rosuvastatin (Crestor)

Summary

Statins are a class of medications used to lower high levels of cholesterol and triglycerides in the blood and reduce the risk of cardiovascular disease. They are classified as low-intensity, moderate-intensity, or high-intensity based on their ability to lower LDL-cholesterol levels. Statins work by inhibiting an enzyme in the liver that is responsible for producing cholesterol.

The American College of Cardiology (ACC) and American Heart Association (AHA) recommend using high-intensity statins as the first-line treatment for people who require cholesterol-lowering medication. The recommended daily dose for atorvastatin is 40-80 mg, and 20-40 mg for rosuvastatin.

Table 1: Statins (hydroxymethylglutaryl-CoA reductase inhibitors) Intensity

Generic name	High intensity	Moderate intensity	Low intensity
Atorvastatin	40 to 80 mg	10 to 20 mg	
Rosuvastatin	20 to 40 mg	5 to 10 mg	
Simvastatin		20 to 40 mg	10 mg
Pravastatin		40 to 80 mg	10 to 20 mg

Lovastatin		40 to 80 mg	20 mg
Fluvastatin		80 mg daily (extended-release) or 40 mg twice daily	20 to 40 mg
Pitavastatin		1 to 4 mg	

Rosuvastatin, marketed under the brand name Crestor, is a medication belonging to the "statin" drug class, used to lower high levels of cholesterol and triglycerides in the blood.

- Rosuvastatin is indicated for the treatment of hyperlipidemia, which is characterized by high levels of low-density lipoprotein (LDL) cholesterol, also known as "bad" cholesterol, in the blood. Elevated levels of LDL cholesterol (LDL-C) can lead to the development of atherosclerosis, a condition in which plaque builds up inside the arteries, increasing the risk of heart attack and stroke.
- Rosuvastatin is also indicated for the prevention of cardiovascular disease in individuals who are at high risk for developing heart disease. This includes people with diabetes, a history of heart attack or stroke, or other risk factors such as high blood pressure or smoking.

Statin Use for the Primary Prevention of Cardiovascular Disease in Adults:

The United States Preventive Services Task Force (USPSTF) also provides recommendations based on population groups and cardiovascular risk:

1. For adults aged 40 to 75 years with one or more cardiovascular risk factors and an estimated 10-year cardiovascular disease (CVD) risk of 10% or greater, the USPSTF recommends initiating a statin (Grade: B). (See Definitions below for a complete list of USPSTF defined risk factors)
2. For adults aged 40 to 75 years with one or more cardiovascular risk factors and an estimated 10-year CVD risk of 7.5% to less than 10%, the USPSTF recommends selectively offering statins for primary prevention of CVD (Grade: C).
3. The current evidence is insufficient to assess the benefits and harms of initiating a statin for the primary prevention of CVD events and mortality in adults 76 years or older. (Grade: I)

These recommendations apply to adults 40 years or older without established CVD or signs of CVD. They do not apply to adults with a LDL cholesterol level greater than 190 mg/dL (4.92 mmol/L) or known familial hypercholesterolemia.

I. Initiate a moderate-intensity statin for those with a risk factor and a 10-year CVD risk of 10% or greater, after patient agreement.
II. For those with a risk factor and a 10-year CVD risk of 7.5% to less than 10%, selectively offer a statin considering patient values and preferences.
III. To implement these recommendations, clinicians should consider the patient's age, presence of cardiovascular risk factors, and estimated CVD risk.
    A. CVD is the leading cause of mortality in the US, making these recommendations crucial.
    B. Age is a significant risk factor for CVD.

Additional resources can be found on the Million Hearts initiative and Centers for Disease Control and Prevention websites. For the full recommendation statement, visit the USPSTF or the Journal of the American Medical Association (JAMA) website.

Definitions

"ASCVD" refers to atherosclerotic cardiovascular disease.

"ASCVD Risk Estimator" is a peer-reviewed online calculator which uses the Pooled Cohort Equations to estimate the 10-year primary risk of ASCVD (atherosclerotic cardiovascular disease) among patients without pre-existing cardiovascular disease who are between 40 and 79 years of age.

"Cardiovascular Event" is a health incident that affects the heart or blood vessels, such as a heart attack or stroke.

