CCHCS Care Guide: Dyslipidemia

SUMMARY

GOALS
- Identify and treat patients on the basis of Primary vs Secondary Prevention for atherosclerotic cardiovascular disease (ASCVD)
- Counsel all patients on healthy lifestyle choices
- Prescribe high-intensity statin therapy for ALL ASCVD patients
- Decrease morbidity and mortality related to ASCVD

DETECTION SUPPORT

ALERTS
- Statin related adverse effects & potential drug interactions
- Evaluate patient for familial hypercholesterolemia (FH) if LDL-C ≥ 190 mg/dL
- DO NOT start dialysis if the patient is on statin

DYSLIPIDEMIA DIAGNOSTIC CRITERIA/EVALUATION

Diagnosis of dyslipidemia is made by measuring serum levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG). Causes may be genetic (see Attachment A), lifestyle factors or medical conditions that interfere with blood lipid levels. Evaluation includes:

- **History:** Assess each patient for personal ASCVD risk factors and family history of ASCVD (see page 5)
  - Estimate patient’s 10-year ASCVD risk based on sex, age, race, total cholesterol, HDL-C, blood pressure, history of diabetes mellitus (DM), and smoking history using American College of Cardiology’s (ACC) new ASCVD Risk Estimator Plus Equation and determine appropriate statin benefit group (see chart below for details).
- **Physical exam:** Height, weight, body mass index (BMI), waist circumference, blood pressure, cardiac evaluation, peripheral and carotid pulses, vascular bruits, check for tendon xanthomas and xanthelasmas.
- **Labs:** Non-fasting lipid panel (LP) is acceptable for initial screening, comprehensive metabolic panel (CMP) including uric acid, thyroid stimulating hormone (TSH), Hemoglobin A1c (HbA1c) if DM status is unknown (see page 6 for additional labs)
- **Patient education:** Explain relationship of dyslipidemia to ASCVD and importance of addressing ASCVD risk factors. Use patient education pages PE1-PE3 for guidance.

TREATMENT

- **Therapeutic Lifestyle Changes:** Recommend 3 month trial of lifestyle changes such as low fat diet, increased exercise, weight loss, adequate sleep, smoking cessation, and control of hypertension (HTN) and/or DM for groups 2, 3, 4 (see below)
- Treatment is managed according to patient’s ASCVD risk per table (see Attachment C for Hypertriglyceridemia details)

<table>
<thead>
<tr>
<th>SECONDARY ASCVD PREVENTION (AGE 18+)</th>
<th>Very High Risk ASCVD</th>
<th>Maximum tolerated statin is recommended:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>(See algorithm page 3)</td>
<td>If LDL-C ≥ 70 mg/dL: Consider adding ezetimibe</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If LDL-C remains ≥ 70 mg/dL (or non-HDL-C ≥ 100): Consider PCSK-9</td>
</tr>
<tr>
<td>Stable ASCVD</td>
<td>(See algorithm page 3)</td>
<td>High-or moderate-intensity statin is recommended:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If High-Intensity statin: Aim for LDL-C lowering by at least 50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If Moderate statin: Aim for LDL-C lowering 30-50%</td>
</tr>
<tr>
<td>PRIMARY PREVENTION</td>
<td>Severe Hypercholesterolemia</td>
<td>LDL-C ≥ 190 mg/dL → No risk assessment needed → High-Intensity statin. If LDL-C 50% reduction not achieved and fasting TG’s ≥ 300 mg/dL, after maximal statin and ezetimibe, bile acid sequestrant may be considered.</td>
</tr>
<tr>
<td>Asses ASCVD risk in each age group</td>
<td>Diabetes Mellitus in Adults</td>
<td>DM and age 40-75 years → Moderate-intensity statin or do risk assessment to consider high-intensity statin</td>
</tr>
<tr>
<td>emphasize adherence to a heart healthy lifestyle</td>
<td>Age 18-39 years</td>
<td>Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk. Consider statin if family history, premature ASCVD and LDL-C of ≥ 160 mg/dL</td>
</tr>
<tr>
<td></td>
<td>Age 40-75 years with LDL-C of ≥ 70&lt; 190 mg/dL and a 10-year ASCVD risk:</td>
<td>&lt; 5% “Low Risk”: Risk discussion. Emphasize healthy lifestyle changes.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 to &lt; 7.5%: If Risk enhancers discuss moderate-intensity statin.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5% - &lt; 20% “Intermediate Risk”: Discussion if risk estimate + risk enhancer favor moderate-intensity statin to reduce LDL-C by 30%-49%.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 20% “High Risk”: Initiate statin to reduce LDL-C ≥ 50%</td>
</tr>
<tr>
<td></td>
<td>Age &gt; 75 years Clinical Assessment → Risk discussion</td>
<td></td>
</tr>
</tbody>
</table>

MONITORING

**If on statin:** Once lipid-lowering drug therapy has started check patient’s fasting lipids:
- 1-3 months after starting treatment
- 1-3 months after dose adjustment until within the therapeutic range (See page 18 for information on monitoring side effects)

Once a patient has reached the appropriate/optimal lipid levels:
- Check fasting lipids every 12 months (unless there are adherence problems or other reasons for more frequent testing, such as changes in therapy)

**If not on statin:** After age 20 years, it is reasonable to assess traditional ASCVD risk factors every 4 to 6 years

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</tr>
</tbody>
</table>

Information contained in the Care Guide is not a substitute for a health care professional’s clinical judgment. Evaluation and treatment should be tailored to the individual patient and the clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to “Disclaimer Regarding Care Guides” for further clarification. https://cchcs.ca.gov/clinical-resources/
CCHCS Care Guide: Dyslipidemia

Summary

**ASCVD Risk Enhancers**
- Family history of premature ASCVD
- Persistently elevated LDL-C ≥ 160 mg/dL
- Chronic Kidney Disease (CKD)
- Metabolic Syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (esp. rheumatoid arthritis, psoriasis, HIV)
- Ethnicity factors: (e.g., South Asian)

Lipid Biomarkers:
- Persistently elevated triglycerides (≥ 175 mg/dL)

In selected individuals if measured:
- Hs-CRP ≥ 2.0 mg/dL
- Lp(a) levels > 50 mg/dL or > 125 nmol/L
- apoB ≥ 130 mg/dL
- Ankle-brachial index < 0.9

Diabetes Specific Risk Factors independent of other Risk Factors in Diabetes
- Long duration (≥ 10 years for type 2 DM or ≥ 20 years for type 1 DM)
- Albuminuria ≥ 30 mcg albumin/mg creatinine
- eGFR < 60 ml/min/1.73 m²
- Retinopathy
- Neuropathy
- ABI < 0.9

Patient presents with suspected dyslipidemia. Perform comprehensive evaluation including:
- Personal and family history, including ASCVD risk factors and physical exam (see pages 5-6)
- Baseline Labs: Fasting lipid panel typically required prior to prescribing statin therapy (may be non-fasting if initial screen), CMP, HbA1c, and TSH (see page 6 for details)
- Diagnostic studies as indicated such as EKG (resting), stress tests (treadmill, chemical, nuclear)

**Primary Prevention: Assess ASCVD Risk**
- Emphasize Adherence to Healthy Lifestyle

Age 18-39

**Estimate Lifetime Risk**
- Encourage lifestyle changes to prevent or reduce ASCVD risk
- Consider statin if family history, premature ASCVD, and LDL-C ≥ 160 mg/dL

*If LDL-C ≥ 190 mg/dL*
- No risk assessment; High intensity statin (Class I)

*Diabetes* and age 40-75

Moderate-intensity statin (Class I)

Age > 75: Clinical assessment, risk discussion

Risk Discussion
- Emphasize lifestyle to reduce risk factors (Class I)
- If Risk Enhancers** present then risk discussion regarding Moderate-intensity statin therapy (Class IIb)

**Risk categories**
- Low Risk (< 5%)
- Borderline Risk (5 - < 7.5%)
- Intermediate Risk (7.5% - < 20%)
- High Risk (≥ 20%)

Risk Discussion
- If risk is uncertain, discuss with patient the consideration of additional risk factors including measuring Coronary Artery Calcium (CAC) in selected adults. For additional information on CAC including scoring see page 6.

ACC/AHA Class of Recommendations
- Class I (Strong/Recommended) Benefit >>> Risk
- Class IIa (Moderate) Benefit > Risk
- Class IIb (Weak) Benefit ≥ Risk

**Class IIa**
- Risk Discussion
- Risk Assessment to consider High-intensity statin (Class IIa)

**Class IIb**
- Risk Discussion
- Estimate ASCVD Risk
- Perform comprehensive evaluation including:
  - Personal and family history
  - Baseline Labs
  - Diagnostic studies

**Diabetes Specific Risk Factors independent of other Risk Factors in Diabetes**
- Long duration (≥ 10 years for type 2 DM or ≥ 20 years for type 1 DM)
- Albuminuria ≥ 30 mcg albumin/mg creatinine
- eGFR < 60 ml/min/1.73 m²

- Retinopathy
- Neuropathy
- ABI < 0.9
Patient presents with clinical ASCVD

Recommend Therapeutic Lifestyle Changes
(See page 7)

ASCVD not at very high risk*

Age ≤ 75 yrs

ASCVD at very high risk*

Age > 75 yrs

High-intensity statin (Goal: LDL-C ≥ 50% (Class I)

If High-intensity statin not tolerated, use Moderate-intensity statin (Class I)

High-intensity or maximal statin (Class I)

If on maximal statin and LDL-C ≥ 70 mg/dL, adding ezetimibe may be reasonable (Class IIb)

If on clinically judged-maximal LDL-C lowering therapy & LDL-C ≥ 70 mg/dL or non HDL-C ≥ 100 mg/dL, adding PCSK9-I is reasonable (Class IIa)

Note: PCSK9-I is Non-Formulary with Use Criteria; Lipid Specialist referral needed prior to prescribing; administration by subQ injection (see page 10 for details)

ACC/AHA Class of Recommendations
• Class I (Strong/Recommended) Benefit >>> Risk
• Class IIa (Moderate) Benefit >> Risk
• Class IIb (Weak) Benefit ≥ Risk

*Very High-Risk for Future ASCVD Events
Includes a history of multiple major ASCVD events or one major event and multiple (> 3) high-risk conditions.

