QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and The Department of Defense (DoD) guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision-making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

Variations in practice will inevitably and appropriately occur when providers take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health care professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

Version 3.0 – 2014
BACKGROUND

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in the United States (US) and globally. In Western countries, most CVD is due to atherosclerosis. [1] Atherosclerosis is the buildup of plaque (cholesterol, proteins, calcium and inflammatory cells) in the walls of arteries that carry oxygenated blood to the heart and other parts of the body. This plaque narrows the opening of the arteries, limiting the flow of oxygenated blood and increasing the risk of chronic and acute ischemia. If a plaque ruptures within a vital artery, a blood clot forms on the plaque and may obstruct the flow of oxygenated blood to the heart or brain, resulting in an acute coronary syndrome (ACS), myocardial infarction (heart attack; MI) or stroke with potentially irreversible damage to the tissue of the heart or brain.

Control and reduction of atherosclerotic cardiovascular disease (ASCVD) risk factors, including high cholesterol levels, elevated blood pressure (BP), insulin resistance, smoking and a sedentary lifestyle, can contribute to a reduction in ASCVD morbidity and mortality.

Dyslipidemia is defined as one or more of the following: low density lipoprotein cholesterol (LDL-C) >130 mg/dL, high density lipoprotein cholesterol (HDL-C) <40 milligram per deciliter (mg/dL), or triglyceride (TG) >200 mg/dL. [2] In patients with known CVD or high risk for CVD, even “normal” levels of lipids can be deemed amenable to intervention for the purpose of reducing CVD risk.

Dyslipidemia may remain clinically silent until the development of complications. This condition can be diagnosed with a blood test measuring plasma levels of total cholesterol (TC), HDL-C, TG, or individual lipoproteins. LDL-C is measured directly or determined by the following equation: TC-HDL-(TG/5). Sometimes, non-HDL cholesterol is also determined as TC minus HDL. A TC of less than 180 mg/dL is thought to be optimal. [3] Yet, the average TC for American adults is about 200 mg/dL. [4]

The etiology of dyslipidemia involves genetic, lifestyle and other factors. Genetic factors that result in either overproduction or slow clearance of TGs and LDL-C, or underproduction or fast clearance of HDL-C, can lead to dyslipidemia. A sedentary lifestyle with excessive dietary intake of saturated fat, trans fats, added sugars, and cholesterol can also lead to dyslipidemia. Other risk factors include insulin resistance, diabetes mellitus (DM or diabetes), central obesity, and chronic kidney disease (CKD).

About 71 million adults in the US (33.4%) have high LDL-C and only one out of every three adults with high LDL-C has the condition under control. [4] The percentage of American adults with high LDL-C has remained around 34 percent over the past decade, but treatment of high LDL-C has increased from 28.4 percent in 1999-2002 to 48.1 percent in 2005–2008. [4] Treatment usually involves dietary changes and lipid-lowering drugs. However, the management of dyslipidemia has shifted away from treating the dyslipidemia itself as a discrete entity, and moved toward managing dyslipidemia in the context of overall risk for CVD.

This guideline addresses the various treatment and management strategies for managing overall CVD risk among patients with dyslipidemia. As TG levels above 300mg/dl are above the 95th percentile, few patients in the US will have levels above 300mg/dl. Even fewer patients will have TGs >500mg/dl (99th percentile). Due to the infrequency of clinically significant hypertriglyceridemia this guideline does not address hypertriglyceridemia other than to look for secondary causes and non-pharmacologic interventions. Interested readers can refer to Lederle and Bloomfield’s 2012 article for additional information. [5]
BACKGROUND

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in the United States (US) and globally. In Western countries, most CVD is due to atherosclerosis. [1] Atherosclerosis is the buildup of plaque (cholesterol, proteins, calcium and inflammatory cells) in the walls of arteries that carry oxygenated blood to the heart and other parts of the body. This plaque narrows the opening of the arteries, limiting the flow of oxygenated blood and increasing the risk of chronic and acute ischemia. If a plaque ruptures within a vital artery, a blood clot forms on the plaque and may obstruct the flow of oxygenated blood to the heart or brain, resulting in an acute coronary syndrome (ACS), myocardial infarction (heart attack; MI) or stroke with potentially irreversible damage to the tissue of the heart or brain.

