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Management of Hypercholesterolemia

Clinical Practice Guideline

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"These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider-in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication, but should be used with the clear understanding that continued research may result in new knowledge and recommendations".

The following guideline is based on the report by American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ATP IV), published in November 2013.
Statins have been shown to prevent fatal and non-fatal ASCVD events (except in those w/ NYHA class II-IV heart failure or chronic dialysis patients) in both the primary prevention and secondary prevention settings. Many studies also demonstrate a reduction in all cause mortality. The ATP IV proposed treatment method abandons a "treat to target" paradigm and embraces a method of using the maximum tolerated statin intensity in the groups known to benefit. Prior proposed approaches to statin treatment lack supporting randomized controlled trial (RCT) data. Global Risk Assessment for Primary Prevention using the new Pooled Cohort Equations to estimate 10-year ASCVD (first occurrence nonfatal and fatal MI and fatal stroke) risk in non-Hispanic white and black patients without clinical ASCVD identifies those most likely to benefit from statins for primary prevention. Most studies of non-statin cholesterol lowering drugs do not demonstrate significant risk reduction above statin treatment alone, and their use should be confined to select patients based on clinical judgment and emerging trial data. The ATP IV guidelines continue to recommend a heart healthy diet, regular exercise, avoidance of tobacco products, and maintenance of a healthy weight and stress that all of these interventions were included as background therapy of RCTs of pharmacological cholesterol therapy.

Statin Benefit Groups

There are four groups of age ≥ 21 yo men and non-pregnant/non-nursing women for whom atherosclerotic cardiovascular disease benefit from statins clearly exceeds adverse event risk (w/o NYHA II-IV HF and/or on hemodialysis). ATP IV guidelines recommend which intensity statin should be initiated in these cases, with some caveats:

1) **Individuals with clinical ASCVD** (ACS, h/o MI, stable or unstable angina, coronary or arterial revascularization, CVA, TIA or PAD presumed atherosclerotic)→ High-Intensity statin preferred
2) **Individuals with LDL-C >= 190 mg/dL**→ High-Intensity statin preferred
3) **Individuals 40-75 years of age *with diabetes and* LDL-C 70-189 mg/dL**: If 10-yr ASCVD risk>= 7.5% → High-Intensity Statin preferred, otherwise use Moderate-Intensity
4) **Individuals 40-75 years of age *without* diabetes *or* clinical ASCVD *and* with LDL 70-189 mg/dL *and* an estimated 10-year ASCVD risk of 7.5% or higher** → Moderate to High-Intensity Statin

When risk is 5-7.5%, there can still be net benefit with *moderate-intensity* statin therapy but should be weighed against possible adverse events and treatment should be individualized

1) Rate of excess diabetes onset varies by statin intensity; for moderate-intensity it is ~0.1 excess cases per 100 treated patients per yr; for high intensity it is ~0.3
2) Myopathy (~ 0.01 excesses case/100 treated/yr) and hemorrhagic stroke (~ 0.01 excesses cases/100 treated/ yr)

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1/04, revised 11/5, 4/09, 4/2010, 4/2012, 4/2014 , 4/2016, 4/2018		April 2020

While ATP IV endorses the new clinical calculator, concerns have been raised as the Pooled Cohort Equations still lack validation in certain ethnic groups and does not include family history. Further studies may help clarify the calculator's broad utility. All calculators have benefits and drawbacks; clinician judgment may be used in choice of calculator, but the clinician should be well acquainted with the calculator they are using. For practical purposes, the provider may decide to quantify risk using another calculator, for example:

- Framingham Coronary Heart Disease 10-year Risk which is validated in whites, African Americans and Hispanic women, but may be less accurate in certain patients and *does not estimate stroke risk*
- Framingham General Cardiovascular Disease 10-year Risk which is based on data from primarily *white patients*

"Nontraditional" risk factors may be taken into account when considering statin initiation for selected individuals when use of the Pooled Cohort Equations alone does not seem to be useful. These include: LDL-C >=160 mg/dL or other evidence of genetic hyperlipidemia, family h/o premature ASCVD (first degree male relative with onset < 55 yo or female < 65 yo), hs-CRP ≥2 mg/dL, CAC score > = 300 Agatson units or ≥ 75th percentile for age, sex, and ethnicity, ABI < 0.9, or elevated lifetime risk of ASCVD.