Major ASCVD Events
• Recent acute coronary syndrome (within the past 12 months)
• History of myocardial infarction (other than recent acute coronary syndrome event listed above)
• History of ischemic stroke
• Symptomatic peripheral arterial disease (history of claudication with ankle brachial index < 0.85, or previous revascularization or amputation)

High-Risk Conditions
• Age ≥ 65 years
• Current smoking
• History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event (s)
• Chronic Kidney Disease (eGFR 15-59 mL/1.73m²)

Note: In adults with dialysis-dependent CKD, KDIGO recommends avoiding initiation of statins or statin/ezetimibe combinations. However, there is no recommendation to stop therapy in dialysis patients who are already receiving statins or statin/ezetimibe combinations.13
• Diabetes
• Hypertension
• Heterozygous familial hypercholesterolemia
• Persistently elevated LDL-C ≥ 100 mg/dL despite normally tolerated statin therapy and ezetimibe
• History of congestive heart failure
Blood lipids, such as cholesterol and TG, are insoluble in plasma. They are made soluble by inclusion into circulating lipoproteins. The lipoprotein consists of esterified and unesterified cholesterol, TGs, phospholipids, and protein. There are five major lipoproteins in blood: chylomicrons, very low-density lipoprotein (VLDL), intermediate-density lipoprotein, LDL-C, and HDL-C.

Dyslipidemia are disorders of lipoprotein metabolism that can lead to atherosclerosis. Dyslipidemias were traditionally classified by patterns of elevation in lipids and lipoproteins (Fredrickson phenotype). A more practical system categorizes dyslipidemias as primary or secondary and characterizes them by:
- Increases in cholesterol only (pure or isolated hypercholesterolemia)
- Increases in TGs only (pure or isolated hypertriglyceridemia) - covered in Attachment C
- Increases in both cholesterol and TGs (mixed or combined hyperlipidemias) - most common

This system does not take into account specific lipoprotein abnormalities (e.g., low HDL-C or high LDL-C) that may contribute to disease despite normal cholesterol and TG levels.

Primary and secondary dyslipidemia is discussed below:

**Primary Genetic Causes**
- **Genetic dyslipidemia** caused by single or multiple gene mutations that result in either overproduction or defective clearance of LDL-C, or TGs, or underproduction or excessive clearance of HDL-C
- Familial combined hyperlipidemia, familial hypertriglyceridemia, and homozygous familial or polygenic hypercholesterolemia are genetic dyslipidemias and currently excluded from these guidelines given their uncommon occurrence and scarce clinical trial data (see Attachment A)

**Secondary Lifestyle or Medical Causes**
- Caused by lifestyle factors or medical conditions that interfere with blood lipid levels over time
  - **Lifestyle Factors**: Obesity (especially excess weight around the waist), smoking, excess consumption of fats (especially saturated and trans fats), and diet high in refined carbohydrates
  - Levels of cholesterol and TGs naturally increase during pregnancy. Statins are contraindicated during pregnancy and lactation
  - **Medical Conditions**: Diabetes, hypothyroidism, alcohol use disorder, metabolic syndrome, severe infections such as human immunodeficiency virus (HIV), cholestatic liver disease, nephrotic syndrome, chronic renal failure
  - **Certain medications**: e.g., thiazide diuretics, beta blockers, oral estrogens, atypical antipsychotics (metabolic syndrome), tamoxifen, glucocorticoids, antiretroviral regimens used for HIV, retinoids, and cyclosporine

Additional factors affecting severity of dyslipidemia/cardiovascular risk:
- **ASCVD risk factors**: Severity of ASCVD 10 year risk estimate is based on sex, age, race, total cholesterol, HDL-C, blood pressure, history of DM, and smoking history (see page 5)
- **ASCVD Risk Enhancers**: In intermediate-risk adults, risk-enhancers are factors which, if present, favor statin initiation/intensification. These include (see page 5 for additional details):
  - Chronic conditions such as metabolic syndrome, chronic kidney disease (CKD), premature menopause
  - Lab abnormalities such as hypertriglyceridemia or elevated Lp(a) or apoB
  - High risk race/ethnicity: American Heart Association (AHA) recommends clinicians review racial/ethnic features that can influence ASCVD risk when making treatment decisions. Different cardiovascular outcomes persist based on sociodemographic characteristics that include, but are not limited to, age, sex, and race/ethnicity. There are specific race/ethnic issues to consider for Asian, Hispanic/Latino, and Black Americans in the evaluation, risk decisions, and treatment due to potential for underestimation of risk when using Cohort Equations derived for whites, and potential for overestimation of risk for East Asians

Important characteristics to consider include:
- Higher ASCVD risk in South Asians
- ASCVD risk higher among individuals from Puerto Rico than from Mexico
- Black women show increased ASCVD risk compared to otherwise similar white counterparts
- Native American/Alaskan have higher rates of risk factors for ASCVD vs non-Hispanic whites
EVALUATING FOR DYSLIPIDEMIA

History

- **Personal**: Smoking, diet, physical activity, impaired glucose tolerance, metabolic syndrome, DM, obesity, HTN, dyslipidemia, cardiovascular or cerebrovascular events, CKD, Non-Alcoholic Fatty Liver Disease (NAFLD)/Non-Alcoholic SteatoHepatitis (NASH), autoimmune/inflammatory disease (e.g., lupus, rheumatoid arthritis, psoriasis), hepatitis C, history of pancreatitis, medications that alter lipids (e.g., steroids, retinoids, HIV therapy, anti-rejection medications)

  ⇒ Evidence supports the association between ASCVD and mental health issues. Depression is an independent risk factor as well as more prevalent in patients with ASCVD. Also schizophrenia, bipolar disorder, anxiety and post traumatic stress disorder have been found to increase the risk for ASCVD. Care coordination and collaboration with mental health is very important.

- **Family**: Cardiovascular disease (CVD), HTN, dyslipidemia

Identify medical conditions that increase a patient’s risk of dyslipidemia and/or ASCVD:
- Impaired glucose tolerance
- Metabolic syndrome
- DM
- Obesity
- HTN
- Prior cardiovascular or cerebrovascular event(s)
- NAFLD

Determine ASCVD Risk

Assessment of ASCVD risk is the foundation of primary prevention with the aim of treating dyslipidemia to delay or prevent new-onset ASCVD. **Note**: In patients without known ASCVD (Primary Prevention) no risk assessment is needed for those with LDL ≥ 190 mg/dL—these patients have a high lifetime risk of ASCVD and high intensity statins should be started.

**ASCVD Risk Factors**: For most patients estimating the individual’s 10-year absolute ASCVD risk is fundamental in establishing appropriate medical management and enables matching the intensity of preventive interventions to the patient’s absolute risk. This helps to maximize anticipated benefit and minimize potential harm from overtreatment. The estimate is based on sex, age, race, total cholesterol, HDL, blood pressure, history of DM, and smoking history.

Use ACC’s new **ASCVD Risk Estimator Plus Equation** to determine patient’s 10-year ASCVD risk.

This tool gives an estimate of the patient’s risk of a cardiovascular event within the next 10 years, categorized as follows:

- **Low risk**: < 5%
- **Borderline risk**: 5% - < 7.5%
- **Intermediate risk**: 7.5% - < 20%
- **High risk**: ≥ 20%

After evaluating 10-year risk, clinicians should discuss it with the patient before initiating statin therapy. Risk discussions are the cornerstone of the shared decision-making process.

**Additional Risk “Enhancers”**: In intermediate-risk adults, risk-enhancing factors favor statin initiation or intensification include:
- Metabolic syndrome
- CKD
- Chronic inflammatory conditions
- Premature menopause and preeclampsia
  - High-risk race/ethnicity (see page 4)
  - Persistent triglycerides ≥ 175 mg/dL
  - Elevated Lp(a) or apoB

(See algorithm on page 3 for list of risk enhancing factors)
# CCHCS Care Guide: Dyslipidemia

## Evaluating for Dyslipidemia Continued

### Physical Exam

Complete comprehensive physical exam, paying particular attention to the following:
- Height, weight, BMI, waist circumference, blood pressure, cardiac evaluation, peripheral and carotid pulses, vascular bruises

High LDL-C can cause tendinous xanthomas and xanthelasmas (lipid rich yellow plaques on the medial eyelids)
- Severe hypertriglyceridemia (> 2000 mg/dL [> 22.6 mmol/L]) may present with gastrointestinal pain (TGs > 150 mg/dL can cause acute pancreatitis), paresthesias, dyspnea, confusion, and dementia

### Labs

Order the following initial labs:
- Lipid Panel includes: Total Cholesterol, HDL-C, TGs, LDL-C, and calculated non-HDL-C (see Attachment B)
  - ACC/AHA note that the maximal difference between random non-fasting lipids (1-6 hours after meal) and fasting lipids is **not clinically significant** (26 mg/dL for TG and 8 mg/dL for total cholesterol, LDL-C and non-HDL-C). The HDL-C does not change. They recommend:
    - General screening LP can be done non-fasting
    - Do fasting LP prior to starting statins, when TG > 500 mg/dL and while on statin therapy
    - Some guidelines recommend checking LP twice before beginning lipid-lowering drug treatment
- CMP including uric acid
- HbA1c
- TSH

Tests for secondary causes of dyslipidemia should be done in most patients with newly diagnosed dyslipidemia and when a component of the lipid profile has inexplicably changed for the worse. Such tests include:
- Fasting glucose
- Liver enzymes

Additional labs only to be considered based on individual patient circumstances:
- **CAC testing:** If uncertain about the need for statin this test can be done to add to the information on future ASCVD risk. AHA considers it an option in patients in intermediate-risk (7.5% - < 20%) or selected borderline-risk adults with uncertainty about statins)
  - CAC=0, indicates low ASCVD risk for 10 years, reasonable to withhold statins and reassess
  - CAC 1-99 and age ≥ 55 years, reasonable to initiate statins
  - CAC ≥ 100 or ≥ 75th percentile, reasonable to initiate statins
- **ApoB:** May be measured when trying to evaluate a patient’s risk of developing ASCVD and when there is a personal or family history of heart disease and/or abnormal lipid levels, especially in patients with significantly elevated TGs
- **Lp(a):** May be considered for patients with a family history of early ASCVD or to refine the evaluation of patients at moderate-risk; high concentrations may support more aggressive control of other lipoprotein factors
- **High-sensitivity C reactive protein (hsCRP):** May help stratify risk in individuals with a borderline risk assessment or with intermediate or high risk and an LDL-C measurement of < 130 mg/dL. A hsCRP test should not be performed in patients with current acute illness associated with the presence of heart disease

### Diagnostic Studies

- EKG resting, stress tests (treadmill, chemical, nuclear) as appropriate
- Imaging: CAC scoring if risk decision is uncertain in selected adults, consider carotid and/or femoral ultrasound and/or carotid intima-media thickness test (CIMT)

### Patient Education

- Review therapeutic lifestyle recommendations (see page 7)
- Explain relationship of dyslipidemia to ASCVD and importance of overall attention to ASCVD risk factors to empower patients to participate in their care
- If the patient is prescribed medication, discuss importance of taking as prescribed, and encourage the patient to be open with their primary care team if they have concerns or side effects that may cause them to non-adhere
- Discuss potential side effects of medications
- See PE-1 through PE-3 for details
The main indication for dyslipidemia treatment is prevention of ASCVD, including acute coronary syndromes, stroke, transient ischemic attack (TIA), or peripheral arterial disease, presumed to be caused by atherosclerosis.