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**Management of Dyslipidemia**

**Algorithm**

1. **Men >35 and women > 45 or any patient with ASCVD**
2. **Does patient have:**
   - CHF (EF < 35% & NYHA Class > 1), or
   - ESRD on Dialysis, or
   - Life expectancy < 5 years?
3. **Exit algorithm**
4. **Discuss treatment benefit with patient**
5. **Does patient have a history of ASCVD or ACS?**
6. **Calculate 10-year CVD risk:**
   - Measure lipids, blood pressure,
   - Assess risk factors for CVD and medications
7. **Recent ACS or recurrent ASCVD?**
   - Yes
8. **10-year CVD risk > 12%, or LDL-C ≥ 190, or DM with HTN or smoking?**
   - Yes
9. **Advertise moderate dose statin Consider titrating to high dose as tolerated**
10. **10-year CVD risk 6 - 12%**
11. **Shared decision making results in statin initiation or continuation?**
12. **Positive lifestyle changes:**
   - Smoking, diet & exercise
   - Optimize comorbid conditions
13. **Repeat CVD risk evaluation:**
   - IF 6 - 12% risk every 2 years
   - IF < 6% risk every 5 years

**ASCVD and Equivalents**

- All ACS and MI
- CABG or PCI
- Stable obstructive CAD (stable symptoms of angina or equivalent)
- CVA or TIA
- Atherosclerotic PVD (claudication or AAA)

**Statin Dose (by 10-yr CVD Risk)**

<table>
<thead>
<tr>
<th>10-yr Risk</th>
<th>Statin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;12%</td>
<td>Mod - Hi</td>
</tr>
<tr>
<td>6-12% (with SDM)</td>
<td>Mod</td>
</tr>
<tr>
<td>&lt; 6%</td>
<td>None</td>
</tr>
</tbody>
</table>

**Statin Dose**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Moderate (mg)</th>
<th>High (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>10-20</td>
<td>40-80</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20-40</td>
<td>-</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>40</td>
<td>-</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>40-80</td>
<td>-</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>80</td>
<td>(80 XL QD or 40 BID)</td>
</tr>
</tbody>
</table>

**Brand**

- Rosuvastatin 5-10 20-40

**Acronym List**

| AAA | abdominal aortic aneurysm |
| ABI | ankle brachial index |
| ACS | acute coronary syndrome |
| ASCVD | atherosclerotic cardiovascular disease |
| BAS | body mass index |
| BID | twice a day |
| BP | blood pressure |
| CABG | coronary artery bypass graft |
| CAC | coronary artery calcium |
| CAD | coronary artery disease |
| CVA | cerebral vascular accident |
| CVD | cardiovascular disease |
| DM | diabetes mellitus |
| EF | ejection fraction |
| ESRD | end stage renal disease |
| HDL-C | high density lipoprotein cholesterol |
| IMT | intimal media thickness |
| LDL-C | low density lipoprotein cholesterol |
| LE | liver expectancy |
| LFT | liver function tests |
| MI | myocardial infarction |
| Mod-HI | moderate to high |
| NYHA | New York Heart Association |
| PCI | percutaneous coronary intervention |
| PVD | peripheral vascular disease |
| OD | once a day |
| RF | risk factors |
| SDM | shared decision making |
| TC | total cholesterol |
| TG | triglycerides |
| TIA | transient ischemic attack |
| TLC | therapeutic lifestyle changes |
Management of Dyslipidemia