Clinician decisions should also take into account patient preferences and individualized risks and benefits.

The age at which screening should begin should be based on an individual's other cardiac risk factors and desire to be screened. Screening may begin in non-pregnant adults at any age but no later than age 40 (the age at which statin therapy for primary prevention is recommended). 10-year risk should be re-evaluated every 4-6 yrs between 40-75 years old. The development of diabetes or clinical ASCVD should prompt evaluation as well.

Statin Choice

Choose medication and dose to achieve the desired LDL-C reduction intensity.

High-Intensity Statin Therapy	**Moderate-Intensity Statin Therapy**	**Low-Intensity Statin Therapy**
Lowers LDL-C >=50%	*Lowers LDL-C 30-50%*	*Lowers LDL-C < 30%*
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mgSimvastatin 10-40 mg -FDA does not recommend use of simvastatin 80 mg due to increased risk of myopathy Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg* ($252) Fluvastatin 40 mg BID ($299)	Simvastatin 10 mg* Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg * Pitavastatin 1 mg*

* Never tested in RCT

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Modification of Statin Choice

1) Since the following patient characteristics predispose to adverse statin effects, a moderate-intensity statin should be used:

A) Multiple or serious co-morbidities, including impaired renal/ hepatic function
B) H/o previous statin intolerance or muscle disorder
C) Unexplained elevation of ALT > 3 x upper limit of normal
D) Patient characteristics or concomitant use of medicines affecting statin metabolism
E) Age >= 75 yo

1) Fewer people > 75 were included in the reviewed RCTs but evidence supports continuing tolerated statins. The small amount of available data does not clearly support starting high-intensity statins for secondary prevention; a larger amount of data does support the use of moderate-intensity statins.

2) Few data in this group indicate a primary prevention benefit, so one must consider risk and benefits; Pooled Cohort Equations can be used in ages 76-79

2) A lower intensity than recommended statin may be considered for other compelling indications including a history of hemorrhagic stroke or Asian ancestry

3) ATP IV makes no recommendations regarding initiation or discontinuation of statins in NYHA II-IV ischemic systolic HF or in patients on maintenance hemodialysis as they have been identified to be less
likely to benefit from statin therapy.

Initial Evaluation for those not currently on statin

1. **Clinical ASCVD**: fasting (preferred) lipid panel, ALT, CK (if indicated)
    a. CK should not routinely be measured during statin therapy
    b. Baseline measurement of CK may be reasonable if there is concern for risk based on personal or family history of statin intolerance or muscle disease, clinical presentation, or concomitant drug treatment that may increase myopathy risk
    c. During statin treatment, it is reasonable to measure CK in individuals with muscle symptoms (pain, tenderness, stiffness, cramping, weakness, generalized fatigue)
    d. Routine monitoring of transaminases during statin therapy is no longer recommended. It is reasonable, however, to re-measure ALT in the setting of unusual fatigue, weakness, appetite loss, abdominal pain, dark urine, jaundice/icterus. For elevations in ALT > 3 times upper limit of normal, further investigation and either reducing statin dose, change to a different statin or stopping the medication are warranted.
2. **No Clinical ASCVD:** as above and screen for diabetes with HgbA1c or fasting glucose if diabetes status unknown
3. **Evaluate for secondary causes as appropriate, particularly if Triglycerides are ≥ 500 mg/dL or LDL-C ≥190 mg/dL.**

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Common Secondary Causes of Hyperlipidemia Seen in Clinical Practice