Lifestyle management is the foundation of all lipid-reduction treatment regimens. Managing patients with dyslipidemia, begins with implementation of lifestyle changes including nutrition therapy, physical activity, smoking cessation, and assessment of sleep issues.

### Therapeutic Lifestyle Recommendations

<table>
<thead>
<tr>
<th>Lifestyle Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nutrition</strong> For primary and secondary prevention of ASCVD, encourage patients to consume CDCR Heart Healthy Diet with a focus on fruits and vegetables, whole grains, legumes, high soluble fiber, and moderate intake of low-fat dairy products while avoiding processed foods and saturated fat. Encourage patients to make healthier canteen choices.</td>
</tr>
</tbody>
</table>
| **Physical Activity** For primary and secondary prevention of ASCVD, recommend regular aerobic physical activity. Specific lipid-level improvements associated with regular exercise include:  
  - Reduced triglyceride and VLDL-C levels  
  - Reduction in total cholesterol  
  - Increased HDL-C |
| **Sleep** Sleep deprivation aggravates insulin resistance, HTN, hyperglycemia, and dyslipidemia, and increases inflammatory cytokines. Encourage patients to get 6-8 hours/night and avoid sleeping pills. |
| **Smoking** Smoking is a major risk factor for ASCVD and may triple the risk of death due to atherosclerosis. Encourage abstinence/exposure from tobacco or nicotine related products; avoid passive exposure to tobacco smoke. |
### CCHCS Care Guide: Dyslipidemia

### Treatment: Pharmacological Management

**First Line Therapy: Statins**

Statins (HMG-CoA reductase inhibitors) should be used as first-line cholesterol-lowering therapy, unless contraindicated. However, considerable residual risk often persists even after aggressive statin monotherapy in primary prevention in patients with multiple cardiovascular risk factors and in secondary prevention patients with stable clinical ASCVD.

**Statin Groups:** The April 2020 AHA/Cholesterol Management Guidelines recommend treatment with a statin for four different groups of patients as listed in the following table:

<table>
<thead>
<tr>
<th>4 Defined Statin Benefit Groups and Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary ASCVD Prevention (Age 18+)</strong></td>
</tr>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td><strong>Maximum tolerated statin is recommended:</strong></td>
</tr>
<tr>
<td>♦ If LDL-C ≥ 70 mg/dL: Consider adding ezetimibe</td>
</tr>
<tr>
<td>♦ If LDL-C remains ≥ 70 mg/dL or non-HDL-C ≥ 100 mg/dL: Consider PCSK-9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Primary Prevention</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
</tr>
<tr>
<td><strong>LDL-C ≥ 190 mg/dL – No risk assessment → High-Intensity statin</strong></td>
</tr>
<tr>
<td>If LDL-C 50% reduction not achieved and fasting TG’s ≥ 300 mg/dL, after maximal statin and ezetimibe, bile acid sequestrant may be considered.</td>
</tr>
</tbody>
</table>

| **Age 18-39 years** | Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk. Consider statin if family history, premature ASCVD and LDL-C of ≥ 160 mg/dL |
| **Age 40-75 years** | with LDL-C of ≥ 70-190 mg/dL and a 10-year ASCVD risk: |
| ♦ < 5% "Low Risk": Risk discussion. Emphasize healthy lifestyle changes. | ♦ 5 to < 7.5%: If Risk enhancers discuss moderate-intensity statin. |
| ♦ 7.5% - < 20% "Intermediate Risk": Discussion: If risk estimate + risk enhancers favor moderate-intensity statin to reduce LDL-C by 30%-49%. | ♦ ≥ 20% "High Risk": Initiate statin to reduce LDL-C ≥ 50% |
| **Age > 75 years Clinical Assessment – Risk discussion** |

**Statin Intensity:** Based on the defined statin group above, select the appropriate statin intensity as listed below and options for specific medications.

<table>
<thead>
<tr>
<th><strong>High-Intensity</strong></th>
<th><strong>Moderate -Intensity</strong></th>
<th><strong>Low-Intensity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C Lowering*</td>
<td>≥ 50%</td>
<td>30% to 49%</td>
</tr>
<tr>
<td>First Line Statins</td>
<td><strong>Atorvastatin (40 mg) 80 mg</strong></td>
<td><strong>Atorvastatin 10 mg (20 mg)</strong></td>
</tr>
<tr>
<td><strong>Rosuvastatin 20 (40 mg)</strong></td>
<td><strong>Rosuvastatin (5 mg) 10 mg</strong></td>
<td><strong>Pravastatin 40 mg (80 mg)</strong></td>
</tr>
<tr>
<td>Other Statins</td>
<td>—</td>
<td><strong>Simvastatin 20–40 mg</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Lovastatin 40 mg (80 mg)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Fluvastatin XL 80 mg</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Fluvastatin 40 mg BID</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Pitavastatin 2–4 mg</strong></td>
</tr>
</tbody>
</table>

*It is important to note that percent reductions are estimates from data across large populations. Individual responses to statin therapy varied in the randomized control trials and should be expected to vary in clinical practice.

**Statin Selection:** Once you have identified the intensity of statin needed you may be able to select a preferred statin based on other factors. See table below with CCHCS Formulary preferred agents followed by non-formulary. See medication pages 14 -17 for non-statin medications.

### Factors to Consider in Statin Selection

<table>
<thead>
<tr>
<th><strong>Most reduction in LDL</strong></th>
<th><strong>Preferred with renal impairment</strong></th>
<th><strong>Preferred with significant liver disease</strong></th>
<th><strong>Fewer drug interactions</strong></th>
<th><strong>Possibly less myopathy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atorvastatin</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Pravastatin</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Rosuvastatin</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Fluvastatin (NF)</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Pitavastatin (NF)</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
SUMMARY

Dyslipidemia

TREATMENT: PHARMACOLOGICAL MANAGEMENT

Non-Statin Drugs

Under certain circumstances, non-statin medications (ezetimibe, bile acid sequestrants, and PCSK9 inhibitors) may be useful in combination with statin therapy.

For secondary prevention: LDL-C ≥ 70 mg/dL is threshold for non-statin drug consideration.

For General Dyslipidemia:

**Ezetimibe** is the most commonly used non-statin agent. It lowers LDL-C levels by 13% to 20% and has a low incidence of side effects.
- Recommended in combination with statin therapy in patients who do not meet LDL-C goals (threshold levels) with dietary modification and maximally tolerated statin therapy
- Ezetimibe may also be used in situations of statin-associated muscle symptoms. The combination therapy is relatively safe

**Bile acid sequestrants** reduce LDL-C levels by 15% to 30% depending on the dose. Bile acid sequestrants are not absorbed and do not cause systemic side effects, but they are associated with gastrointestinal complaints (e.g., constipation) and can cause severe hypertriglyceridemia when fasting triglycerides are ≥ 300 mg/dL (≥ 3.4 mmol/L).
- Recommended use in patients 20 to 75 years of age with a baseline LDL-C 190 mg/dL or higher (4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides 300 mg/dL or lower (≥ 3.4 mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered

**PCSK9 inhibitors** are powerful LDL-lowering drugs. They generally are well tolerated, but long-term safety remains to be proven. They further reduce LDL-C levels by 43% to 64%. These medications are given subQ every two weeks and are non-formulary (see restrictions on pages 14-15). Adding a PCSK9 inhibitor may be considered in the following:
- In patients with very high-risk ASCVD (history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions) and LDL-C level remains ≥ 70 mg/dL on maximally tolerated statin plus ezetimibe therapy
- In patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL) and the LDL-C level on high-intensity or maximally tolerated statin plus ezetimibe remains ≥ 100 mg/dL and the patient has multiple factors that increase subsequent risk of ASCVD events
- In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL or higher while taking maximally tolerated statin and ezetimibe therapy
- In patients 40 to 75 years of age with a baseline LDL-C level of 220 mg/dL or higher who have an on-treatment LDL-C level of 130 mg/dL or higher while receiving maximally tolerated statin and ezetimibe therapy

Additional Medications for Hypertriglyceridemia (See Attachment C):

Patients occasionally have isolated hypertriglyceridemia. ACC/AHA guidelines recognize two categories:
- Moderate hypertriglyceridemia is defined as TG (fasting or nonfasting) 175 - 499 mg/dl
- Severe hypertriglyceridemia is defined as fasting TG ≥ 500 mg/dl

Statins remain first line therapy. In cases where ASCVD risk is high or other complications exist (e.g., pancreatitis) and patient requires more than lifestyle/diet change and statin the following medications can be considered.

**Fibrates:** Triglyceride-lowering medication may also mildly lower LDL-C levels in patients with normal TGs.
- Fenofibrate (formulary) may be considered concomitantly with a low or moderate-intensity statin only if the patient benefits from ASCVD risk reduction or TG lowering when TGs are > 500 mg/dL. They may be useful in some patients with severe hypertriglyceridemia.
- Gemfibrozil (formulary) should not be initiated in patients on statin therapy because of an increased risk for muscle symptoms and rhabdomyolysis.

**Omega-3 fatty acids:** There is evidence that omega-3 fatty acids can reduce blood TG levels (third line therapy). Note: CCHCS/CDCR currently “Non-Formulary.”
### SUMMARY

#### TREATMENT: PHARMACOLOGICAL MANAGEMENT

#### Statin Contraindications

For a majority of patients, statins are safe, however:

- Statins are contraindicated for use by patients with active hepatic disease or unexplained persistent elevations in aminotransferase levels.
- Statins are also contraindicated during pregnancy and while breastfeeding because of the effects on the cholesterol pathway.
- CKD patients NOT on dialysis may be started and continued on statins.

  - Patients starting dialysis may continue a statin if already on a statin.
  - Patients on dialysis should NOT be started on statins.

#### Statin-Associated Side Effects

For most patients, statins are safe and well-tolerated. However, statin-associated side effects (SASE) may occur in a significant subset of statin-treated patients.

Instead of the label *statin intolerance*, the present AHA guideline prefers *statin-associated side effects* because the large majority of patients are able to tolerate statin rechallenge with an alternative statin or alternative regimen, such as reduced dose or in combination with non-statins.

1. **Statin-associated muscle symptoms (SAMS):** The most frequent SASE, SAMS are usually subjective myalgia, reported observationally in 5% to 20% of patients. SAMS often result in nonadherence and can adversely impact ASCVD outcomes. An elevated creatine kinase (CK) level is not required for establishing the diagnosis, although SAMS may be corroborated by CK $\geq 4 \times$ the upper limit of normal (ULN). For management see page 18.