"Cardiovascular Risk Factors" are conditions or habits that increase the chances of developing cardiovascular disease. They encompass a wide range of factors, such as:

1. Age: Men aged 45 years or older and women aged 55 years or older are at higher risk.
2. Diabetes: A chronic condition that affects the body's ability to use sugar for energy and can cause damage to the blood vessels.
3. Dyslipidemia: An abnormal amount of lipids (like cholesterol and/or fat) in the blood.
4. Excessive Alcohol Use: Drinking too much alcohol can raise blood pressure and contribute to heart disease.
5. Family history of early heart disease: Heart disease in a father or brother before age 55, or in a mother or sister before age 65, can indicate a genetic predisposition to cardiovascular conditions.
6. Hypertension: High blood pressure, which can cause strain on the heart and contribute to atherosclerosis (hardening of the arteries).
7. Obesity: A body mass index (BMI) of 30 or higher, which puts strain on the heart.
8. Poor Diet: Diets high in saturated fats, trans fats, sodium, and cholesterol can raise blood cholesterol levels and contribute to heart disease.
9. Sedentary Lifestyle: Lack of physical activity can contribute to the development of heart disease.
10. Smoking: Tobacco use contributes to the buildup of plaque in the blood vessels and can lead to heart disease.

"Cholesterol" is a type of fat molecule that is essential for building cell membranes and producing hormones, but high levels of cholesterol in the blood can increase the risk of cardiovascular disease.

"Familial Hypercholesterolemia" is a genetic disorder characterized by high cholesterol levels, specifically high levels of LDL-C, in the blood.

"High-intensity statin" is a statin with LDL-lowering capacity of 50% or greater.

"High-sensitvity C-reactive protein" refers to a blood test that measures C-reactive protein, which is a marker of inflammation. It is commonly used to assess one's cardiovascular risk.

"Hyperlipidemia" is a condition characterized by high levels of lipids (fats) in the blood, including cholesterol and triglycerides.

"Low-density lipoprotein cholesterol (LDL-C)" is a type of cholesterol that is often referred to as "bad" cholesterol because high levels of LDL-C can increase the risk of cardiovascular disease. Statins and other medications are often used to lower LDL-C levels.

"Moderate-Intensity statin" is a statin with LDL-lowering capacity of 30-49%.

"Preventive Services Statins Zero Copay Exception" is a provision in the health plan where the member doesn't have to pay any out-of-pocket costs (copay) for statins when used for the primary prevention of cardiovascular disease.

"Primary prevention" is used to reduce the risk of future atherosclerotic cardiovascular disease (ASCVD) events.

"Secondary prevention" is used to treat existing ASCVD and to prevent it from getting worse.

"Statins" is a class of medications used to lower cholesterol levels and reduce the risk of cardiovascular disease by inhibiting an enzyme involved in cholesterol synthesis.

"Triglycerides" is a type of fat molecule that is used for energy storage in the body, but high levels of triglycerides in the blood can increase the risk of cardiovascular disease.

"U.S. Preventive Services Task Force (USPSTF) recommendations" are based on a rigorous review of existing peer-reviewed evidence and are intended to help primary care clinicians and patients decide together whether a preventive service is right for a patient's needs.

Coverage Criteria

Medical Necessity Criteria for Authorization

The Plan considers rosuvastatin (Cestor) medically necessary when the following criterion is met:

1. The member is unable to use, or has adequately tried and failed atorvastatin at doses of 40-80 mg per day.

If the above prior authorization criteria is met, rosuvastatin will be approved for up to 36 months.

Preventive Services Statins Zero Copay Exception

The Plan is committed to facilitating a $0 member cost share for a brand low/moderate intensity statin or brand/generic high intensity statin when it's determined to be medically necessary for primary prevention of cardiovascular disease in adults aged 40 to 75 years. Please note that this coverage does not extend to individuals with a low-density lipoprotein cholesterol (LDL-C) level greater than 190 mg/dL (4.92 mmol/L) or known familial hypercholesterolemia, as the USPSTF recommendation does not apply to these cases. It is also important to note that the initiation or titration to 80 mg of simvastatin is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.

The requested product will be covered at $0 member cost share when the following criteria are met:

1. The member is aged 40 to 75 years, and the statin is needed for primary prevention of cardiovascular disease*; AND*
2. The member has an estimated 10-year risk of a cardiovascular event of 10 percent or greater*; AND*
3. The member has ONE or more cardiovascular risk factors, which may include but are not limited to the following:
    a. Age (men aged 45 years or older; women aged 55 years or older)*; and/or*
    b. Diabetes*; and/or*
    c. Dyslipidemia*; and/or*
    d. Family history of early heart disease (heart disease in father or brother before age 55; heart disease in mother or sister before age 65)*; and/or*
    e. Hypertension*; and/or*
    f. Obesity (Body Mass Index (BMI) of 30 or higher)*; and/or*
    g. Smoking*; AND*
4. The member is not characterized by ONE or more of the following:
    a. Adults with a low-density lipoprotein cholesterol (LDL-C) level greater than 190 mg/dL (4.92 mmol/L)*; and/or*
    b. The member has a known familial hypercholesterolemia*; and/or*
    c. The member has existing atherosclerotic cardiovascular disease (this is considered secondary prevention of cardiovascular disease).