Secondary Cause	Elevated LDL-C	Elevated Triglyceride
Diet	Saturated or trans-fat, weight gain, anorexia	Weight gain, very low-fat diets, high intake of refined carbohydrates, excessive alcohol intake
Drugs	Diuretics, cyclosporine, glucocorticoids, amiodarone	Oral estrogens, glucocorticoids, bile acid sequestrants, protease inhibitors, retinoic acid, anabolic steroids, sirolimus, raloxifeine, tamoxifen, most beta blockers (carvedilol – most favorable)
Diseases	Biliary obstructions, nephrotic syndrome	Nephrotic syndrome, chronic renal failure, lidodystrophies
Disorders, altered metabolism	Hypothyroidism, obesity, pregnancy	Diabetes (poorly controlled), hypothyroidism, obesity, pregnancy

Monitoring Therapy

1) Lipid lowering agents should be taken indefinitely or as long as treating hypercholesterolemia remains consistent with the patient's health and treatment goals. Lipid levels return to baseline once medication is stopped.
2) Lipid panel 4-12 weeks after starting statin to determine adherence and then every 3-12 months as clinically indicated
    a. High-intensity statin therapy generally results in >=50% decrease from untreated baseline (if baseline is unknown, LDL-C < 100 has generally been observed)
    b. Moderate-intensity statin therapy generally results in 30-50% reduction
    c. Percent reduction may be used to indicate adherence (but can also indicate biologic variability); attention should be paid to adherence and lifestyle therapy, evaluation and treatment for secondary causes; clinical judgment should be used to decide if any therapy should be increased
3) A decrease in statin dose may be considered when 2 consecutive LDL-C values are < 40 mg/dL
4) It may be harmful to initiate or increase a simvastatin dose to 80 mg/dL due to the risk of rhabdomyolysis; lovastatin should be avoided in the setting of several medicines and dose limitations exist for other medicines; make sure to check labeling
5) Current diabetes screening guidelines should be maintained for those on statins
6) A review of manufacturer's prescribing information may be useful prior to initiation of any cholesterol lowering drug
7) To evaluate and treat muscle symptoms:
    a. Obtain a history of baseline symptoms prior to starting therapy
    b. For unexplained severe symptoms, discontinue statin and evaluate CK, Cr, UA
    c. For mild-moderate symptoms
        i. Discontinue statin until symptoms can be evaluated
        ii. Evaluate for conditions that might increase risk (hypothyroidism, reduced renal or hepatic function, rheumatologic disorder like polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, primary muscle disease)
            1. If symptoms resolve and there is no contraindication, give the same statin at an original or lower dose and observe for symptoms

   a. If causal relationship exists, discontinue original statin and when symptoms resolve, use a low dose of different statin. Pravastatin and fluvastatin are the statins with the least intrinsic muscle toxicity.
   b. Once that dose is tolerated, it can be gradually increased
2. If symptoms do not resolve after 2 mo without statin, or CK does not return to normal, consider other causes
3. If the statin is determined to not be the cause, or if the predisposing condition has been treated, the original statin at the original dose can be resumed

8) For presentation with a confusional state or memory impairment, it may be reasonable to evaluate for nonstatin causes (e.g. exposure to other drugs, systemic, or neuropsychiatric causes) in addition to possible statin adverse effects
9) Statins used in combination with other cholesterol-lowering drug therapies may require more intensive monitoring
10) Even lower-intensity statin therapy can reduce ASCVD events, so maximum intensity that does not cause adverse events should be used
11) Adverse events involving statins should be reported to the FDA MedWatch program

Non-statin Therapy

Non-statin therapy can be considered in high-risk patients (including those with clinical ASCVD less than
75 yo, those with LDL-C > 190 or diabetes) who have a less-than-anticipated response to statins, or are unable to tolerate the recommended statin intensity; clinicians should preferentially prescribe drugs w/ RCT proof of ASCVD risk reduction that exceeds risk of adverse effects.