Factors that may increase the risk for statin-induced myopathy include:

- Female sex
- Small body size
- Age $> 65$ years
- Frailty
- Asian ancestry
- Personal or family history of myopathy
- Poorly controlled hypothyroidism
- Subnormal vitamin D
- The use of medications that raise circulating levels of statins and/or their active metabolites (e.g., erythromycin, amlodipine, fluconazole)

Muscle adverse events remain important side effects usually manifested by muscle discomfort, including muscle aches, soreness, stiffness and weakness. In these cases current guidelines recommend to check CK.

#### Spectrum of Statin-Associated Muscle Adverse Events (See Page 18 for details on managing)

<table>
<thead>
<tr>
<th>Myalgias</th>
<th>CK Normal</th>
<th>Musculoskeletal manifestations are well-recognized side effects of treatment with statins. These side effects are reported to occur in about 10% of people prescribed statins.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myositis/Myopathy</td>
<td>CK $&gt; ULN$</td>
<td>Characterized most of the time by mild to moderate hypercreatinemia. Rare incidence.</td>
</tr>
<tr>
<td>Myonecrosis w/ myoglobinuria (rhabdomyolysis)</td>
<td>CK $&gt; 10xULN +$ renal injury</td>
<td>Defined by the Task Force as myonecrosis with myoglobinuria or acute renal failure. Patients with symptomatic or asymptomatic rhabdomyolysis from a statin should discontinue therapy immediately.</td>
</tr>
</tbody>
</table>

2. **New Onset DM:** More frequent if associated with BMI $\geq 30$, FBS $\geq 100$ mg/dL, or A1c $\geq 6%$

3. **Hepatic Dysfunction:** Transaminase elevation $3x$ULN – Infrequent

4. **CKD/End Stage Renal Disease:** Patients on hemodialysis should NOT be started on a statin
## CCHCS Care Guide: Dyslipidemia

### SUMMARY

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>DOsing</th>
<th>ADVERSE EFFECTS/INTERACTIONS</th>
<th>COMMENTS</th>
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<tr>
<td><strong>HMG CoA Reductase inhibitors (statins)</strong> - Risk of skeletal muscle effects (e.g., myopathy, rhabdomyolysis) increases with higher doses and concomitant use of certain drugs. Predisposing factors include age &gt; 65, female gender, uncontrolled hypothyroidism, and renal impairment.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin (Lipitor®)</td>
<td>Usual dose: 10-80 mg orally once daily</td>
<td>Adverse Reactions: myopathy, rhabdomyolysis, elevated liver enzymes, diarrhea, arthralgia, myalgia, nasopharyngitis, nausea, dyspepsia, urinary tract infection, insomnia, rhabdomyolysis</td>
<td>CCHCS PREFERRED AGENT</td>
</tr>
<tr>
<td>Tablet: 10 mg, 20 mg, 40 mg, 80 mg $</td>
<td>MODERATE-INTENSITY: 30% to &lt; 50% reduction in LDL: 10-20 mg orally once daily</td>
<td>Conttraindications: hypersensitivity to atorvastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevations of serum transaminases, pregnancy, breast-feeding, concomitant use with certain HIV protease inhibitors (tipranavir plus ritonavir), glecaprevir/pibrentasvir, cyclosporine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIGH-INTENSITY: ≥ 50% reduction in LDL: 80 mg orally once daily; 40 mg orally once if 80 mg not tolerated</td>
<td>Caution in the following: heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, pre-existing amyotrophic lateral sclerosis (ALS), the elderly</td>
<td></td>
</tr>
<tr>
<td>Dose adjustments:</td>
<td>Max dose 20 mg/day: concomitant use with clarithromycin, erythromycin, itraconazole, ketoconazole, voriconazole, saquinavir plus ritonavir, darunavir plus ritonavir, fosamprenavir, atazanavir plus ritonavir, elbasvir/grazoprevir</td>
<td>Use caution and lowest dose necessary with HIV protease inhibitor (lopinavir plus ritonavir), glecaprevir/pibrentasvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Max dose 40 mg/day: concomitant use with neflinavir</td>
<td>Use caution with niacin, fibrates (avoid gemfibrozil if possible)</td>
<td></td>
</tr>
<tr>
<td>Renal Impairment: No adjustment needed</td>
<td>Renal Impairment:</td>
<td>Use caution with digoxin, oral contraceptives, warfarin, colchicine</td>
<td></td>
</tr>
<tr>
<td>Hepatic Impairment: Contraindicated in active liver disease or unexplained/persistent transaminase elevations</td>
<td>Hepatic Impairment: Contraindicated in active liver disease or unexplained/persistent transaminase elevations</td>
<td>Consider temporarily suspending use while patient is on daptomycin</td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin (Crestor®)</td>
<td>Usual dose: 5-40 mg orally once daily</td>
<td>Adverse Reactions: myopathy, rhabdomyolysis, elevated liver enzymes, diarrhea, arthralgia, myalgia, headache, dizziness, constipation, nausea, dyspepsia, rash, rhabdomyolysis</td>
<td>CCHCS PREFERRED AGENT</td>
</tr>
<tr>
<td>Tablet: 5 mg, 10 mg, 20 mg, 40 mg $</td>
<td>MODERATE-INTENSITY: 30% to &lt; 50% LDL reduction: 5-10 mg orally once daily</td>
<td>Conttraindications: hypersensitivity to rosuvastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevations of serum transaminases, pregnancy, breast-feeding, concomitant use with sofosbuvir/velpatasvir, lasmiditan</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIGH-INTENSITY: ≥ 50% LDL reduction: 20-40 mg orally once daily</td>
<td>For Asian patients, consider 5 mg/day starting dose</td>
<td></td>
</tr>
<tr>
<td>Dose adjustments:</td>
<td>Asian patients: consider lower starting (5 mg/day) and maximum doses</td>
<td>Caution in the following: patients of Asian descent, heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, pre-existing amyotrophic lateral sclerosis (ALS), the elderly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Max dose 5 mg/day: concomitant use with cyclosporine</td>
<td>Rosuvastatin may be less likely to interact with other drugs</td>
<td></td>
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<tr>
<td></td>
<td>Max dose 10 mg/day: concomitant use with lopinavir plus ritonavir, atazanavir plus ritonavir, elbasvir/grazoprevir, glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, gemfibrozil</td>
<td>Use caution with niacin, fibrates (avoid gemfibrozil if possible)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal Impairment:</td>
<td>Use caution with protease inhibitor/ritonavir combinations, warfarin, colchicine</td>
<td></td>
</tr>
<tr>
<td>CrCl &lt; 30 mL/min (not on hemodialysis):</td>
<td>Renal Impairment:</td>
<td>Consider temporarily suspending use while patient is on daptomycin</td>
<td></td>
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<tr>
<td></td>
<td>Initial dose: 5 mg/day;</td>
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<tr>
<td></td>
<td>Max dose 10 mg/day</td>
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<td></td>
<td>Rosuvastatin levels in hemodialysis patients are about 50% higher than in normal renal function.</td>
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<tr>
<td></td>
<td>Hepatic Impairment:</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Contraindicated in active liver disease or unexplained/persistent transaminase elevations</td>
<td></td>
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**Bold = Formulary**  
*See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions and contraindications.  
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<tr>
<td><strong>HMG CoA Reductase inhibitors (Statins)</strong> - Risk of skeletal muscle effects (e.g., myopathy, rhabdomyolysis) increases with higher doses and concomitant use of certain drugs. Predisposing factors include: age &gt;65, female gender, uncontrolled hypothyroidism, and renal impairment.</td>
<td></td>
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</tr>
<tr>
<td><strong>Pravastatin</strong> (Pravachol&lt;sup&gt;®&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tablet: 10 mg, 20 mg, 40 mg</td>
<td>$</td>
<td><strong>Adverse Reactions</strong>: myopathy, rhabdomyolysis, elevated liver enzymes, diarrhea, constipation, nausea, vomiting, musculoskeletal pain, myalgia, rash, headache, dizziness, cough, rhinitis, upper respiratory infection</td>
<td><strong>Contraindications</strong>: hypersensitivity to pravastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevation serum transaminases, pregnancy, breast-feeding. Caution in the following: heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, preexisting amyotrophic lateral sclerosis (ALS), the elderly.</td>
</tr>
<tr>
<td>Usual dose: 20-80 mg orally once daily</td>
<td><strong>MODERATE-INTENSITY</strong> 30% to &lt; 50% reduction in LDL: 40-80 mg orally once daily</td>
<td><strong>Drug interactions</strong>: - Pravastatin may be less likely to interact with other drugs - Use caution with niacin, fibrates (avoid gemfibrozil) - Consider dose reduction with niacin dose ≥ 1000 mg/day - Consider temporarily suspending use while patient is on daptomycin</td>
<td></td>
</tr>
<tr>
<td>Dose adjustments: Max dose 20 mg/day: concomitant use with cyclosporine</td>
<td>Max dose 40 mg/day: concomitant use with clarithromycin, sofosbuvir/velpatasvir/voxilaprevir</td>
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<td></td>
<td>Reduce dose by 50%: concomitant use with glecaprevir/pibrentasvir</td>
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</tr>
<tr>
<td>Renal Impairment: Severe renal impairment (CrCl &lt; 30 mL/min): Initial dose: 10 mg/day</td>
<td>Hepatic Impairment: Contraindicated in active liver disease or unexplained/persistent transaminase elevations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin (Zocor&lt;sup&gt;®&lt;/sup&gt;)</td>
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<tr>
<td>Tablet: 5 mg, 10 mg, 20 mg, 40 mg</td>
<td>$</td>
<td><strong>Adverse Reactions</strong>: myopathy, rhabdomyolysis, elevated liver enzymes, arthralgia, myalgia, vertigo, headache, abdominal pain, gastritis, nausea, constipation, edema, upper respiratory infection, atrial fibrillation, insomnia, sinusitis</td>
<td><strong>Note</strong>: 80 mg dose is associated with elevated risk of muscle injury. FDA recommends 80 mg dose only for patients who have been taking this dose for at least 12 months without evidence of muscle injury. 80 mg dose should not be started in new patients, including patients already taking lower doses. <strong>Contraindications</strong>: hypersensitivity to simvastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevations of serum transaminases, pregnancy, breast-feeding, concomitant use with strong CYP3A4 inhibitors (e.g., erythromycin, clarithromycin, itraconazole, ketoconazole, posaconazole, voriconazole, HIV protease inhibitors, nefazodone, cobicistat), cyclosporine, danazol, gemfibrozil. Caution in the following: heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, patients of Chinese decent, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, preexisting amyotrophic lateral sclerosis (ALS), the elderly.</td>
</tr>
<tr>
<td>Usual dose: 10-40 mg once daily in evening</td>
<td><strong>MODERATE-INTENSITY</strong> 30% to &lt; 50% reduction in LDL: 20-40 mg once daily in evening</td>
<td><strong>Drug interactions</strong>: - Contraindicated with strong CYP3A4 inhibitors (e.g., erythromycin, clarithromycin, itraconazole, ketoconazole, posaconazole, voriconazole, HIV protease inhibitors, nefazodone, cobicistat), cyclosporine, danazol, gemfibrozil</td>
<td></td>
</tr>
<tr>
<td>Dose adjustments: Max dose 10 mg/day: concomitant use with verapamil, diiltiazem, dronedarone</td>
<td>Max dose 20 mg/day: concomitant use with amiodarone, amiodipine, ranolazine, lomitapide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Impairment: CrCl &lt; 30 mL/min: initial dose, 5 mg/day, close monitoring is advised</td>
<td>Hepatic Impairment: Contraindicated in active liver disease or unexplained/persistent transaminase elevations</td>
<td></td>
<td></td>
</tr>
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*See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions and contraindications.*  