If the above prior authorization criteria are met, the requested product will be authorized for up to 36 months at a $0 member cost share.

Appendix

Reduction in Risk of Cardiovascular Events

General Recommendation

1. The American Heart Association (AHA)/American College of Cardiology (ACC) cholesterol management guideline recommends statins as first-line therapy for reducing the risk of atherosclerotic cardiovascular disease (ASCVD) in adults.
2. Evidence shows that statins substantially reduce low-density lipoprotein (LDL)-cholesterol concentrations and associated ASCVD risk.
3. The maximum tolerated statin intensity should be used to achieve optimum ASCVD benefits.
4. The ACC/AHA guideline recommends statin therapy for primary prevention of CVD in the following populations:
    a. Those 40-75 years with an LDL-cholesterol ≥70 - <190 mg/dl without Diabetes Mellitus and 10-year ASCVD risk of 5- <7.5%: consider a risk discussion" "if risk enhancers present then risk discussion regarding moderate-intensity statin therapy." (Class IIb)
    b. Those 40-75 years with an LDL-cholesterol ≥70 - <190 mg/dl without Diabetes Mellitus and 10-year ASCVD risk of ≥7.5% - <20%: consider a risk discussion: "If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LCL-C by 30-49%" (Class I)
    c. Those 40-75 years with an LDL-cholesterol ≥70 - <190 mg/dl without Diabetes Mellitus and 10-year ASCVD risk of ≥20%: consider a risk discussion: "Initiate statin to reduce LDL-C by ≥50%." (Class I)
    d. In those with LDL-C ≥190 mg/dl (≥4.9 mmol/L): "No risk assessment; High intensity statin." (Class I)
    e. In those with Diabetes mellitus and age 40-75 years: "Moderate intensity statin." (Class I)
    f. In those with Diabetes Mellitus and age 40-75 years: "Risk assessment to consider high intensity statin." (Class IIa)
    g. In those 20-39 years: "To encourage lifestyle to reduce ASCV risk; consider statin if family history [of] premature ASCVD and LDL-C ≥160 mg/dl (≥4.1 mmol/L)."
5. ACA/AHA guidelines define "risk enhancers" as the following:
    a. Family history of premature ASCVD
    b. Persistent elevated LDL-C ≥160 mg/dl (≥4.1 mmol/L)
    c. Chronic kidney disease
    d. Metabolic syndrome
    e. Conditions specific to women (e.g., preeclampsia, premature menopause)
    f. Inflammatory disease (especially rheumatoid arthritis, psoriasis, HIV)
    g. Ethnicity (e.g., South Asian ancestry)
    h. Lipid biomarkers:
        i. Persistently elevated triglycerides (≥175 mg/dl, (≥2.0 mmol/L))
    i. In selected individuals if measured:
        i. High-sensitivity C-reactive protein (hs-CRP) ≤2.0 mg/L

ii. Lp(a) levels > 50 mg/dl or >125 nmol/L
iii. apoB ≥130 mg/dl
iv. Ankle-brachial index (ABI) <0.9

Primary Prevention with Rosuvastatin

1. Rosuvastatin is used with diet and lifestyle modifications in patients without clinical evidence of coronary heart disease but with an increased risk of cardiovascular disease.
2. High-risk patients are identified by age, high-sensitivity C-reactive protein concentrations, and additional cardiovascular disease risk factors.
3. A shared decision-making approach between the patient and clinician is recommended when considering statin therapy for primary prevention.
4. Rosuvastatin therapy in high-risk patients has been shown to reduce the risk of major cardiovascular events.

Reducing Progression of Coronary Atherosclerosis

1. Rosuvastatin is used to slow the progression of atherosclerosis as part of a treatment strategy to lower total and LDL-cholesterol concentrations to target levels.
2. Studies have shown that rosuvastatin slows the progression of atherosclerosis in patients with elevated LDL-cholesterol concentrations and subclinical atherosclerosis.

Secondary Prevention with Rosuvastatin

1. Rosuvastatin is used for secondary prevention in patients with established ASCVD.
2. The 2018 AHA/ACC cholesterol management guideline emphasizes lifestyle modification as the foundation of ASCVD risk reduction.
3. Patients with clinical ASCVD should also be treated with a statin in conjunction with lifestyle modification to reduce LDL-cholesterol concentrations.
4. AHA/ACC recommends the use of high-intensity statin therapy.

Intensity of Statin Therapy

1. The appropriate intensity of a statin should be used to reduce the risk of ASCVD following a risk discussion between the individual and their care provider
2. Rosuvastatin at different doses is considered to be high-intensity or moderate-intensity statin based on LDL-cholesterol reduction (see Table 1).

