Table 13–8

Risk-Enhancing Factors for Clinician-Patient Risk Discussion According to American Heart Association/ American College of Cardiology (AHA/ACC)[4]

Risk-Enhancing Factors
• **Family history of premature ASCVD** (male < 55 years; female, < 65 years)
• **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.14–4.89 mmol/L); non–HDL-C 190–219 mg/dL [4.91–5.66 mmol/L])[a]
• **Metabolic syndrome**
• **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
• **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS
• **History of premature menopause** (before age 40 years) and **history of pregnancy-associated conditions that increase later ASCVD risk** such as preeclampsia
• **High-risk race/ethnicities** (eg, South Asian ancestry)
• **Lipid/biomarkers**: Associated with increased ASCVD risk
• Persistently[a] elevated, primary hypertriglyceridemia (≥ 175 mg/dL [1.98 mmol/L])
• If measured:
1. **Elevated high-sensitivity C-reactive protein** (≥ 2 mg/L)
2. **Elevated Lp(a)**: A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥ 50 mg/dL (0.5 g/L; 125 nmol/L) constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
3. **Elevated apoB** ≥ 130 mg/dL (1.3 g/L): A relative indication for its measurement would be triglycerides ≥ 200 mg/dL (2.26 mmol/L). ApoB level ≥ 130 mg/dL (1.3 g/L) corresponds to an LDL-C > 160 mg/dL (4.14 mmol/L) and constitutes a risk-enhancing factor.
4. **ABI** < 0.9

Table 13–9

Effects of Lipid-Lowering Drugs on Serum Lipids at FDA-Approved Doses

Lipid-Lowering Drug	LDL Cholesterol	HDL Cholesterol	Triglycerides	Total Cholesterol
Statins				
Atorvastatin	−26% to −60%	+5% to +13%	−17% to −53%	−25% to −45%
Fluvastatin	−22% to −36%	+3% to +11%	−12% to −25%	−16% to −27%
Fluvastatin ER	−33% to −35%	+7% to +11%	−19% to −25%	−25%
Lovastatin	−21% to −42%	+2% to +10%	−6% to −27%	−16% to −34%
Pitavastatin	−31% to −45%	+1% to +8%	−13% to −22%	−23% to −31%
Pravastatin	−22% to −34%	+2% to +12%	−15% to −24%	−16% to −25%
Rosuvastatin	−45% to −63%	+8% to +14%	−10% to −35%	−33% to −46%
Simvastatin	−26% to −47%	+8% to +16%	−12% to −34%	−19% to −36%
Cholesterol Absorption Inhibitor				
Ezetimibe	−18%	+1% to +2%	−7% to −9%	−12% to −13%
Bile Acid Sequestrants				
Cholestyramine	−15% to −30%	+3% to +5%	May increase in patients with elevated triglycerides	−10% to −25%
Colesevelam	−15% to −18%	+3% to +5%		−70% to −10%
Colestipol	−15% to −30%	+3% to +5%		−10% to 25%
Nicotinic Acid				
Niacin ER	−5% to −17%	+14% to +26%	−11% to −38%	−3% to −12%
Niacin IR	−5% to −25%	+15% to +39%	−20% to −60%	−3% to −25%
Fibric Acid Derivatives				
Fenofibrate	−31% to +45%	+9% to +23%	−23% to −54%	−9% to −22%
Gemfibrozil	−30% to +30%	+10% to +30%	−20% to −60%	−2% to −16%
Omega-3-Fatty Acids				
Omega-3 ethyl esters	+45%	+9%	−45%	−10%
Icosapent ethyl	−5%	−4%	−27%	−7%
Microsomal Transfer Protein Inhibitors				
Lomitapide	−40%	−7%	−45%	−36%
Antisense Oligonucleotide				
Mipomersen	−25%	+15%	−18%	−21%
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors				
Alirocumab	−48% to −71%			−46% to −59%
Evolocumab	−48% to −71%			−46% to −59%
Adenosine Triphosphate Citrate Lyase (ACL) Inhibitors				