1) **Niacin**
   a. Obtain transaminases, fasting glucose or A1c and uric acid before initiation, during up- titration to maintenance dose, then every 6 months
   b. Niacin should not be used if LFTs are > 2-3 x ULN; there are persistent severe cutaneous
   symptoms, persistent hyperglycemia, acute gout, unexplained abdominal pain, or GI symptoms, or if new onset atrial fibrillation or weight loss occurs
   c. If an adverse effect occurs, risk: benefit ratio must be considered before restarting
   d. To reduce cutaneous symptoms:
      i. Start low dose and titrate over weeks as tolerated
      ii. Take w/ food or premedicate w/ 325 mg ASA 30 min prior to dose
      iii. If using extended-release preparation: increase from 500 mg to 2000 mg/day over 4-8 weeks, <= weekly
      iv. If using immediate-release preparation: increase from 100 mg TID and up-titrate to 3g/daily, in 2-3 divided doses
2) **Bile Acid Sequestrants**
   a. Do not use if baseline fasting trig > 300 mg/dL or type III hyperlipoproteinemia; fasting lipids should be obtained at baseline, at 3 mo and then Q6-12 mo
   b. May be used with caution if baseline trig is 250-299 with fasting lipids at 6 weeks; discontinue if triglycerides exceed 400 mg/dL

3) **Cholesterol-Absorption Inhibitor (Ezetimibe)**
   a. Reasonable to obtain transaminases at baseline; when co-administered with statin, monitor LFTs as clinically indicated and stop if ALT > 3x ULN
4) **Fibrates**
   a. Gemfibrozil should not be initiated in patients on statin therapy due to increased risk of muscle symptoms and rhabdomyolysis
   b. Fenofibrate –concurrent use with statin therapy is no longer recommended. FDA has deemed that benefits of combined therapy do not outweigh risks.
5) **Omega-3 Fatty Acids**
   a. If EPA and/or DHA are used for trig > 500 mg/dL, evaluate in setting of GI disturbance, skin changes, bleeding

6) PCSK9 Inhibitors
   a. Evolocumab (Repatha, Repatha SureClick) and Alirocumab (Praluent)
   b. Reduce LDL_C by as much as 60% in patients on statins; Evolocumab has been shown to reduce cardiovascular events but not mortality.
   c. Indications

      i. **Homozygous familial hypercholesterolemia:** Adjunct to diet and other LDL-lowering therapies (eg, statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C. (evolocumab only)

      ii. **Hyperlipidemia, primary:** Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C). (evolocumab and alirocumab)

   d. Administered subcutaneously monthly evolocumab (Repatha) or every 2 weeks alirocumab
   e. (Praluent). Evolocumab does have an alternate q 2 week regimen for primary hyperlipidemia)
   f. Repatha (140 mg) $651 per dose; Praluent (75 mg – 150 mg) $672 per dose; Repatha –
   utilizing monthly dosing regimen $1853

Lipid Lifestyle Management Guideline

A separate Lifestyle Management Guideline was also issued, with the following recommendations for adults who would benefit from LDL-C lowering: consume a dietary pattern high in vegetables, fruits, and whole grains with low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils and nuts; limit sweets, sugar-sweetened beverages, and red meat. The *DASH dietary plan*, *USDA Food Pattern* (which offers lacto-ovo vegetarian and vegan options), and *AHA Diet* are plans that can achieve these recommendations. This pattern should be individualized, keeping patient preferences and other dietary needs in mind. The pattern should aim to achieve 5-6% of calories from saturated fat and reduce the percent of calories from saturated and trans-fat.

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Aerobic exercise of moderate or vigorous intensity should be performed 3-4 sessions per week, an average of 40 minutes per session. The separate Guideline on Lifestyle Management published in 2013 has specific recommendations for patients who would benefit from LDL-C lowering and blood pressure lowering and can be referred to for more details.