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<td><strong>HMG CoA Reductase Inhibitors (Statins)</strong> - Risk of skeletal muscle effects (e.g., myopathy, rhabdomyolysis) increase with higher doses and concomitant use of certain drugs. Predisposing factors include: age &gt;65, female gender, uncontrolled hypothyroidism, and renal impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin Lesco®, Lesco® XL Capsule, immediate-release (IR): 20 mg, 40 mg</td>
<td>Usual dose: 20-40 mg orally once daily in the evening, titrated up to 40 mg orally twice daily</td>
<td><strong>Adverse Reactions</strong>: myopathy, rhabdomyolysis, elevated liver enzymes, arthralgia, headache, atrial fibrillation, HTN, nausea, dyspepsia, fatigue, myalgia, sinusitis, pharyngitis, peripheral edema, rash, syncope, urinary tract infection</td>
<td><strong>Contraindications</strong>: hypersensitivity to fluvastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevation serum transaminases, pregnancy, breast-feeding</td>
</tr>
<tr>
<td>Table: extended-release (XL): 80 mg</td>
<td>Dose adjustments: Max dose 20 mg orally twice daily: concomitant use with cyclosporine, fluconazole</td>
<td><strong>Drug interactions</strong>: • Fluvastatin may be less likely to interact with other drugs • Use caution with niacin, fibrates (avoid gemfibrozil), glibenclamide, phenytoin, warfarin, colchicine</td>
<td><strong>Caution in the following</strong>: heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, preexisting amyotrophic lateral sclerosis (ALS), the elderly</td>
</tr>
<tr>
<td>Renal Impairment: <strong>Mild-moderate impairment</strong>: no adjustment; <strong>Severe impairment</strong>: doses &gt; 40 mg/day have not been evaluated</td>
<td><strong>Hepatic Impairment</strong>: Contraindicated in active liver disease or unexplained/persistent transaminase elevations</td>
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<td>$$$-$$$$</td>
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</tr>
<tr>
<td>Pitavastatin Livalo® Tablet: 1 mg, 2 mg, 4 mg</td>
<td>Usual dose: 1-4 mg orally once daily</td>
<td><strong>Adverse Reactions</strong>: myopathy, rhabdomyolysis, elevated liver enzymes, headache, nausea, dyspepsia, constipation, diarrhea, backache, myalgia, limb pain, arthralgia, rash, dizziness, memory impairment, peripheral neuropathy</td>
<td><strong>Contraindications</strong>: hypersensitivity to pitavastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevation serum transaminases, pregnancy, breast-feeding, concomitant use with cyclosporine</td>
</tr>
<tr>
<td>$$$</td>
<td><strong>MODERATE-INTENSITY</strong>: 30% to &lt; 50% reduction in LDL: 2-4 mg orally once daily in the evening</td>
<td><strong>Drug interactions</strong>: • Pitavastatin may be less likely to interact with other drugs • Contraindicated with cyclosporine • Use caution with fibrates (avoid gemfibrozil), niacin, colchicine</td>
<td><strong>Caution in the following</strong>: heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, the elderly</td>
</tr>
<tr>
<td>Dose adjustments: Max dose 1 mg/day: concomitant use with erythromycin Max dose 2 mg/day: concomitant use with rifampin</td>
<td><strong>Renal Impairment</strong>: CrCl &lt; 60 mL/min or HD: start 1 mg orally daily, max 2 mg/day</td>
<td><strong>Hepatic Impairment</strong>: Contraindicated in active liver disease or unexplained/persistent transaminase elevations</td>
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<td>$$$</td>
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*See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions and contraindications.

The cost scale $$$-$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.
Azetidinone - Use may be considered in patients who do not meet cholesterol treatment goals with dietary modification and maximally-tolerated statin therapy. 2018 Guideline on the Management of Blood Cholesterol from the ACC/American Heart Association Task Force found no proof that adding a non-statin to a statin prevents ASCVD events in patients without clinical ASCVD.

**Ezetimibe**

**Zetia® Tablet:**

- Dose: 10 mg orally once daily
- Renal Impairment: No dose adjustment needed.
- Hepatic Impairment: Moderate to severe hepatic impairment: Not recommended

**Adverse Reactions:** diarrhea, abdominal pain, myalgia, arthralgia, back pain, fatigue, cough, sinusitis, pharyngitis, upper respiratory infection, hepatitis, elevated hepatic enzymes, rhabdomyolysis, anaphylaxis, pruritus

**Drug interactions:**
- Use caution with fibrates (avoid gemfibrozil), cyclosporine, warfarin, antacids, bile acid sequestrants

**Contraindications:** hypersensitivity to ezetimibe or any component of the formulation, concomitant use with statin in patients with active hepatic disease or unexplained persistent elevations in serum transaminases; pregnancy and breastfeeding (when used with a statin)

**Caution in the following:** hepatic impairment (use not recommended in moderate or severe impairment), renal impairment, concomitant use with statins, concomitant use with fibrates, pregnancy, breastfeeding, the elderly

**Use Restrictions:** For the addition of Ezetimibe see “Memorandum—Ezetimibe” located on Pharmacy LifeLine page under Memos tab.

http://lifeline/HealthCareOperations/MedicalServices/Pharmacy/Pages/Resources.aspx

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**Bile Acid Sequestrants**

**Cholestyramine QUESTRAN® Powder:**

- Initial dose: 4 g orally 1 to 2 times daily before meals (mixed in 60-180 ml of noncarbonated beverage)
- Maintenance dose: 8-16 g/day in 2 divided doses before meals
- Max dose: 24 g/day
- Renal Impairment: No adjustment needed
- Hepatic Impairment: No adjustment needed

**Adverse Reactions:** constipation, abdominal discomfort, flatulence, nausea, vomiting, dental caries, anxiety, dizziness, drowsiness, fatigue, headache, osteoporosis

**Drug interactions:**
- Decreases absorption of other drugs
- Administer other drugs at least 1 hour before or at least 4-6 hours after each dose

**Contraindications:** Complete biliary obstruction (bile is not secreted into the intestine), patients with TG > 400 mg/dl, GI obstruction, hypersensitivity to cholestyramine or any component of the product

**Caution in the following:** primary biliary cirrhosis, hypertriglyceridemia, renal impairment, patients susceptible to fat-soluble vitamin deficiencies, constipation, coagulopathy, dysphagia, cholelithiasis, hemorrhoids, pregnancy, breast-feeding, the elderly

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**Lorem ipsum...**

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<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCSK9</strong> Alirocumab Praluent® Solution for Injection, Prefilled pen device:</td>
<td>Usual dose: Treatment of primary hyperlipidemia, including heterozygous familial hypercholesterolemia, to lower LDL-C: 75 mg subcutaneously once every 2 weeks. If response is inadequate, increase to 150 mg subcutaneously once every 2 weeks</td>
<td>Adverse Reactions: chest pain, pharyngitis, antibody formation, injection site reaction, cough, diarrhea, myalgia, elevated hepatic enzymes, influenza, sinusitis, allergic reaction, angioedema, anaphylaxis</td>
<td>Contraindications: hypersensitivity to alirocumab or any component of the formulation</td>
</tr>
<tr>
<td>75 mg/mL 150 mg/mL</td>
<td>Treatment of patients with heterozygous familial hypercholesterolemia who are undergoing LDL apheresis: 150 mg subcutaneously every 2 weeks; administer without regard to timing of apheresis. For myocardial infarction prophylaxis, stroke prophylaxis, and to reduce the risk of unstable angina requiring hospitalization in patients with established cardiovascular disease: 75 mg subcutaneously once every 2 weeks. If response is inadequate, increase to 150 mg subcutaneously once every 2 weeks</td>
<td>Note: Alirocumab is recommended as second-line therapy in addition to maximally tolerated statin therapy in patients with clinical ASCVD and comorbidities that still require 25% or greater LDL reduction. Factors to consider include cost, benefit of ASCVD risk reduction, dosing frequency requirements, and administration by subcutaneous injection</td>
<td></td>
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<tr>
<td>$$$$$</td>
<td>Renal Impairment: Mild to moderate impairment: No dose adjustment needed Severe impairment: specific guidelines for dose adjustment not available</td>
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<td></td>
<td>Hepatic Impairment: Mild to moderate impairment: No dose adjustment needed Severe impairment: specific guidelines for dose adjustment not available</td>
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<tr>
<td><strong>Renal Impairment</strong></td>
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</tbody>
</table>

**Bold = Formulary** *

*See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions and contraindications.

The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.
### Medications* Continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects/Interactions</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9)</strong></td>
<td>Recommended as third-line therapy in addition to maximally tolerated statin therapy and ezetimibe in patients with clinical ASCVD and comorbidities that still require greater LDL reduction. The addition of a PCSK9 inhibitor may be considered for patients that meet the non-formulary criteria upon the recommendation of a specialist (cardiologist or endocrinologist).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCSK9 Evolocumab Repatha® Solution for Injection, Prefilled syringe: 140 mg/mL Prefilled pen device: 140 mg/mL</td>
<td>Usual dose: Treatment of primary hypercholesterolemia (including heterozygous familial hypercholesterolemia): 140 mg subcutaneously every 2 weeks or 420 mg subcutaneously once monthly Adjunct to diet and other LDL-C lowering therapies for the treatment of homozygous familial hypercholesterolemia in patients who require additional lowering of LDL-C: 420 mg subcutaneously once monthly Myocardial infarction prophylaxis, stroke prophylaxis, and to reduce the risk of coronary revascularization in patients with established cardiovascular disease: 140 mg subcutaneously every 2 weeks or 420 mg subcutaneously once monthly</td>
<td>Adverse Reactions: back pain, pharyngitis, antibody formation, injection site reaction, diarrhea, myalgia, arthralgia, cough, dizziness, HTN, headache, hyperglycemia, influenza, sinusitis, allergic reaction, angioedema, anaphylaxis</td>
<td>Contraindications: hypersensitivity to evolocumab or any component of the formulation, Caution in the following: latex hypersensitivity, pregnancy, breast-feeding</td>
</tr>
<tr>
<td></td>
<td>Note: Evolocumab is recommended as second-line therapy in addition to maximally tolerated statin therapy in patients with clinical ASCVD and comorbidities that still require 25% or greater LDL reduction. Factors to consider include cost, benefit of ASCVD risk reduction, dosing frequency requirements, and administration by subcutaneous injection Renal Impairment: Mild to moderate impairment: No dose adjustment needed Severe impairment: specific guidelines for dose adjustment not available Hepatic Impairment: Mild to moderate impairment: No dose adjustment needed Severe impairment: specific guidelines for dose adjustment not available</td>
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**Summary**

**Decision Support**

**Patient Education/Self Management**
**Fibric Acid Derivatives**

**Note:** Increases in CK, increased risk of rhabdomyolysis, and myoglobinuria leading to acute renal failure are associated with concurrent use of fibrates and statins (significantly higher rate observed with gemfibrozil), particularly in the elderly, patients with diabetes, renal failure, or hypothyroidism.