Combination Antilipemic Therapy

1. Combination therapy with a non-statin drug may be useful in high-risk patients who require further reduction in LDL-cholesterol concentrations.
2. If combination therapy is necessary, selection of the non-statin drug should be based on the risk and benefit profile and patient preferences.

Patients with Chronic Kidney Disease (CKD)

1. Some studies on rosuvastatin's benefits in patients with chronic kidney disease showed that therapy did not substantially reduce the primary composite endpoint of cardiovascular death, nonfatal MI, or nonfatal stroke compared with placebo.
2. Chronic kidney disease is considered a "risk enhancer" per the 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease.
3. A secondary analysis of the JUPITER (Justification for the Use of statins in Prevention-an Intervention Trial Evaluating Rosuvastatin), which recruited n=3,267 participants with reduced kidney function, identified that those with moderate CKD experienced a 45% reduction in composite primary outcome of myocardial infarction, stroke, hospital stay for unstable angina, arterial revascularization or confirmed cardiovascular death (HR 0.55, 95% CI: 0.38-0.82, p=0.002). They also realized a 44% reduction in all-cause mortality (HR 0.56, 95% CI:0.37-0.85, p=0.005). These results were similar for those with preserved kidney function in the JUPTER study.

References

1. American College of Endocrinology Guidelines for the Management of Dyslipidemia and Prevention of Cardiovascular Disease- 2017. Endocrine Practice - 2017 April; 23(Supplement 2): S97-S115.
2. Arnett DK et al: 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. J Am Coll Cardiol. 74(10):e177-232, 2019
3. Asians. Int J Endocrinol Metab. 2017 Apr; 15(2): e43319. Published online 2017 Apr 22. doi: 10.5812/ijem.43319.
4. AstraZeneca. Crestor® (rosuvastatin calcium) tablets prescribing information. Wilmington, DE; 2020 Sept.
5. Chou R, Cantor A, Dana T, et al. Statin use for the primary prevention of cardiovascular disease in adults: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. Published August 23, 2022. doi:10.1001/jama.2022.12138
6. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines J Am Coll Cardiol. 2013 Nov; S0735-1097(13)06029-4.
7. Grundy SM, Stone NJ, Bailey AL et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019; 139:e1082-e1143
8. Hla D, Blumenthal RS, Martin SS, et al. Assessing Severity of Statin Side Effects: Fact Versus Fiction. American College of Cardiology. Apr 09, 2018.
9. Kostapanos MS, Elisaf MS. JUPITER and satellites: clinical implication of the JUPITER study and its secondary analyses. World J Cardiol. 2011 Jul 26; 3(7):207-14. doi:10.4330/wjc.v3.i7.207.
10. Kostapanos MS, Liberopoulos EN, Elisaf MS. Statin pleiotropy against renal injury. J Cardiometab Syndr. 2009;4:E4–E9. doi: 10.1111/j.1559-4572.2008.00052.x.
11. Mach F et al: 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 41(1):111-88, 2020
12. O'Malley PG et al: Management of dyslipidemia for cardiovascular disease risk reduction: synopsis of the 2020 updated U.S. Department of Veterans Affairs and U.S. Department of Defense clinical practice guideline. Ann Intern Med. 173(10):822-9, 2020.

13. Ridker PM, MacFadyen J, Cressman M, Glynn RJ. Efficacy of rosuvastatin among men and women with moderate chronic kidney disease and elevated high-sensitivity C-reactive protein: a secondary analysis from the JUPITER (Justification for the Use of Statins in Prevention-an Intervention Trial Evaluating Rosuvastatin) trial. J Am Coll Cardiol. 2010 Mar 23;55(12):1266-1273. doi: 10.1016/j.jacc.2010.01.020. Epub 2010 Mar 4.
14. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2013 Nov 12.
15. US Preventive Services Task Force. Collaboration and shared decision-making between patients and clinicians in preventive health care decisions and US Preventive Services Task Force recommendations. JAMA. 2022;327(12):1171-1176. doi:10.1001/jama.2022.3267
16. US Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. JAMA. 2016;316(19):1997-2007. doi:10.1001/jama.2016.15450
17. US Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: preventive medication. August 23, 2022. https://uspreventiveservicestaskforce.org/uspstf/recommendation/statin-use-in-adults-preventive-medication. (Accessed July 13, 2023).
18. Virani SS, Newby LK, Arnold SV, Bittner V, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. Circulation. 2023;148:e9–e119. doi: 10.1161/CIR.0000000000001168.

Clinical Guideline Revision / History Information

Original Date: 08/06/2020

Reviewed/Revised: 06/24/2021, 12/01/2021, 06/23/2022, 3/23/2023, 07/31/2023, 06/27/2024, 10/01/2025