Table 13–9

Effects of Lipid-Lowering Drugs on Serum Lipids at FDA-Approved Doses

Lipid-Lowering Drug	LDL Cholesterol	HDL Cholesterol	Triglycerides	Total Cholesterol
Statins				
Atorvastatin	−26% to −60%	+5% to +13%	−17% to −53%	−25% to −45%
Fluvastatin	−22% to −36%	+3% to +11%	−12% to −25%	−16% to −27%
Fluvastatin ER	−33% to −35%	+7% to +11%	−19% to −25%	−25%
Lovastatin	−21% to −42%	+2% to +10%	−6% to −27%	−16% to −34%
Pitavastatin	−31% to −45%	+1% to +8%	−13% to −22%	−23% to −31%
Pravastatin	−22% to −34%	+2% to +12%	−15% to −24%	−16% to −25%
Rosuvastatin	−45% to −63%	+8% to +14%	−10% to −35%	−33% to −46%
Simvastatin	−26% to −47%	+8% to +16%	−12% to −34%	−19% to −36%
Cholesterol Absorption Inhibitor				
Ezetimibe	−18%	+1% to +2%	−7% to −9%	−12% to −13%
Bile Acid Sequestrants				
Cholestyramine	−15% to −30%	+3% to +5%	May increase in patients with elevated triglycerides	−10% to −25%
Colesevelam	−15% to −18%	+3% to +5%		−70% to −10%
Colestipol	−15% to −30%	+3% to +5%		−10% to 25%
Nicotinic Acid				
Niacin ER	−5% to −17%	+14% to +26%	−11% to −38%	−3% to −12%
Niacin IR	−5% to −25%	+15% to +39%	−20% to −60%	−3% to −25%
Fibric Acid Derivatives				
Fenofibrate	−31% to +45%	+9% to +23%	−23% to −54%	−9% to −22%
Gemfibrozil	−30% to +30%	+10% to +30%	−20% to −60%	−2% to −16%
Omega-3-Fatty Acids				
Omega-3 ethyl esters	+45%	+9%	−45%	−10%
Icosapent ethyl	−5%	−4%	−27%	−7%
Microsomal Transfer Protein Inhibitors				
Lomitapide	−40%	−7%	−45%	−36%
Antisense Oligonucleotide				
Mipomersen	−25%	+15%	−18%	−21%
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors				
Alirocumab	−48% to −71%			−46% to −59%
Evolocumab	−48% to −71%			−46% to −59%
Adenosine Triphosphate Citrate Lyase (ACL) Inhibitors				
Bempedoic Acid	−15% to −25%	−5%		−11%

Table 13–10

Formulation, Dosing, and Common Adverse Effects of Lipid-Lowering Drugs

Lipid-Lowering Drug	Dosage Forms	Usual Adult Maintenance Dose Range	Adverse Effects
Statins			
Atorvastatin	10-, 20-, 40-, 80-mg tablets	10–80 mg once daily (at any time of day). Dose adjustment in patients with renal dysfunction is not necessary	Most frequent side effects are constipation, abdominal pain, diarrhea, and nausea. Statins should be dose reduced and/or discontinued promptly if serum transaminase levels (liver function tests) rise to three times upper limit of normal or if patient develops signs or symptoms of myopathy. Dose equivalence should be considered when switching HMG-CoA reductase inhibitors
Fluvastatin	20-, 40-mg capsules; 80-mg extended-release tablets	20–40 mg/day as a single dose (evening) or 40 mg twice daily; 80-mg extended-release once daily. Dose adjustments for mild-to-moderate renal impairment are not necessary	
Lovastatin	10-, 20-, 40-mg tablets	10–80 mg/day as a single dose (with evening meal) or divided twice daily with food; 20–60 mg/day as a single dose. In patients with severe renal insufficiency (creatinine clearance < 30 mL/min [0.5 mL/s]), dosage increases above 20 mg/day should be carefully considered and, if deemed necessary, implemented cautiously	
Pravastatin	10-, 20-, 40-, 80-mg tablets	10–80 mg/day as a single dose at bedtime. In patients with a history of significant renal or hepatic dysfunction, a starting dose of 10 mg daily is recommended	
Pitavastatin	1-, 2-, 4-mg tablets	1–4 mg/day as a single dose can be taken with or without food, at any time of day. Moderate renal impairment (glomerular filtration rate 30–60 mL/min/1.73 m^2 [0.29–0.58 mL/s/m^2]) and end-stage renal disease on hemodialysis: Starting dose of 1 mg once daily and maximum dose of 2 mg once daily	
Rosuvastatin	5-, 10-, 20-, 40-mg tablets	5–40 mg/day (at any time of day); 40 mg reserved for those who do not achieve LDL cholesterol goal on 20 mg. In patients with history of significant renal dysfunction or Asian, starting dose of 5 mg daily is recommended	
Simvastatin	5-, 10-, 20-, 40-, 80-mg tablets	5–40 mg/day as a single dose in the evening, or divided. Recommended starting dose for patients at high risk of CHD is 40 mg/day. In patients with mild-to-moderate renal insufficiency, dosage adjustment is not necessary. However, caution should be exercised in patients with severe renal insufficiency; such patients should be started at 5 mg/day and be closely monitored. Due to increased risk of myopathy, including rhabdomyolysis, use of the 80-mg dose should be restricted to patients who have been taking simvastatin 80 mg chronically (eg, for 12 months or more) without	