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>DOSING</th>
<th>ADVERSE EFFECTS/INTERACTIONS</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fenofibrate</strong> <em>(Lofibra®, Tricor®)</em></td>
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<tr>
<td>Tablet:</td>
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<tr>
<td>Generic Lofibra® 54 mg, 160 mg</td>
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<td></td>
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<tr>
<td>Generic Tricor® 48 mg, 145 mg</td>
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<td>$-$ $$</td>
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</tbody>
</table>

**Primary hypercholesterolemia or mixed dyslipidemia:**
- Generic Lofibra®: 160 mg orally once daily
- Generic Tricor®: 145 mg orally once daily
Withdraw therapy in patients who do not have an adequate response after two months of treatment with the maximum recommended dose of 160 mg/day (Generic Lofibra®); 145 mg/day (Generic Tricor®)

- Severe hypertriglyceridemia:
  - Generic Lofibra®: 54-160 mg orally once daily
  - Generic Tricor®: 48-145 mg orally once daily
Consider dosage reduction if serum lipid concentrations fall significantly below target goals.

- Max dose:
  - Generic Lofibra®: 160 mg/day
  - Generic Tricor®: 145 mg/day

**Renal Impairment:**
CrCl 30-80 mL/min: Initially
- Generic Lofibra®: 54 mg orally once daily
- Generic Tricor®: 48 mg orally once daily
Do not increase dose until effects of the initial dose on renal function and serum lipid concentrations have been fully evaluated.
CrCl < 30 mL/min: Contraindicated

**Hepatic Impairment:** Contraindicated in hepatic dysfunction, including primary biliary cirrhosis or unexplained, persistent liver function abnormality

**Adverse Reactions:** elevated hepatic enzymes, abdominal pain, nausea, constipation, diarrhea, asthenia, dyspepsia, gallstones, myopathy, backache, rhinitis, rash urticarial, pulmonary embolism, thrombosis

**Drug interactions:**
- Use caution with warfarin, statins, bile acid sequestrants, immunosuppressants (e.g., cyclosporine, tacrolimus), colchicine

**Contraindications:**
- Hypersensitivity to fenofibrate, fenofibric acid or any component of the formulation, severe renal dysfunction (CrCl < 30 mL/min) including patients receiving dialysis, hepatic disease including primary biliary cirrhosis or unexplained persistent liver function abnormalities, gallbladder disease, breastfeeding

**Caution in the following:** diabetes, hypothyroidism, mild to moderate renal impairment, thromboembolic disease, pregnancy, the elderly

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*Bold = Formulary*  
*See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions and contraindications.*

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### SUMMARY

**Patient Is On Statin**

Check patient’s fasting lipids:
- 1-3 months after starting treatment
- 1-3 months after adjustment of treatment until within the threshold range

Once a patient has reached the appropriate threshold or optimal lipid levels:
- Check fasting lipids every 12 months (unless there are adherence problems or other reasons for more frequent testing, such as efficacy checks, changes in therapy, etc.)
  - Discontinuation/non-adherence remains a major gap in the primary/secondary prevention of ASCVD.
  - The major reason for statin discontinuation is because of the development of SAMS. See below.

**Statin-Associated Side Effects:** Adverse reactions occur less frequently with statins than with most other classes of lipid-lowering agents. However, muscle events remain important side effects.

**Statin Associated Muscle Symptoms (SAMS)**

**Myalgia:** Measure CK if patient develops myalgia(s). If muscle enzyme CK remains normal, statin therapy may continue if the symptoms are acceptable to the patient.

**Myositis/Myopathy:** Statin treatment should be discontinued immediately. Monitor CK levels weekly and seek specialist advice if:
- There is a moderate rise in the CK level (i.e., 3-10 x upper limit of normal)
- An elevated CK level is found (i.e., CK > 10 x upper limit of normal), or where myopathy is suspected or diagnosed

**Myonecrosis with myoglobinuria (rhabdomyolysis):** Stop statin immediately and refer to specialist

**Hepatic dysfunction:** Borderline elevations are almost always benign (LFTs < 2x ULN). Stop statin if signs/symptoms of liver disease occur or LFTs <3x ULN. Measure liver function and monitor.

**Type 2 DM:** Patients at increased risk of type 2 DM are recommended to continue statin therapy with added emphasis given to lifestyle changes.

**Behavioral and cognitive:** Concerns have been raised about increased suicide in patients treated with some lipid-lowering therapies, but statins do not appear to be associated with an increased risk of suicide or depression. Some reports indicate a possible correlation between statins and short-term memory loss. Cognitive impairment is usually reversible upon discontinuation of statin.

### Decision Support

**Patient Is Not On Statin**

After age 20 years, it is reasonable to measure traditional ASCVD risk factors at least every 4 to 6 years. Traditional ASCVD risk factors refers to HTN, tobacco use, DM, premature family history of cardiovascular disease, CKD, and obesity.

**Managing Patient Adherence**

The clinician should reassess, rediscuss, and encourage rechallenge as the initial approach unless side effects are severe. Ongoing communication is integral to patient care, as is regular monitoring to check for adherence, adequacy of response, new associated symptoms, and reaffirmation of benefit.

**Patient Adherence:** Despite the well-documented benefits from statins, patient adherence to therapy is frequently challenged by adverse effects and it is important to discuss these with each patient prior to prescribing (see PE-3 for details).
- In such cases, consider using smaller statin doses and/or less potent statins with lower incidence of myopathy, along with cautious up-titration of dose.
- Some lipid specialists prescribe fluvastatin or pitavastatin in patients intolerant to other members of the HMG-CoA reductase inhibitor class.
3. Newburger, Jane W., and de Ferranti Sarah D. Dyslipidemia: Definition, screening, and diagnosis. UpToDate 03/03/2020.
CCHCS Care Guide: Dyslipidemia

PATIENT EDUCATION/Self-Management

Dyslipidemia

What You Should Know

What is dyslipidemia? (Also called “high cholesterol”)
- Dyslipidemia refers to unhealthy levels of one or more kinds of lipid (fat) in your blood. Your blood contains three main types of lipid: high-density lipoprotein (HDL) low-density lipoprotein (LDL) and triglycerides.

Why is treating dyslipidemia important?
- Dyslipidemia is a risk factor for heart attacks and strokes.
- Treating dyslipidemia will help you avoid a heart attack or stroke.

How can I tell if I have dyslipidemia?
- When you have dyslipidemia, you may not have symptoms.
- Your health care provider will order a test that measures the amount of lipids in your blood.

How do I know if I need the test?
- Your health care provider will check your lipids/cholesterol if:
  - You have a history of:
    - Previous heart attack
    - Diabetes mellitus
    - High blood pressure
    - Cigarette smoking
  - You are:
    - Overweight or obese
    - Physically Inactive
  - You have:
    - Family history of early heart disease

How is dyslipidemia treated?
- Treatment depends on your:
  - Lipid (cholesterol) levels
  - Your risk of heart attacks based on other things like do you smoke, or have high blood pressure or diabetes
  - General health

Your primary care provider may give you a lipid-lowering medication to lower your cholesterol.

What You Should Do

Change your daily routine and activities to lower your cholesterol:
- Lose weight if you are overweight
- Exercise
- Stop smoking
- Eat more fruits and vegetables
- Reduce fat in your diet (meat, milk, eggs, butter, cheese, packaged foods and snack items like cookies, crackers and chips)
- Take any medications you are given as directed
- Report medication side effects
  - Muscle aches are commonly reported and may or may not be due to your medicine
- Get blood tests as recommended by your health care team.
What is cholesterol?
- **Blood cholesterol** is waxy and fat-like and is made by your liver. It is needed for good health. Your body needs it to perform important jobs, like making hormones, Vitamin D and parts of cells and protecting nerves fibers.
- Your body makes all the blood cholesterol it needs, which is why experts recommend that people eat as little dietary cholesterol as possible while on a healthy eating plan.
- **Dietary cholesterol** is found in animal foods, including meat, seafood, poultry, eggs, and dairy products.

What is the difference between LDL and HDL Cholesterol?
- LDL makes up most of your body’s cholesterol.
- High levels of LDL cholesterol can build up on the walls of your blood vessels (called plaque) and raise your risk for heart disease and stroke.
- HDL absorbs cholesterol and carries it back to the liver. The liver then flushes it from the body.
- High levels of HDL cholesterol can lower your risk for heart disease and stroke.

How do I find out my cholesterol levels?
- Your health care team can do a simple blood test, called a “lipid profile,” to measure your cholesterol levels.
- This information helps your health care team determine your risk for heart disease or stroke.

How do I know my risk for high cholesterol?
- Certain health conditions, your lifestyle, and your family history can raise your risk for high cholesterol.
- These are called “risk factors.” These are listed in below in detail.

<table>
<thead>
<tr>
<th>Risk Factors for High Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health Conditions</strong></td>
</tr>
<tr>
<td><strong>Behaviors</strong></td>
</tr>
<tr>
<td><strong>Family History</strong></td>
</tr>
<tr>
<td><strong>Age and Gender</strong></td>
</tr>
</tbody>
</table>
# Statin Medications

## What You Should Know

### What are statins?
- Statin medications are usually the first type of drug that doctors prescribe to lower LDL. They also lower triglycerides, which are another type of blood fat, and can mildly raise your "good" (HDL) cholesterol level.

### What happens when I take this medication?
- You should have a blood test before starting treatment. This checks the level of cholesterol. It also checks if your liver is working properly.
- After starting treatment you should have a blood test within 1-3 months and again at 12 months.
- The blood is checked to measure the cholesterol level to see how well the statin is working.

