cannot tolerate statins, and as add-on therapy in people who are taking statins at the maximum tolerated dose but need additional LDL-C reduction. The effects of ezetimibe on cardiovascular morbidity and mortality have not been evaluated, therefore statins, because of their proven outcome and safety data, remain the first-line therapy for people who require LDL-C reduction.

**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. To date, the 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 rich 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.

<table>
<thead>
<tr>
<th>CHOLESTEROL ABSORPTION INHIBITOR DOSING</th>
<th>LDL-C EFFECTS</th>
<th>HDL-C EFFECTS</th>
<th>TG EFFECTS</th>
<th>COST/ YEAR*</th>
<th>SAFETY COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NF-EZETIMIBE (ZETIA)-B</strong></td>
<td>10 mg daily</td>
<td>18-20%↓</td>
<td>0-5%↑</td>
<td>5-10%↓</td>
<td>$$$$$</td>
</tr>
<tr>
<td><strong>EZETIMIBE/SIMVASTATIN (VYTORIN)-B</strong></td>
<td>10 mg/10 mg daily</td>
<td>45%↓</td>
<td>52%↓</td>
<td>55%↓</td>
<td>60%↓</td>
</tr>
</tbody>
</table>

### 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 2a 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

**For Triglyceride >500 mg/dL Reduction:**

- **NF - Omega-3-acid ethyl esters 1 gm capsule (Lovaza) – B** (465 mg EPA + 375 mg DHA per capsule)
  - 4 caps/day
  - LDL-C EFFECTS: 4-45%↑
  - HDL-C EFFECTS: 0-3%↑
  - TG EFFECTS: 45%↓
  - COST/ YEAR*: $$$$$

- **NF - Kirkland Signature™ EC Fish Oil Concentrate 1200 mg Softgels (374 mg EPA + 310 mg DHA per capsule) – OTC**
  - 6 caps/day
  - LDL-C EFFECTS: 4-45%↑
  - HDL-C EFFECTS: 0-3%↑
  - TG EFFECTS: 45%↓
  - COST/ YEAR*: $$

- **NF - NVC Omega-3 Fish Oil/Vit E Soft Gels (180 mg EPA + 120 mg DHA + 5 IU Vit E) – OTC**
  - 12 caps/day
  - LDL-C EFFECTS: 4-45%↑
  - HDL-C EFFECTS: 0-3%↑
  - TG EFFECTS: 45%↓
  - COST/ YEAR*: $$

**For Post-MI or Secondary Prevention:**

- **NF - Omega-3-acid ethyl esters 1 gm capsule (Lovaza) – B, NF (465 mg EPA + 375 mg DHA per capsule)**
  - 1 cap/day
  - No effect
  - No effect
  - No effect
  - COST/ YEAR*: $$$

- **NF - Kirkland Signature™ EC Fish Oil Concentrate 1200 mg Softgels (374 mg EPA + 310 mg DHA per capsule) – OTC**
  - 2 caps/day
  - No effect
  - No effect
  - No effect
  - COST/ YEAR*: $

- **NF - NVC Omega-3 Fish Oil/Vit E Soft Gels (180 mg EPA + 120 mg DHA) – KP OTC**
  - 3 cap/day
  - No effect
  - No effect
  - No effect
  - COST/ YEAR*: $

#### 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".


**NOTE:** These guidelines are informational only. They are neither intended nor designed as a substitute for the reasonable exercise of independent clinical judgment by practitioners, considering each patient’s needs on an individual basis. Guideline recommendations apply to populations of patients. Clinical judgment is necessary to design treatment plans for individual patients.

**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 (12/12) or OTC for niacin; patient costs against caps will be higher.