Patient education:

http://www.uptodate.com/contents/high-cholesterol-treatment-options-beyond-the-basics?source=see_link

http://www.uptodate.com/contents/diet-and-health-the-basics?source=see_link

https://healthyforgood.heart.org/eat-smart
http://health.gov/dietaryguidelines/2015/guidelines/

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FDA Drug Safety Communication: Important safety label changes to cholesterol-lowering statin drugs, 2-28-2012.

PL Detail-Document, Common Cardiovascular Risk Calculators. Pharmacist's

Letter/Prescriber's Letter. January 2014. PL Detail-Document, Common Cardiovascular

Risk Calculators. Pharmacist's Letter/Prescriber's Letter. January 2014

Alirocumab (Praluent) to Lower LDL-Cholesterol. The Medical Letter August 17, 2015

Evolucumab (Repatha)—A Second PCSK9 Inhibitor to Lower LDL-Cholesterol. The Medical Letter. October 12, 2015.

Lipid Lowering Drugs. The Medical Letter October 24, 2016.

Reduction of Cardiovascular Risk with Evolucomab (Repatha). The Medical Letter April 24, 2017.

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Medications for Cholesterol Reduction

HMG- CoA Reductase Inhibitors (Statins)			
Average LDL-C reduction: Low Intensity <30%, Moderate Intensity 30% to <50%, High Intensity ≥50%			
Drug		**Dose**	**Comments /Safety**
Atorvastatin (Lipitor) ($116-$173)	Moderate Intensity	10 -20 mg daily	(see guideline pages 3-5 for additional recommendations)
	High Intensity	40 - 80 mg daily *Only one RCT with 40 mg dose; down-titration if unable to tolerate 80 mg dose*	Baseline measurement of CK is reasonable for individuals believed to be at increased risk for adverse muscle events During statin therapy, it is reasonable to measure CK in individuals with muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or generalized fatigue. Baseline measurement of hepatic transaminase levels (ALT) should be performed before initiating statin therapy. During statin therapy, it is reasonable to measure hepatic function if symptoms suggesting hepatotoxicity arise Individuals receiving statin therapy should be evaluated for new-onset diabetes mellitus If unexplained severe muscle symptoms or fatigue develop during statin therapy, promptly discontinue the statin and address the possibility of rhabdomyolysis by evaluating CK, creatinine, and a urinalysis for myoglobinuria.
Fluvastatin ($150)	Low Intensity	20-40 mg nightly	
	Moderate Intensity	40 mg twice daily	
Fluvastatin XL (Lescol XL) ($263)	Moderate Intensity	80 mg daily	
Lovastatin ($71-$128) Lovastatin extended release (Altoprev) ($1000 – brand only)	Low Intensity	20 mg nightly	
	Moderate Intensity	40 mg nightly *(60 mg dose is not included in ACC/AHA guidelines)*	
Pitavastatin (Livalo) ($332 – brand only)	Low Intensity	1 mg daily	
	Moderate Intensity	2-4 mg daily	
Pravastatin (Pravachol ($96-$144)	Low Intensity	10-20 mg daily	
	Moderate Intensity	40-80 mg daily	
Rosuvastatin (Crestor) ($268)	Moderate Intensity	5-10 mg daily, do not crush or chew	
	High Intensity	20-40 mg daily, do not crush or chew	
Simvastatin (Zocor) ($84-$147)	Low Intensity	10 mg nightly	
	Moderate Intensity	20-40 mg nightly *80 mg dose is not recommended due to increased risk of myopathy, including rhabdomyolysis, unless patient has already been stable on this dose for >12 mos and no other contraindications*	