### What are side effects of this medication?
- Most people who take a statin medication have no side-effects, or only minor ones.
- Possible side-effects include:
  - Headache
  - Muscle aches
  - Stomach pain
  - Bloating
  - Diarrhea
  - Feeling sick (nausea)
  - A rash
  - Pins and needles feeling
- Tell your doctor if you have any of these, especially muscle pains, tenderness, cramps or weakness. This may happen as a rare side-effect of statins and is a severe form of muscle inflammation.
- Muscle pains may be more likely if you are also taking a medicine called amlodipine or diltiazem.
- Your doctor may need to adjust your dose of statin to reduce the risk of muscle damage.

### How do I know if I should not take this medication?
- You should not take a statin if you have active liver disease, if you are pregnant or intend to be pregnant, or if you are breastfeeding.
- You should stop a statin if you develop liver disease.

### What should I avoid when taking this medication?
- Do not eat grapefruit or drink grapefruit juice if you are taking some statins.
- A chemical in grapefruit can increase the level of statin in the bloodstream, which can make side-effects from the statin more likely. This is only a problem with simvastatin, atorvastatin and lovastatin. Other statins, such as pravastatin, do not interact with grapefruit.
- Medicines can sometimes interfere with statins. For example, some antibiotics and cyclosporin. The doses of either the statin or the other interacting medicine may need to be adjusted.
- If you are prescribed (or buy) another medicine, remind the doctor or pharmacist that you are on a statin in case an interaction is likely.
Dislipidemia

Lo que debe saber

¿Qué es la dislipidemia? (También llamada “colesterol alto”)
- La dislipidemia se refiere a niveles poco saludables de uno o más tipos de lípidos (grasas) en la sangre. Su sangre contiene tres tipos principales de lípidos: lipoproteínas de alta densidad (high-density lipoprotein, HDL), lipoproteínas de baja densidad (low-density lipoprotein, LDL) y triglicéridos.

¿Por qué es importante tratar la dislipidemia?
- La dislipidemia es un factor de riesgo para ataques cardíacos y derrames cerebrales.
- El tratamiento de la dislipidemia lo ayudará a evitar un ataque cardíaco o un derrame cerebral.

¿Cómo puedo saber si tengo dislipidemia?
- Cuando se tiene dislipidemia, es posible no presentar síntomas.
- Su proveedor de atención médica ordenará una prueba que mide la cantidad de lípidos en la sangre.

¿Cómo sé si necesito la prueba?
- Su proveedor de atención médica revisará sus lípidos/colesterol:
  - Si tiene antecedentes de:
    - Ataque cardíaco previo
    - Diabetes mellitus
    - Hipertensión
    - Tabaquismo
  - Si tiende:
    - Tiene sobrepeso o es obeso
    - Es físicamente inactivo
    - Antecedentes familiares de una enfermedad cardíaca a temprana edad

¿Cómo se trata la dislipidemia?
El tratamiento depende de:
- Sus niveles de lípidos (colesterol)
- Su riesgo de sufrir ataques cardíacos con base en otros aspectos: si fuma, si tiene hipertensión o diabetes
- Salud general

Su proveedor de atención primaria puede proporcionarle un medicamento que reduce los lípidos para bajar su colesterol.

Lo que debe hacer
Cambié su rutina y actividades diarias para bajar su colesterol:
- Pierda peso si tiene sobrepeso
- Ejercítense
- Deje de fumar
- Coma más frutas y verduras
- Reduzca la grasa en su dieta (carne, leche, huevos, mantequilla, queso, alimentos envasados y meriendas como galletas dulces o saladas y papas fritas)
- Tome cualquier medicamento que se le proporcione según lo indicado
- Informe sobre cualquier efecto secundario de los medicamentos
  ⇒ Se reportan comúnmente dolores musculares y pueden deberse o no a su medicamento
- Realícese análisis de sangre según las recomendaciones de su equipo de atención médica
Colesterol alto – Hipercolesterolemia

Lo que debe saber

¿Qué es el colesterol?
- El colesterol en sangre es ceroso y similar a la grasa y es producido por el hígado. Es necesario para una buena salud. Su cuerpo lo necesita para realizar trabajos importantes, como producir hormonas, vitamina D y partes de las células y proteger las fibras nerviosas.
- Su cuerpo produce todo el colesterol en sangre que necesita, por lo que los expertos recomiendan que las personas consuman la menor cantidad posible de colesterol en la dieta mientras siguen un plan de alimentación saludable.
- El colesterol dietético se encuentra en los alimentos de origen animal, como la carne, el marisco, las aves de corral, los huevos y los productos lácteos.

¿Cuál es la diferencia entre el colesterol LDL y el colesterol HDL?
- El colesterol viaja a través de la sangre en proteínas llamadas “lipoproteínas”. Hay 2 tipos:
  - El LDL constituye la mayor parte del colesterol de su cuerpo.
  - Los niveles altos de colesterol LDL pueden acumularse en las paredes de los vasos sanguíneos (llamado placa) y aumentar su riesgo de enfermedad cardíaca y derrame cerebral.
  - El HDL absorbe el colesterol y lo lleva de regreso al hígado. Luego, el hígado lo elimina del cuerpo.
  - Los niveles altos de colesterol HDL pueden reducir su riesgo de enfermedad cardíaca y derrame cerebral.

¿Cómo determino mis niveles de colesterol?
- Su equipo de atención médica puede realizar un análisis de sangre simple, llamado “perfil lipídico,” para medir sus niveles de colesterol.
- Esta información ayuda a su equipo de atención médica a determinar su riesgo de enfermedad cardíaca o derrame cerebral.

¿Cómo sé mi riesgo de colesterol alto?
- Ciertas afecciones de salud, su estilo de vida y sus antecedentes familiares pueden aumentar su riesgo de colesterol alto.
- Estos se denominan “factores de riesgo” y se enumeran a continuación en detalle.

### Factores de riesgo para el colesterol alto

<table>
<thead>
<tr>
<th>Afecciones de salud</th>
<th>La diabetes tipo 2 y la obesidad pueden elevar los niveles de colesterol y grasas en sangre (triglicéridos).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comportamientos</td>
<td>Una dieta alta en grasas saturadas y grasas trans, no hacer suficiente ejercicio, fumar, beber en exceso.</td>
</tr>
<tr>
<td>Antecedentes</td>
<td>Algunas personas tienen una afección genética poco común llamada hipercolesterolemia familiar (familiar hypercolesterolemia, FH).</td>
</tr>
<tr>
<td>Familiares</td>
<td>Esta afección causa niveles muy altos de colesterol de lipoproteínas de baja densidad (LDL o “malo”) a partir de una edad temprana que, si no se tratan, empeoran con la edad.</td>
</tr>
<tr>
<td></td>
<td>Si alguien de su familia sufre un ataque cardíaco a una edad temprana, hable con su equipo de atención médica sobre su riesgo de sufrir de FH.</td>
</tr>
<tr>
<td></td>
<td>Si tiene antecedentes familiares de colesterol alto, es más probable que tenga colesterol alto. Es posible que necesite controlar sus niveles de colesterol con más frecuencia que las personas que no tienen antecedentes familiares de colesterol alto.</td>
</tr>
<tr>
<td>Edad y género</td>
<td>El riesgo de tener colesterol alto aumenta con la edad. Esto se debe a que, a medida que envejecemos, nuestros cuerpos no pueden eliminar el colesterol de la sangre tan bien como lo hacían cuando éramos más jóvenes. Esto resulta en niveles más altos de colesterol, lo que aumenta el riesgo de enfermedad cardíaca y derrame cerebral.</td>
</tr>
</tbody>
</table>
Medicamentos con estatinas

¿Qué son las estatinas?
- Los medicamentos con estatinas generalmente son el primer tipo de medicamento que los médicos recetan para reducir las LDL. También reducen los triglicéridos, que son otro tipo de grasa en la sangre y pueden elevar levemente su nivel de colesterol “bueno” (HDL).

¿Qué ocurre cuando tomo este medicamento?
- Debe hacerse un análisis de sangre antes de comenzar el tratamiento. Esto verifica el nivel de colesterol. También verifica si su hígado está funcionando de forma adecuada.
- Después de comenzar el tratamiento, debe realizarse un análisis de sangre dentro de 1 a 3 meses y de nuevo a los 12 meses.
- Se revisa la sangre para medir el nivel de colesterol y ver qué tan bien está funcionando la estatina.

¿Cuáles son los efectos secundarios de este medicamento?
- La mayoría de las personas que toman estatinas no presentan efectos secundarios o solo presentan efectos secundarios menores.
- Los posibles efectos secundarios incluyen:
  - Dolor de cabeza
  - Dolores musculares
  - Dolor estomacal
  - Inflamación
  - Sensación de mareo (náuseas)
  - Sarpullido
  - Hormigueo
- Informe a su médico si tiene alguno de estos, especialmente dolores musculares, sensibilidad, calambres o debilidad. Esto puede ocurrir como un efecto secundario poco común de las estatinas y es una forma grave de inflamación muscular.
- Los dolores musculares pueden ser más probables si también está tomando un medicamento llamado amlodipino o diltiazem.
- Es posible que su médico tenga que ajustar su dosis de estatina para reducir el riesgo de daño muscular.

¿Cómo puedo saber si no debo tomar este medicamento?
- No debe tomar estatina si tiene una enfermedad hepática activa, si está embarazada o tiene la intención de quedarse embarazada, o si está amamantando.
- Debe dejar de tomar estatina si desarrolla una enfermedad hepática.

¿Qué debo evitar cuando tomo este medicamento?
- No coma toronja ni beba jugo de toronja si está tomando estatinas.
- Una sustancia química en la toronja puede aumentar el nivel de estatinas en el torrente sanguíneo, lo que aumenta la probabilidad de sufrir los efectos secundarios de la estatina. Este problema solo sucede con simvastatina, atorvastatina y lovastatina. Otras estatinas, como pravastatina, no interfieren con la toronja.
- En ocasiones, los medicamentos pueden interferir con las estatinas. Por ejemplo, algunos antibióticos y la ciclosporina. Es posible que se tengan que ajustar las dosis de la estatina o del otro medicamento que interactúa.
- Si le recetan (o compra) otro medicamento, recuérdelo al médico o farmacéutico que está tomando una estatina en caso de que puedan interferir.
The terminology surrounding the hereditary disorders of LDL-C metabolism can be confusing. Individual patients may have one (monogenetic) or more (polygenetic) genetic defects that lead to a particular phenotype.

Below is a brief summary of some of the more common genetic causes, see references for more information.