**Algorithm**

1. Men >35 and women > 45 or any patient with ASCVD
   - **Yes**
   - Exit algorithm

2. Does patient have:
   - CHF (EF < 35% & NYHA Class > 1), or
   - ESRD on Dialysis, or
   - Life expectancy < 5 years?
   - **Yes**
   - Exit algorithm
   - **No**

3. Discuss treatment benefit with patient

4. Does patient have a history of ASCVD or ACS?
   - **Yes**
   - **No**

5. Recent ACS or recurrent ASCVD?
   - **Yes**
   - Advise moderate dose statin
     Consider titrating to high dose as tolerated
   - **No**

6. Calculate 10-year CVD risk:
   - Measure lipids, blood pressure,
   - Assess risk factors for CVD and medications
   - **Yes**
   - 10-year CVD risk ≥ 12%, or LDL-C ≥ 190, or DM with HTN or smoking?
     - **Yes**
     - Advise moderate dose statin
       Consider titrating to high dose as tolerated
     - **No**
     - 10-year CVD risk 6-12%?
       - **Yes**
       - Advise moderate dose statin
       - **No**

7. Shared decision making results in statin initiation or continuation?
   - **Yes**
   - **No**

8. Positive lifestyle changes:
   (Smoking, diet & exercise)
   Optimize comorbid conditions

9. Mediterranean diet plus positive lifestyle changes

10. Repeat CVD risk evaluation:
    - IF 6-12% risk every 2 years
    - IF < 6% risk every 5 years

11. Routine monitoring and follow-up, including for adverse drug effects

12. ASCVD and Equivalents
   - All ACS and MI
   - CABG or PCI
   - Stable obstructive CAD (stable symptoms of angina or equivalent)
   - CVA or TIA
   - Atherosclerotic PVD (claudication or AAA)
   - Does not include asymptomatic atherosclerotic (CAC, exercise test, IMT, ABI, brachial reactivity)

13. Statin Dose (by 10-yr CVD Risk)
   - **10-yr Risk**
   - **Statin Dose**
     - >12 % Mod - Hi
     - 6-12 % (with SDM) Mod
     - < 6 % None

14. Statin Dose
   - Generic [mg] High [mg]
     - Atorvastatin 10-20 40-80
     - Simvastatin 20-40 -
     - Pravastatin 40 -
     - Lovastatin 40-80 -
     - Fluvastatin 80 (80 XL QD or 40 BID) -

15. Brand
   - Rosuvastatin 5-10 20-40

In patients unable to tolerate appropriate mod-hi dose statin according to their risk, use the highest tolerable statin dose as treatment option.
Assessment of Cardiovascular Risk

A. We recommend CVD risk screening for men > age 35 and women > age 45, including a lipid profile and a risk calculation. [Strong For]

B. We recommend against routine screening for dyslipidemia outside of the context of a cardiovascular risk assessment. [Strong Against]

C. Patients with Severe Systolic Chronic Heart Failure (CHF), End Stage Renal Disease (ESRD) and on Dialysis, or a Limited Life Expectancy are excluded from this guideline

D. For risk calculation, we suggest a 10-year risk calculator. [Weak For]

Pharmacotherapy for Primary Prevention (Patients without a history of ASCVD or ACS)

E. F.

7. We suggest shared decision making regarding pharmacologic treatment for patients with an estimated 10-year CVD risk of 12% or greater that takes into consideration the known minimal harms and substantial benefits of moderate-dose therapy in this group of patients. [Weak For]

8. We suggest initiation of a moderate-dose statin for patients with an estimated 10-year CVD risk of 12% or greater. [Weak For]

9. We suggest considering a moderate-dose statin for patients with a 10-year CVD risk between 6% and 12% following a discussion of the known minimal harms, benefits derived from limited evidence, and an exploration of the patient’s values and preferences. [Weak For]

10. For primary prevention, we recommend a moderate-dose statin as the agent of choice to reduce CVD risk if the patient chooses pharmacologic therapy. [Strong For]