		hemodialysis: starting dose of 1 mg once daily and maximum dose of 2 mg once daily	
Rosuvastatin	5-, 10-, 20-, 40-mg tablets	5–40 mg/day (at any time of day); 40 mg reserved for those who do not achieve LDL cholesterol goal on 20 mg. In patients with history of significant renal dysfunction or Asian, starting dose of 5 mg daily is recommended	
Simvastatin	5-, 10-, 20-, 40-, 80-mg tablets	5–40 mg/day as a single dose in the evening, or divided. Recommended starting dose for patients at high risk of CHD is 40 mg/day. In patients with mild-to-moderate renal insufficiency, dosage adjustment is not necessary. However, caution should be exercised in patients with severe renal insufficiency; such patients should be started at 5 mg/day and be closely monitored. Due to increased risk of myopathy, including rhabdomyolysis, use of the 80-mg dose should be restricted to patients who have been taking simvastatin 80 mg chronically (eg, for 12 months or more) without evidence of muscle toxicity.	
Cholesterol Absorption Inhibitors			
Ezetimibe	10-mg tablets	10 mg once daily. No dosage adjustment is necessary in patients with renal or mild hepatic insufficiency	Overall incidence of adverse events reported with ezetimibe alone was similar to that reported with placebo and generally similar between ezetimibe with a statin and statin alone. The frequency of increased transaminases was slightly higher in patients receiving ezetimibe plus a statin compared with those receiving statin monotherapy (1.3% vs 0.4%)
Bile Acid Sequestrants			
Cholestyramine	4-g packets	4–24 g/day in two or more divided doses	Main side effects are nausea, constipation, bloating, and flatulence, although these may be less with colesevelam. Increasing fluid and dietary fiber intake may relieve constipation and bloating. Impairs absorption of fat-soluble vitamins
Colesevelam	625-mg tablets	3750 mg/day as a single dose or divided twice daily, with meals	
	3.75-g oral suspension packet	One packet once a day with meals	
Colestipol	5-g packets	5–30 g/day as a single dose or divided	
	1-g tablets	2–16 g/day as a single dose or divided	

(*Continued*)

Table 13–10

Formulation, Dosing, and Common Adverse Effects of Lipid-Lowering Drugs (*Continued*)