Cost per 30 days of generic medication unless otherwise specified

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Significant Statin Drug Interactions	
Atorvastatin	Use with caution in patients in patients taking strong CYP34A inhibitors. Consider alternate agents. Examples of common medications to avoid with atorvastatin: • Cyclosporine • Gemfibrozil • Tipranavir plus ritonavir • Telaprevir • Itraconazole Use with caution and use with the lowest atorvastatin dose necessary: Lopinavir + ritonavir Amiodarone Do not exceed 20 mg daily atorvastatin with the following agents: • Darunavir + ritonavir • Fosamprenavir • Fosamprenavir + ritonavir • Saquinavir + ritonavir Administer 1 hr before or at least 4 hours after cholestyramine or colestipol Use statins with caution with niacin ≥1000 mg/day Experts suggest avoiding grapefruit with atorvastatin due to inhibition of the CYP3A4 enzyme
Fluvastatin	Do not exceed fluvastatin 20 mg twice daily (fluvastatin may be least likely to interact): Cyclosporine Administer 1 hr before or at least 4 hours after cholestyramine or colestipol Avoid with fluvastatin: Gemfibrozil , Fenofibrate Use statins with caution with niacin ≥1000 mg/day
Lovastatin	Use with caution in patients in patients taking strong CYP34A inhibitors. Consider alternate agents. Contraindicated with lovastatin: • Itraconazole • Ketoconazole • Posaconazole • Erythromycin • Clarithromycin • Telithromycin • HIV protease inhibitors • Boceprevir • Telaprevir • Nefazodone Avoid with lovastatin: • Cyclosporine • Gemfibrozil Do not exceed 20 mg lovastatin daily with: Danazol

	• Diltiazem • Verapamil • Clarithromycin Administer 1 hr before or at least 4 hours after cholestyramine or colestipol. Use statins with caution with niacin ≥1000 mg/day. Limit extended release niacin to 2000 mg and lovastatin dose to 40mg daily when used in combination. Experts suggest avoiding grapefruit with lovastatin.
Pitavastatin	Contraindicated with pitavastin: Cyclosporine Limit dose to 1 mg daily with: Erythromycin Limit dose to 2 mg daily with: Rifampin
Pravastatin	Administer 1 hr before or at least 4 hours after cholestyramine or colestipol Avoid use with pravastatin: Gemfibrozil Do not exceed pravastatin 20 mg daily: Cyclopsorine Do not exceed pravastatin 40 mg daily: • Clarithromycin • Azithromycin Use statins with caution with niacin ≥1000 mg/day
Rosuvastatin	Do not exceed rosuvastatin 5 mg: • Cyclosporine Do not exceed rosuvastatin 10 mg daily: • Atazanavir ± ritonavir • Lopinavir + ritonavir Avoid use with rosuvastatin: • Gemfibrozil Administer 1 hr before or at least 4 hours after cholestyramine or colestipol Use statins with caution with niacin ≥1000 mg/day
Simvastatin	Contraindicated with simvastatin: • HIV protease inhibitors • Boceprevir • Telaprevir • Itraconcazole • Ketoconazole • Posaconazole • Danazol • Clarithromycin • Erythromycin Do not exceed simvastatin 20 mg: • Amiodarone • Amlopidine Administer 1 hr before or at least 4 hours after cholestyramine or colestipol Use statins with caution with niacin ≥1000 mg/day. Limit extended release niacin to 2000 mg and simvastatin dose to 40mg daily when used in combination Experts suggest avoiding grapefruit with simvastatin.