11. For primary prevention in patients who are unable to tolerate statins, we suggest reinforcing adherence to positive lifestyle changes. For patients who prefer to try pharmacotherapy, we suggest considering treatment with gemfibrozil or bile acid sequestrants (BAS), noting that these agents have been associated with only a small CVD risk reduction and studied in limited populations, e.g., males with LDL-C >190 mg/dL. [Weak For]

12. We suggest establishing baseline liver function tests (LFTs) and creatinine kinase (CK) before initiation of drug therapy. [Weak For]

13. We recommend against routinely measuring LFTs or CK after a moderate-dose statin is initiated. [Strong Against]

Pharmacotherapy for Secondary Prevention (Patients with a History of ASCVD or ACS)

14. In patients with established ASCVD, we recommend use of a moderate-dose statin following a discussion of the minimal harms, substantial benefits, and an exploration of the patient’s values and preferences. [Strong For]

15. In patients with ASCVD who are able to tolerate statins, we recommend against the routine use of non-statin lipid lowering drugs (e.g., fibrates, niacin, ezetimibe, omega-3 fatty acids, etc.) either alone as mono-therapy or added to statins. [Strong Against]

16. In patients with ASCVD who are unable to tolerate statins, we suggest reinforcing adherence to positive lifestyle changes and suggest offering niacin or gemfibrozil, noting that these agents have been associated with only a small CVD risk reduction and studied in limited populations (e.g., males with low HDL-C). [Weak For]

17. We strongly recommend against the routine use of LDL–C and non-HDL–C goals for the secondary prevention of ASCVD. [Strong Against]

18. We suggest offering a high-dose statin only in select patient populations (e.g., ACS, multiple uncontrolled risk factors or recurrent CVD events on moderate-dose statin) following a discussion of the added harms, small additional benefits, and an exploration of the patient’s values and preferences. [Weak For]

I.

19. We suggest measuring LFTs 4–12 weeks after the initiation of high-dose statin. [Weak For]
**Assessment of Cardiovascular Risk**

**Recommendations**

**A.** We recommend CVD risk screening for men > age 35 and women > age 45, including a lipid profile and a risk calculation. [Strong For]

**B.** We recommend against routine screening for dyslipidemia outside of the context of a cardiovascular risk assessment. [Strong Against]

**C.** We suggest against the routine use of high-sensitivity C-reactive protein (hsCRP) testing. [Weak Against]

1. We suggest the routine use of coronary artery calcium (CAC) testing. [Weak Against]

**Pharmacotherapy for Primary Prevention (Patients without a history of ASCVD or ACS)**

**E, F**

7. We suggest shared decision making regarding pharmacologic treatment for patients with an estimated 10-year CVD risk of 12% or greater that takes into consideration the known minimal harms and substantial benefits of moderate-dose therapy in this group of patients. [Weak For]

8. We suggest initiation of a moderate-dose statin for patients with an estimated 10-year CVD risk of 12% or greater. [Weak For]

9. We suggest considering a moderate-dose statin for patients with a 10-year CVD risk between 6% and 12% following a discussion of the known minimal harms, benefits derived from limited evidence, and an exploration of the patient’s values and preferences. [Weak For]

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11. For primary prevention in patients who are unable to tolerate statins, we suggest reinforcing adherence to positive lifestyle changes. For patients who prefer to try pharmacotherapy, we suggest considering treatment with gemfibrozil or bile acid sequestrants (BASs), noting that these agents have been associated with only a small CVD risk reduction and studied in limited populations, e.g., males with LDL-C >190 mg/dL. [Weak For]

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19. We suggest measuring LFTs 4-12 weeks after the initiation of high-dose statin. [Weak For]
Non-pharmacological Approaches

H.

