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Statins and Other Hypercholesteromia Treatments

What Is a Statin?[1]

Definition

- Statins are a class of lipid-lowering agents that inhibit HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol biosynthesis.

Clinical Purpose

- Reduce low-density lipoprotein cholesterol (LDL-C)
- Lower the risk of atherosclerotic cardiovascular disease (ASCVD), including myocardial infarction, stroke, and cardiovascular mortality

Mechanism of Action

- By inhibiting cholesterol synthesis in the liver, statins increase the expression of LDL receptors on hepatocytes, thereby enhancing clearance of circulating LDL-C.

Patient Risk Categories & Recommended Statin Therapy[1,2]

Patient Category	Recommended Statin Intensity
Clinical ASCVD (MI, stroke, PAD)	High-intensity (atorvastatin 40–80 mg, rosuvastatin 20–40 mg)
LDL-C ≥190 mg/dL	High-intensity regardless of 10-year ASCVD risk
Diabetes (Age 40–75)	Moderate-intensity (atorvastatin 10-20 mg, rosuvastatin 5-10 mg); consider high-intensity dose if risk enhancers present
ASCVD risk ≥20%	High-intensity statin
ASCVD risk 7.5–19.9% + risk enhancers (e.g., FH, CKD)	Moderate–high, shared decision
Age >75 & on statin	Continue if tolerated

Statin therapy is categorized based on the average expected LDL-C reduction[1]:

Intensity	Average LDL-C Reduction
High-Intensity	↓ LDL-C by ≥50%
Moderate-Intensity	↓ LDL-C by 30% to <50%
Low-Intensity	↓ LDL-C by <30%

Statin	High-Intensity Dose	Moderate-Intensity Dose	Low-Intensity Dose
Atorvastatin	40–80 mg	10–20 mg	—
Rosuvastatin	20–40 mg	5–10 mg	—
Simvastatin	—	20–40 mg	10 mg
Pravastatin	—	40–80 mg	10–20 mg
Lovastatin	—	40 mg	20 mg
Fluvastatin XL	—	80 mg (40 mg BID)	20–40 mg
Pitavastatin	—	2–4 mg	1 mg

Statin Safety and Monitoring[1,2]

Hepatic Function:

- Obtain baseline liver function tests (LFTs) prior to statin initiation.
- Repeat LFTs at least annually, more frequently if clinically indicated, such as in cases of unexplained fatigue, right upper quadrant pain, or jaundice.

Muscle Symptoms:

- Routine creatine kinase (CK) monitoring is not recommended.
- Check CK levels only if the patient reports signs or symptoms of myopathy, such as muscle pain, weakness, or dark urine.

Drug-Drug Interactions:

- Avoid coadministration of simvastatin with strong CYP3A4 inhibitors (e.g., diltiazem, amiodarone) due to increased risk of myopathy.
- Avoid combining statins with gemfibrozil as this significantly increases the risk of rhabdomyolysis.

Role of Non-Statin Therapies in Hypercholesterolemia[2]

When to Consider Non-Statin Therapy

Addition of non-statin lipid-lowering agents should be considered in the following scenarios:

- Clinical ASCVD with LDL-C ≥70 mg/dL despite maximally tolerated statin therapy
    - Add ezetimibe
    - If LDL-C remains above goal after ezetimibe,
        - Consider adding a PCSK9 inhibitor (e.g., alirocumab, evolocumab)
- Severe hypercholesterolemia (LDL-C ≥190 mg/dL) with residual L DL-C ≥100 mg/dL
    - Add ezetimibe
    - If LDL-C remains above goal after ezetimibe,
        - Consider adding a PCSK9 inhibitor
- Statin intolerance or partial intolerance
- Presence of high-risk comorbidities, such as familial hypercholesterolemia (FH)

Overview of Available Non-Statin Therapies

1. Ezetimibe[3]
    a. LDL-C Reduction: ~13–20%
    b. Role: First-line adjunct to statins
    c. Key Evidence: IMPROVE-IT (NEJM 2015) demonstrated reduction in CV events in post-ACS patients
    d. Monitoring: LFTs if used concurrently with statin therapy
2. PCSK9 Inhibitors (Alirocumab, Evolocumab)[4,5]
    a. LDL-C Reduction: ~50–60%
    b. Role: High-risk ASCVD or familial hypercholesterolemia
    c. Key Evidence: FOURIER (NEJM 2017): Evolocumab reduced CV events in stable ASCVD ODYSSEY OUTCOMES (NEJM 2018): Alirocumab reduced events post-ACS Monitoring: LDL-C 4 to 12 weeks after initiation
3. Bempedoic Acid (Nexletol)[6]
    a. LDL-C Reduction: ~15–20%
    b. Role: Statin-intolerant patients or in combination with statins
    c. Key Evidence: CLEAR OUTCOMES (NEJM 2023) showed MACE reduction in statin-intolerant population
    d. Monitoring: Uric acid and serum creatinine
4. Bile Acid Sequestrants (e.g., cholestyramine, colesevelam)[7]
    a. LDL-C Reduction: ~15–25%
    b. Role: Consider in patients with TG <300 mg/dL who cannot tolerate statins
    c. Considerations: Can cause gastrointestinal side effects Multiple drug interactions due to binding in the gut
5. Inclisiran (Leqvio)[8]
    a. LDL-C Reduction: ~50%
    b. Role: ASCVD and familial hypercholesterolemia requiring additional LDL-C lowering
    c. Dosing: Subcutaneous injection at baseline, 3 months, then every 6 months
    d. Monitoring: LDL-C levels post-initiation

Statin Approximate LDL-C Reduction[1]

Statin	Approximate LDL Reduction
Atorvastatin	30-55%
Rosuvastatin	35-63%
Simvastatin	30-50%
Pravastatin	20-35%
Lovastatin	20-30%
Fluvastatin	20-35%
Pitavastatin	30-40%

LDL-C Reduction with Non-Statin Therapies

Agent	Approximate LDL Reduction
Ezetimibe	~13-20%
PCSK9 Inhibitors	~50-60%
Bempedoic Acid	~15-20%
Bile Acid Sequestrants	~15-25%
Inclisiran	~50%

Questions?

- For information on how to incorporate these guidelines into your practice, reach out for a free pharmacist consultant: https://illinoisadvance.uic.edu/

References

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