Lipid-Lowering Drug	Dosage Forms	Usual Adult Maintenance Dose Range	Adverse Effects
Nicotinic Acid (Prescription Products)			
Niacin ER	250-, 500-, 750-, 1000-mg extended-release tablets	1000–2000 mg once daily at bedtime. Use with caution in patients with renal impairment	Side effects include flushing, itching, gastric distress, headache, hepatotoxicity, hyperglycemia, and hyperuricemia
Niacin IR	250-, 500-mg tablets	1–6 g/day in two to three divided doses. Do not exceed 6 g daily	
Fibric Acid Derivatives			
Fenofibrate	54-, 160-mg tablets[a]	54–160 mg/day; the dosage should be minimized in severe renal impairment	Most common side effects are nausea diarrhea, abdominal pain, and rash. Increased risk of rhabdomyolysis when given with a statin. Fibric acids are associated with gallstones, myositis, and hepatitis
Gemfibrozil	600-mg tablets	1200 mg/day in two doses, 30 minutes before meals; should be avoided in hepatic or severe renal impairment	
Omega-3-Fatty Acids			
Omega-3 ethyl esters	1-g capsule containing at least 0.9 g of OM3FA ethyl ester (EPA~0.465 g and DHA ~0.375 g)	4 g/day taken as single 4-g dose (four capsules) or two 2-g doses (two capsules twice daily)	All products are obtained from oil of fish. Should be used with caution in patients with known hypersensitivity to fish and/or shellfish. Side effects of Lovaza/Omtryg include • Eructation, 4% • Dyspepsia, 3% • Taste perversion, 4% Side effects of Vascepa include: • Arthralgia, 2.3%
Icosapent ethyl	0.5-, 1-g capsule containing 1 g of icosapent ethyl	2 g twice daily with meals	
Microsomal Transfer Protein Inhibitors			
Lomitapide	5-,10-, 20-, 30-, 40-, and 60-mg capsules	5 mg once daily. Titrate dose based on acceptable safety/tolerability: increase to 10 mg daily after at least 2 weeks; and then, at a minimum of 4-week intervals, to 20 mg, 40 mg, and up to the maximum recommended dose of 60 mg daily	Gastrointestinal side effects and elevation in liver enzymes and hepatic fat are common
Antisense Oligonucleotide			
Mipomersen	200-mg subcutaneous injection	200 mg once weekly as a subcutaneous injection	Injection site reactions, hepatic fat, and liver enzyme elevations are common
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors			
Alirocumab	75- or 150-mg	75–150 mg once every 2 week subcutaneous injection or	Injection site reactions, nasopharyngiti

	containing 1 g of icosapent ethyl		• Taste perversion, 4% Side effects of Vascepa include: • Arthralgia, 2.3%
Microsomal Transfer Protein Inhibitors			
Lomitapide	5-,10-, 20-, 30-, 40-, and 60-mg capsules	5 mg once daily. Titrate dose based on acceptable safety/tolerability: increase to 10 mg daily after at least 2 weeks; and then, at a minimum of 4-week intervals, to 20 mg, 40 mg, and up to the maximum recommended dose of 60 mg daily	Gastrointestinal side effects and elevation in liver enzymes and hepatic fat are common
Antisense Oligonucleotide			
Mipomersen	200-mg subcutaneous injection	200 mg once weekly as a subcutaneous injection	Injection site reactions, hepatic fat, and liver enzyme elevations are common
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors			
Alirocumab	75- or 150-mg subcutaneous injection	75–150 mg once every 2 week subcutaneous injection or 300 mg once every month subcutaneous injection	Injection site reactions, nasopharyngitis, influenza, upper respiratory tract infections, urinary tract infection, elevation in liver enzymes
Evolocumab	140- or 420-mg subcutaneous injection	140 mg once every 2 week subcutaneous injection or 420 mg once every month subcutaneous injection	Injection site reactions, nasopharyngitis, influenza, upper respiratory tract infections, urinary tract infection, back pain
Adenosine Triphosphate Citrate Lyase (ACL) Inhibitors			
Bempedoic acid	180-mg tablets	180 mg once daily. No dosage adjustment for patients with renal or hepatic insufficiency provided in labeling	Hyperuricemia
Combination Products			
Ezetimibe and simvastatin	10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg	Dosage range is 10/10 mg/day through 10/40 mg/day. Recommended usual starting dose is 10/10 or 10/20 mg/day. Initiation of therapy with 10/10 mg/day may be considered for patients requiring less aggressive LDL cholesterol reductions. Due to increased risk of myopathy, including rhabdomyolysis, use of the 10/80-mg dose of Vytorin should be restricted to patients who have been taking Vytorin 10/80 mg chronically (eg, for 12 months or more) without evidence of muscle toxicity	See previous entries for each drug (ezetimibe and simvastatin)
Bempedoic acid and ezetimibe	180 mg/10 mg	180 mg/10 mg once daily	See previous entries for each drug (bempedoic acid and ezetimibe)

[a]Dose strengths vary depending on brand.

CHD, coronary heart disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; ER, extended-release; HMG-CoA, 3-hydroxy-3-methyglutaryl coenzyme A; IR, immediate-release; LDL, low-density lipoprotein; OM3FA, omega-3 fatty acid.