20. We recommend all adults adopt healthy lifestyles to reduce CVD risk, including: [Strong For]

- b. Therapeutic Lifestyle Changes (TLC) diet to optimize nutrition
  (For overweight and/or obese patients, see VA/DoD CPG for Management Of Overweight And Obesity 2014 at: http://www.healthquality.va.gov/guidelines/cd/obesity/index.asp)

Modified from the 2006 CPG without an updated systematic review of the evidence. *

21. We suggest offering high-risk patients (see text for definition) a dietitian-monitored Mediterranean diet supplemented with either extra-virgin olive oil (roughly 1 liter per week) or 30g of mixed nuts per day (15g of walnuts, 7.5g of hazelnuts, and 7.5g of almonds) for the reduction of CVD events. [Weak For]

22. We suggest that each patient's diet be individualized based on a nutrition assessment (preferably by a RD), other CVD risk factors, other disease conditions, and patient's lifestyle. [Weak For]

Modified from the 2006 CPG without an updated systematic review of the evidence. *

23. We recommend treating the common secondary causes of elevated TGs: dietary indiscretion (e.g., refined sugars), alcohol use, hypothyroidism, and hyperglycemia. [Strong For]

Modified from the 2006 CPG without an updated systematic review of the evidence. *

24. We suggest for patients with TGs greater than 500 mg/dL a strict diet therapy including avoidance of alcohol, restriction of dietary fat, and avoidance of refined sugars. We suggest for patients with TGs greater than 1000 mg/dL a very low fat diet to reduce chylomicronemia and risk of acute pancreatitis. [Weak For]

Follow-up

G.

25. We suggest CVD risk assessment every five years for patients with low CVD risk and not on statin therapy. [Weak For]

26. We suggest CVD risk assessment every two years for patients with intermediate CVD risk or with appearance of a new CVD risk factor (e.g., new diagnosis of type 2 DM or hypertension) and not on statin therapy. [Weak For]

* These "modified" recommendations from the previous CPG published in 2006 were considered still relevant to health care providers and were carried forward into this CPG. For additional information please refer to the section Reconciling 2006 CPG Recommendations in the full CPG.
Non-pharmacological Approaches

H.

20. We recommend all adults adopt healthy lifestyles to reduce CVD risk, including: [Strong For]
   a. Tobacco cessation for all smokers (See VA/DoD Tobacco Use CPG 2008 at:
   b. Therapeutic Lifestyle Changes (TLC) diet to optimize nutrition
      (For overweight and/or obese patients, see VA/DoD CPG for Management Of Overweight And Obesity 2014 at:
   c. Optimal physical activity (See 2008 Physical Activity Guidelines for Americans, at

   Modified from the 2006 CPG without an updated systematic review of the evidence. *

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Table 7. Summary of Statin and Non-statin Pharmacologic Agents