Nonstatins		
Clinicians treating high-risk patients who have a less-than-anticipated response to statins, who are unable to tolerate recommended intensity of a statin, or who are completely statin intolerant may consider the addition of a nonstatin cholesterol-lowering therapy.		
Drug	**Dose**	**Other**
Selective Cholesterol Absorption Inhibitor		When ezetimibe is coadministered with a statin, monitor transaminase levels as clinically indicated, and discontinue ezetimibe if persistent ALT elevations >3 times ULN occur Absorption decreased by bile acid sequesterants; administer ezetimibe at least 2hrs before or 4hrs after one
Ezetimibe (Zetia) ($312)	10 mg every day	
Bile Acid Sequestrants		BAS should not be used in individuals with baseline fasting triglyceride levels ≥300 mg/dL or type III hyperlipoproteinemia Use BAS with caution if baseline triglyceride levels are 250 to 299 mg/dL, and evaluate a fasting lipid panel in 4 to 6 weeks after initiation. Discontinue the BAS if triglycerides exceed 400 mg/dL. The bile acid sequestrant should be taken 1 hour after or 4 hours before other medications due to binding interactions Granules must be administered as solution; not to be taken in dry form
Cholestyramine granules • Questran granules $131 • Cholestyramine Light packets • Questran Light $201	Initial: 4g every day with food Usual: 4g 2-6 times a day with food	
• Prevalite packets $214	Initial: 5 g every day-twice a day Usual: 15-30 g divided	
Colestipol (Colestid) • Colestipol granules $234/500g • Colestipol tablets $118	Tabs: Initial: 2 g 1-2 times daily Usual: 2-16 g/day, may be split into divided doses Granules: Initial: 5g 1-2 times daily Usual: 5-30g/day, may be split into divided doses	
Colesevelam (Welchol) $750 (brand only)	3.75 g (oral suspension or 6 tabs) once daily or 1.875g (3 tabs) twice daily with meals	

Fibrates		Gemfibrozil should not be initiated in patients on statin therapy because of an increased risk for muscle symptoms and rhabdomyolysis Fenofibrate dose may need to be adjusted based on patient's renal function
Fenofibrate (TriCor, Lofibra) Generic micronized $208 Generic for TriCor $172 Generic for Lofibra $71	Generic (micronized): 130mg daily Lofibra tab: 160mg daily TriCor: 145mg daily	
Gemfibrozil (Lopid) $139	600 mg twice a day 30 minutes before meals	
Antilipemic Agents		Niacin should not be used if: • Hepatic transaminase elevations are higher than 2 to 3 times ULN. • Persistent severe cutaneous symptoms, persistent hyperglycemia, acute gout or unexplained abdominal pain or gastrointestinal symptoms occur.
Niacin (Most niacin products are available over the counter)		
Immediate-release *Niacor*($5-$8) Extended-release *Niaspan*($3-$5)	Immediate release: Initial: 250mg with evening meal Usual: 2-6 g in 3 divided doses Extended release: Initial: 500 mg every evening Usual: 1-2 g every evening	• New-onset atrial fibrillation or weight loss may occur • Use only if triglyceride goals are not met with other therapies
Omega-3-acid ethyl esters *(Lovaza)$248*	4g/day as single dose or 2 divided doses	If used for the management of • severe hypertriglyceridemia, defined as triglycerides ≥500 mg/dL, it is reasonable to evaluate the patient for gastrointestinal disturbances, skin changes, and bleeding. • Do not crush, break, or chew

Combination Products		(See individual agents)
Ezetimibe/Simvastatin *(Vytorin) $333*	Initial: 10/20 mg daily Usual: 10/20 mg – 10/40 mg daily	
PCSK9 Inhibitors		
Evolocumab (brand name only) Repatha: $670/140mg Repatha SureClick: $670/140mg Repatha Pushtronex: $1452/420mg	**Hyperlipidemia, primary:** SubQ: 140 mg every 2 weeks or 420 mg once monthly **Homozygous familial hypercholesterolemia:** SubQ: 420 mg once monthly	Most common side effect: >10%: Respiratory: Nasopharyngitis (6% to 11%) Influenza 8-9% Hypersensitivity reactions have been reported. Once monthly dose given as SubQ infusion over 9 minutes or as 3 140mg injections within a 30 minute period
Alirocumab (Praluent) $672/mL	**Hyperlipidemia SubQ**: Initial: 75 mg once every 2 weeks or 300mg every 4 weeks Maximum: 150 mg every 2 weeks	Most common side effect: injection site reaction (7%), Influenza (6%), Diarrhea 5%. Liver enzyme disorder 3% Hypersensitivity reactions have been reported. If giving 300mg dose, administer two 150mg injections in two different injection sites

Cost = monthly cost AWP)