

Atherosclerotic Cardiovascular Disease

ASCVD | Staff education reference for the pharmacy team

What It Is

ASCVD is a group of conditions driven by **atherosclerosis**, the slow buildup of cholesterol-rich plaque inside artery walls. Over years the plaque narrows and stiffens the vessel. When a plaque ruptures, a clot forms and abruptly cuts off blood flow, which is what produces most heart attacks and strokes. It is the leading cause of death in the U.S.

Clinical ASCVD includes:

- **Coronary heart disease:** myocardial infarction, stable or unstable angina, coronary revascularization
- **Cerebrovascular disease:** ischemic stroke and transient ischemic attack (TIA)
- **Peripheral artery disease:** including atherosclerotic aortic aneurysm

The core prevention principle: lower cumulative lifetime exposure to LDL cholesterol and other risk factors.

Risk Factors

Non-modifiable Older age, male sex, and family history of premature ASCVD (first-degree male relative before 55, female before 65).

Modifiable High LDL-C, hypertension, diabetes, cigarette smoking, obesity, physical inactivity, atherogenic diet, and chronic kidney disease. These are where pharmacist intervention has the most impact.

Risk enhancers Help tip a borderline or intermediate patient toward therapy: persistently elevated LDL-C 160+, high Lp(a) or apoB, metabolic syndrome, chronic inflammatory disease (RA, psoriasis, HIV), triglycerides 175+, high-risk ethnicity such as South Asian ancestry, history of preeclampsia or premature menopause, and hs-CRP 2.0+.

Estimating 10-Year Risk

For adults without established ASCVD, quantify risk with a validated calculator to guide shared decision-making. Two tools live in the ACC CVD Risk Estimator Plus:

- **Pooled Cohort Equations (PCE, 2013):** long-standing guideline tool; 10-year risk for ages 40 to 79 from age, sex, race, lipids, blood pressure, diabetes, and smoking.
- **PREVENT equations (AHA, 2023):** newer, race-free, ages 30 to 79. Gives 10- and 30-year estimates for ASCVD, heart failure, and total CVD, and adds kidney and metabolic inputs (eGFR, BMI, A1c). PREVENT tends to produce lower estimates, so the tool chosen affects who is flagged for therapy.

Category	10-year risk	General direction
Low	< 5%	Emphasize lifestyle; statin usually not indicated
Borderline	5 to 7.4%	Consider statin if risk enhancers are present
Intermediate	7.5 to 19.9%	Moderate-intensity statin; CAC score can refine the decision
High	≥ 20%	High-intensity statin to lower LDL-C by 50% or more

Categories reflect the PCE thresholds in the 2018 ACC/AHA cholesterol guideline.

Statins: First-Line Therapy

LDL-C is the primary target. Statins are first-line and the only lipid class with consistent mortality benefit. Four groups clearly benefit: clinical ASCVD, LDL-C 190+, diabetes at ages 40 to 75, and selected primary-prevention patients based on calculated risk.

Intensity	LDL-C ↓	Agents
High	≥ 50%	Atorvastatin 40 to 80 mg · Rosuvastatin 20 to 40 mg
Moderate	30 to 49%	Atorvastatin 10 to 20 mg · Rosuvastatin 5 to 10 mg · Simvastatin 20 to 40 mg · Pravastatin 40 to 80 mg · Pitavastatin 1 to 4 mg
Low	< 30%	Simvastatin 10 mg · Pravastatin 10 to 20 mg · Lovastatin 20 mg

Secondary prevention High-intensity statin targeting a 50% or greater LDL-C reduction; consider adding non-statin therapy when LDL-C stays at or above 70 mg/dL (lower thresholds in very high risk).

Statin Solubility: Lipophilic vs Hydrophilic

Solubility shapes a statin's interaction and tolerability profile, which matters when selecting or switching agents.

	Lipophilic	Hydrophilic
Statins	Atorvastatin, Simvastatin, Lovastatin, Fluvastatin, Pitavastatin	Pravastatin, Rosuvastatin
Cell entry	Passive diffusion into many tissues; some CNS penetration	Transporter-dependent (OATP1B1); more liver-selective
Metabolism, DDIs	More CYP450 metabolism (3A4: simva, lova, atorva); more interaction potential	Minimal CYP involvement; generally fewer drug interactions
Practical note	Higher potency options for aggressive LDL lowering	Reasonable switch for muscle symptoms or CYP3A4 interactions

Beyond Statins: Add-On Therapy

For patients not at goal or intolerant of statins, layer on non-statin agents:

Agent	Mechanism / route	LDL ↓	Typical use
Ezetimibe	Blocks intestinal cholesterol absorption; oral	15 to 25%	First add-on when not at goal on a statin
PCSK9 inhibitors	Monoclonal antibody (evolocumab, alirocumab); SC every 2 to 4 wk	50 to 60%	High-risk patients far from goal
Inclisiran	siRNA against PCSK9; SC twice yearly after loading	~50%	Add-on where adherence is a barrier
Bempedoic acid	ACL inhibitor; oral	15 to 25%	Statin-intolerant patients or add-on
Icosapent ethyl	Purified EPA; oral	TG-directed	TG 150+ on statin; lowers ASCVD events (REDUCE-IT)

Monitoring & Safety

- **Lipids:** baseline panel, recheck 4 to 12 weeks after starting or changing, then every 3 to 12 months.
- **Liver:** baseline LFTs; routine monitoring is not needed unless symptoms arise.
- **Glucose:** statins may modestly raise A1c; cardiovascular benefit outweighs this risk.
- **Muscle symptoms (SAMS):** most myalgias are not true intolerance; check CK if severe or with objective weakness. Options: dose reduction, brief drug holiday, switch to a hydrophilic statin, or alternate-day rosuvastatin.
- **Pregnancy:** generally discontinue; counsel on contraception in patients of childbearing potential.

Where the Pharmacist Adds Value

- Reinforce statin adherence and correct the belief that a normal cholesterol reading means the statin can stop.
- Assess statin-associated muscle symptoms and separate true intolerance from nocebo before abandoning therapy.
- Screen for interactions (simvastatin dose limits with amlodipine, diltiazem, or azoles; grapefruit).
- Recommend intensification or an add-on agent when a patient is not at LDL-C goal, and refer when appropriate.
- Counsel on smoking cessation, blood pressure, and glucose control, and deliver guideline-based immunizations as part of total risk reduction.

For staff education and internal reference. Clinical decisions should follow current ACC/AHA guidance and individualized shared decision-making.