<table>
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<tr>
<th>Drug Category</th>
<th>Dose</th>
<th>Adverse Drug Events</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>10-40 mg once daily (high dose = 40-80 mg) / 10-20 mg (moderate dose)</td>
<td>Statins are generally well tolerated. Myalgia, myopathy, and rarely, rhabdomyolysis may occur. Risk of rhabdomyolysis is increased in the presence of interacting drugs, higher statin doses, renal or liver impairment, hypothyroidism, frailty, advanced age, etc. Other adverse events include diabetes, LFT elevation and possible non-serious, reversible cognitive effects including memory loss and confusion. However, an association between statins and an effect on cognition has not been confirmed. First line therapy for primary or secondary prevention of ASCVD. Monotherapy with statins represents the best evidence for cardiovascular risk reduction.</td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>5-40 mg once daily (high dose = 20-40 mg) / 5-10 mg (moderate dose)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>5-40 mg once daily (moderate dose = 10-40 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td>20-40 mg once daily (moderate dose = 40-80 mg)</td>
<td></td>
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<td>Pravastatin</td>
<td>10-40 mg once daily (moderate dose = 40-80 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20-40 mg/day (moderate dose = 40 mg / twice daily or 80 mg 30/day)</td>
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<td></td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>1-4 mg once daily (moderate dose = 2-4 mg)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Fibrates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>Nanocrystal 145 mg/day / Nicoretal 45-200 mg/day / Nicoretal taken with meals. Dose varies depending upon micronized product used.</td>
<td>Skin rash, gastrointestinal (nausea, bloating, dyspepsia, cramping), headache, myalgia, myopathy, increased serum transaminases, elevation in serum creatinine, cholelithiasis, etc. Combination with a statin in the ACCORD trial showed no evidence of improved patient outcomes beyond statin based therapy (Subgroup analysis showed potential harm in women and a potential benefit in those with high TG and low HDL-C). (6) Avoid in patients with CCl = 30 ml/m; active liver disease including primary biliary cirrhosis, and preexisting gallbladder disease.</td>
<td>First line therapy for primary or secondary prevention of ASCVD. Monotherapy with statins represents the best evidence for cardiovascular risk reduction.</td>
</tr>
<tr>
<td>Fenofibrinic Acid</td>
<td>35-155 mg once daily / Taken without regard to meals. See Fenofibrate</td>
<td>Avoid in patients with CCl = 30 ml/m; active liver disease including primary biliary cirrhosis, and preexisting gallbladder disease.</td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>600 mg twice daily / Take 30-60 min before meals. See Fenofibrate</td>
<td>VA-HIT (secondary prevention) gemfibrozil BID for 5 years vs. placebo in men with low HDL-C and moderately elevated LDL-C resulted in a significant reduction in nonfatal MI and death or cardiac origin. (7) Avoid in patients with CCl = 30 ml/m; active liver disease including primary biliary cirrhosis, and preexisting gallbladder disease.</td>
<td></td>
</tr>
</tbody>
</table>

| **Cholesterol Absorption Inhibitors** | | |       |
| Ezetimibe      | 10 mg/day | Unknown benefit for reducing cardiovascular risk in primary or secondary prevention. |       |

| **Cholesterol Lowering Medications** | | |       |
| Cholesterol Absorption Inhibitors | | |       |
| Fish Oil | 1-4 g/day, as single dose or divided twice daily. | Taste perversion, dyspepsia, pruritus, and rash. HMG-CoA reductase inhibitors (statins) in combination with fish oil may potentiate the risk for myopathy. Avoid in patients with active liver disease, active peptic ulcer disease, and arterial bleeding. |       |

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<tbody>
<tr>
<td><strong>Bile Acid Sequestrants (BAS)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>4-12 g/day / Take within 30 min of a meal.</td>
<td>Nausea, bloating, cramping, and constipation, elevations in hepatic transaminases and alkaline phosphatase and increases in triglycerides.</td>
<td>Separate BAS from other medications by taking them at least 1 hour before BAS and at least 4-6 hours after BAS to avoid a reduced effect of other medications.</td>
</tr>
<tr>
<td>Colestipol</td>
<td>5-30 g/day</td>
<td></td>
<td>Colesevelam has less drug interactions than do the older BAS and will not decrease vitamin A, D, E, K absorption as much.</td>
</tr>
<tr>
<td>Colesevelam</td>
<td>3.75 g/day / Take with meals daily or divided twice daily.</td>
<td></td>
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</tr>
</tbody>
</table>

**Niacin Products**

| Niapsan (ER Niacin) | 500-2000 mg/day / Initial: 500 mg at bedtime x 4 weeks, then 1 g at bedtime x 1 week x 4 weeks x 2 weeks x 1 week x 2 weeks | Flushing, edema, glucose intolerance, GI distress (abdominal pain, diarrhea, dyspepsia, nausea, vomiting), pruritus, GI bleeding, elevation of liver transaminases and hepatic toxicity. | Combination with a statin in AIM-HIGH and HPS2-THRIVE showed no evidence of improved patient outcomes beyond statin based therapy in patients with ASCVD with well controlled LDL-C. (8,9) An increased risk for serious adverse events was observed in HPS2-THRIVE in the niacin/tacopirpiran group. (8) The contribution of laropiprant to the increased risk for adverse events is unknown. Avoid in patients with active liver disease, active peptic ulcer disease, and arterial bleeding. |