<table>
<thead>
<tr>
<th>Genetic Cause</th>
<th>Description</th>
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</table>
| Familial Combined Hyperlipidemia (FCHL)| FCHL is a common genetic lipid disorder (1 to 2 percent of the population). Patients present with elevated levels of plasma total cholesterol, LDL-C, triglycerides, and apoB. Premature atherosclerotic cardiovascular disease (ASCVD) is not uncommon. When not initially present, there is an increased future likelihood of impaired glucose tolerance or type 2 diabetes.  
  - **Clinical manifestations** include premature CHD (particularly in patients with concurrent hypertriglyceridemia), xanthelasma (in 10 percent of cases), and obesity  
  - **Diagnosed** in patients with a family history of premature CHD and whose apoB concentration is > 120 mg/dL in combination with either elevations in both LDL-C and triglycerides or either elevated LDL-Col or triglycerides  
  - **Treatment** of FCHL (first line) is a statin, irrespective of whether or not triglyceride levels are elevated, which is effective therapy for lowering apoB levels. The potency and dose of statin should be chosen with the aim of achieving LDL-C < 100 mg/dL in primary prevention and < 70 mg/dL in secondary prevention. If the LDL-C or non-HDL-C therapeutic goals are not reached, addition of ezetimibe can be considered. |
| Familial Hypertriglyceridemia           | Familial Hypertriglyceridemia is a disorder characterized by the overproduction of V-LDL from the liver. As a result, the patient will have an excessive number of triglycerides and V-LDL on the lipid profile.  
  - **Clinical manifestations**: Mild to moderate elevations in triglyceride concentration. Familial Hypertriglyceridemia is typically accompanied by other co-morbidities: obesity, hyperglycemia, and HTN. Patients with this disorder are often heterozygous for inactivating mutations of the lipoprotein lipase (LPL) gene. While this mutation can alone raise triglyceride levels significantly, the combination of other medications or pathology can further increase serum triglyceride to pathologic levels. Significant increases in triglyceride levels can lead to the development of clinical signs and acute pancreatitis. A common sign of severe triglyceride elevation is xanthoma formation on skin exams.  
    - Typically Familial Hypertriglyceridemia is differentiated with significantly high triglycerides and low HDL-C levels in comparison to others in the Fredrickson, Levy and Lees (FLL) phenotypes.  
    - However, the influence of comorbid conditions that often accompany the pathology can skew a patient’s lipid profile.  
  - **Diagnosed** with routine fasting LP in the appropriate individuals. If triglyceride abnormalities are still present in the absence of secondary causes, further investigation could be suggested to screen first degree relatives due to the high prevalence of familial causes.  
  - **Treatment** for Familial Hypertriglyceridemia focuses on reducing the triglyceride levels. Furthermore, if the patient has pathologic triglyceride levels, treating or removing secondary causes would be vital to maintain relatively normal lipid levels. See Attachment C |

- [UpToDate: Inherited disorders of LDL-cholesterol metabolism other than familial hypercholesterolemia](#)
- [NCBI: Familial Hypertriglyceridemia](#)
Homozygous Familial Hypercholesterolemia

Homozygous Familial Hypercholesterolemia is a rare and life-threatening disease originally characterized clinically by plasma cholesterol levels > 13 mmol/L (> 500 mg/dL), extensive xanthomas, and marked premature and progressive ASCVD.

- **Clinical Manifestations:** strikingly elevated levels of low-density lipoprotein cholesterol (LDL-C) cutaneous xanthomas, and family history of premature atherosclerosis
- **Diagnosis:** Historically, the diagnosis of HoFH was based on untreated LDL-C levels of > 500 mg/dL (> 12.9 mmol/L) and treated levels ≥ 300 mg/dL (≥ 7.7 mmol/L); in addition, cutaneous or tendon xanthomas before age 10 and elevated LDL-C in both parents (suggesting HeFH) were also considered. Diagnosis of HoFH should not be excluded based on treated LDL-C levels < 300 mg/dL (< 7.7 mmol/L), but must also include other supportive clinical or genetic evidence.
- **Treatment:** The International FH Foundation recommends that as an initial goal, therapy should aim for a reduction of ≥ 50% in plasma LDL-C levels. In the absence of CHD or other major risk factors, an LDL-C treatment goal of < 100 mg/dL (< 2.5 mmol/L) is recommended, whereas a goal of < 70 mg/dL (< 1.8 mmol/L) is suggested for patients with CHD or other major risk factors
- **Primary goals of management** are prevention of ASCVD by early and comprehensive control of hypercholesterolemia, and early detection of complications, with specific focus on ostial occlusion and aortic stenosis.

Such patients are at increased risk of developing coronary artery disease and also sudden death unless the condition is recognized and treated promptly.

Polygenic Hypercholesterolemia

Many patients with the Familial Hypercholesterolemia clinical phenotype, but without a single mutation of sufficient pathogenicity to produce it, will have multiple (polygenic) gene variants, each of which makes a small independent contribution to a significantly elevated LDL-C. These patients are said to have polygenic hypercholesterolemia.

Some of these individuals express marked hypercholesterolemia when only two or three penetrant gene variants combine, whereas others may require the combination of greater numbers of less penetrant ones.

- **Treatment:** Therapy in polygenic hypercholesterolemia usually begins with a statin; ezetimibe, a bile acid sequestrant, PCSK9 inhibitor, or nicotinic acid are alternatives in patients who cannot tolerate a statin. Further lowering of LDL-C may be accomplished by combining a statin with ezetimibe. Low doses of nicotinic acid (1 to 1.5 g/day) will also raise high-density lipoprotein cholesterol (HDL-C), a desirable effect in patients with hypercholesterolemia and low HDL-C.
Diagnosis of dyslipidemia is made by measuring plasma levels of total cholesterol, triglycerides (TG), and individual lipoproteins. Key components of a standard lipid panel include the following:

<table>
<thead>
<tr>
<th>Component</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol/HDL-C ratio (calculated)</td>
<td>To calculate ratio, divide total cholesterol number by HDL-C (e.g., if total cholesterol is 200 mg/dL and HDL is 50 mg/dL the ratio would be 4-to-1). Higher ratios mean a higher risk of heart disease.</td>
</tr>
<tr>
<td>HDL-C</td>
<td>HDL cholesterol is known as the &quot;good&quot; cholesterol because it helps remove other forms of cholesterol from the bloodstream. Higher levels of HDL cholesterol are associated with a lower risk of heart disease.</td>
</tr>
<tr>
<td>LDL-C (calculated)</td>
<td>The equation calculates LDL-C as total cholesterol minus HDL-C minus TGs divided by five. The result is expressed in milligrams per deciliter. The direct LDL-C test measures the amount of LDL cholesterol, sometimes called &quot;bad&quot; cholesterol, in the blood. Calculated LDL-C is about as accurate as direct LDL-C when TG levels are normal.</td>
</tr>
<tr>
<td>Non-HDL-C (calculated)</td>
<td>Non-HDL-C is calculated as total cholesterol minus HDL cholesterol. According to the European Society of Cardiology cholesterol guideline, non-HDL-C evaluation is recommended for risk assessment, particularly in people with high TG levels, diabetes, obesity, or very low LDL-C levels.</td>
</tr>
<tr>
<td>Non-HDL cholesterol (non-HDL-C)</td>
<td>Represents the cholesterol components carried by atherogenic lipoproteins such as LDL, very low-density lipoprotein (VLDL) and intermediate density lipoprotein (IDL). Higher non-HDL-C levels indicate increased risk of atherosclerosis. Non-HDL-C is calculated as total cholesterol minus HDL cholesterol</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>Total cholesterol is a measure of the total amount of cholesterol in the blood. It includes LDL cholesterol, VLDL, and HDL cholesterol.</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>TGs (excess calories are transformed into TGs) are a type of fat (lipid) found in the blood.</td>
</tr>
</tbody>
</table>
Elevated fasting plasma TG levels are associated with ASCVD burden and events such as myocardial infarction and stroke. The risk of ASCVD events begins to rise with TG level above 150 mg/dL (1.7 mmol/L). Higher TG levels also increase the risk of pancreatitis.

This section will assist clinicians in recognizing and treating patients with hypertriglyceridemia to reduce ASCVD risk, as well as reduce the risk of pancreatitis.¹⁴

### Risk Factors for Hypertriglyceridemia

- Men ≥ 55y, Women ≥ 65y
- Current/Recent smoker
- HTN
- HDL ≤ 40 mg/dL for men, ≤ 50 mg/dL for women
- Hs-CRP > 3 mg/L
- Renal dysfunction, CrCl 30-60 ml/min
- Retinopathy
- Micro- or Macro-albuminuria
- ABI < 0.9 without claudication

### Secondary Factors for Hypertriglyceridemia

The table below lists lifestyle, secondary disorders and medications that influence hypertriglyceridemia.

<table>
<thead>
<tr>
<th>LIFESTYLE</th>
<th>Obesity</th>
<th>Metabolic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2° DISORDERS</td>
<td>DM or Hypothyroidism</td>
<td>Chronic liver disease</td>
</tr>
<tr>
<td>MEDICATIONS</td>
<td>Hormone related: Oral estrogens TamoxifenRaloxifene Retinoids Glucocorticoids</td>
<td>Immune related: Cyclosporine Tacrolimus Sirolimus Cyclophosphamide Interferon</td>
</tr>
</tbody>
</table>

### Treatment of Hypertriglyceridemia

The table below includes treatment recommendations and goals for moderate and severe hypertriglyceridemia.

<table>
<thead>
<tr>
<th>Triglyceride Level</th>
<th>Goal</th>
<th>Intervention</th>
</tr>
</thead>
</table>
| Moderate Hypertriglyceridemia | 150-499 mg/dL | Reduce VLDL (atherogenic) and ASCVD risk | • Lifestyle changes: especially appropriate diet composition, physical activity, weight reduction in overweight and obese
• Evaluate all patients for secondary factors/causes
• Statin recommended in adults age 40-75 with moderate hypertriglyceridemia and an ASCVD risk of 7.5% or higher (proven to be of most benefit to reduce ASCVD risk)

| Severe Hypertriglyceridemia | > 500 mg/dL | Reduce ASCVD risk (↑VLDL) Reduce pancreatitis risk (↑chylomicrons) | • Evaluate and address secondary factors/causes
• Initiation of statins is recommended in patients with severe hypertriglyceridemia and ASCVD risk equal to or greater than 7.5%.
• Recommend very low fat diet.
• Avoid refined carbohydrates and alcohol
• Fenofibrate may be considered concomitantly with a low or moderate-intensity statin only if the benefits from ASCVD risk reduction or triglyceride lowering when benefits are judged to outweigh the potential risk for adverse effects (Renal status should be evaluated before fenofibrate initiation (see page 17).
• Consider Omega-3 fatty acids as needed. Omega-3 Acid Ethyl Esters (Lovaza®) is non-formulary with use criteria (Reserved for patients who fail or are intolerant to fibrate/statin combination after a six month trial). |