**Niacor (IR Niacin)**

| 250-6000 mg/day / Initial: 250 mg daily with evening meal, increase frequency and/or dose every 4-7 days. | | |

**Fish Oil**

| 1-4 g/day, as single dose or divided twice daily. | Taste perversion, dyspepsia, pruritus, and rash. HMG-CoA reductase inhibitors (statins) in combination with fish oil may potentiate the risk for myopathy. Avoid in patients with active liver disease, active peptic ulcer disease, and arterial bleeding. | Meta-Analysis by Rizos et al. (2012) included 60 studies enrolling 68,680 patients. Use of omega-3 fatty acids was not associated with a reduction in all-cause mortality, cardiac death, MI, stroke or sudden death. (10) |

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Table 7. Summary of Statin and Non-statin Pharmacologic Agents

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Dose</th>
<th>Adverse Drug Events</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins</strong></td>
<td></td>
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<tr>
<td>Atorvastatin</td>
<td>10-40 mg once daily (high dose = 40-80 mg) (moderate dose = 10-20 mg)</td>
<td></td>
<td>First line therapy for primary or secondary prevention of ASCVD. Monotherapy with statins represents the best evidence for cardiovascular risk reduction.</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>5-40 mg once daily (high dose = 20-40 mg) (moderate dose = 5-10 mg)</td>
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<tr>
<td>Simvastatin</td>
<td>5-40 mg once daily (moderate dose = 10-40 mg)</td>
<td></td>
<td></td>
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<tr>
<td>Lovastatin</td>
<td>20-40 mg once daily (moderate dose = 40 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>10-40 mg once daily (moderate dose = 40-80 mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20-40 mg/day (moderate dose = 40 mg twice daily or 80 mg 30/day)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>1-4 mg once daily (moderate dose = 2-4 mg)</td>
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<td></td>
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<tr>
<td><strong>Fibrates</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fenofibrate</td>
<td>Nanocrystal 145 mg/day (micronized 45-200 mg/day) (micronized taken with meals). Dose varies depending upon micronized product used.</td>
<td>Skin rash, gastrointestinal (nausea, bloating, dyspepsia, cramping), headache myalgia, myopathy, increased serum transaminases, elevation in serum creatinine, cholesterol, etc.</td>
<td></td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>35-105 mg once daily (taken without regard to meals). See Fenofibrate.</td>
<td>Avoid in patients with CCl = 30 ml/min, active liver disease including primary biliary cirrhosis, and preexisting gallbladder disease.</td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>600 mg twice daily (take 30-60 min before meals). See Fenofibrate</td>
<td>VA-HT (secondary prevention) gemfibrozil BID for 5 years vs. placebo in men with low HDL-C and moderately elevated LDL-C resulted in a significant reduction in nonfatal MI and death or cardiac origin. (7) Avoid in patients with CCl = 30 ml/min, active liver disease including primary biliary cirrhosis, and preexisting gallbladder disease.</td>
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</tr>
<tr>
<td><strong>Cholesterol Absorption Inhibitors</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>10 mg/day</td>
<td>Unknown benefit for reducing cardiovascular risk in primary or secondary prevention.</td>
<td></td>
</tr>
<tr>
<td><strong>Fish Oil</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish Oil</td>
<td>1-4 g/day, at single dose or divided twice daily.</td>
<td>Taste perversion, dyspepsia, pruritus, and rash. Hepatic ALT and AST increased. May increase LDL-C. Meta-Analysis by Rizos et al. (2012) included 60 studies enrolling 66,680 patients. Use of omega 3 fatty acids was not associated with a reduction in all-cause mortality, cardiac death, MI, stroke or sudden death. (10)</td>
<td></td>
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REFERENCES


