

Chronic Coronary Disease Care Guide

July 2024



Information contained in the Care Guide is not a substitute for a health care professional's clinical judgment. Evaluation and treatment should be tailored to the individual patient and the clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to "Disclaimer Regarding Care Guides" for further clarification.

<https://cchcs.ca.gov/clinical-resources/>

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GOALS

- ✓ Identify and treat patients with chronic coronary disease (CCD) to decrease the risk of major adverse cardiovascular events (MACE)
- ✓ Counsel all patients on healthy lifestyle choices.
- ✓ Prescribe statin therapy for patients with CCD.
- ✓ Prescribe antiplatelet therapy as indicated for patients with CCD.

ALERTS

- Consider potential drug-drug interactions (DDI) and adverse effects when prescribing statin therapy.
- Shorter durations of dual antiplatelet therapy (DAPT) are safe and effective in many circumstances.
- Long-term beta blocker use may not be indicated for all patients with CCD.

INTRODUCTION

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of morbidity and mortality globally and in the United States. This care guide aims to provide recommendations for diagnostic evaluation, symptom relief, and reduction of future ASCVD events and heart failure (HF) in patients with CCD.

CCD is a heterogenous group of conditions that include obstructive and nonobstructive coronary artery disease (CAD) with or without previous myocardial infarction (MI) or revascularization. CCD also includes ischemic heart disease that was diagnosed with noninvasive testing as well as chronic angina syndromes. This care guide will apply to the following categories of patients in the outpatient setting:

- Patients discharged after admission for an acute coronary syndrome (ACS) event.
- Patients discharged after coronary revascularization procedure or surgery.
- Patients discharged after stabilization of all acute cardiovascular issues.
- Patients with left ventricular systolic dysfunction with known or suspected CAD
- Patients with an established cardiomyopathy deemed to be of ischemic origin.
- Patients with stable angina symptoms or other ischemic equivalents, such as dyspnea or arm pain with exertion, that is medically managed with or without positive results of an imaging test.
- Patients with angina symptoms and evidence of coronary vasospasm or microvascular angina.
- Patients diagnosed with coronary disease based solely on the results of noninvasive imaging, such as a stress test or coronary computed tomography angiography, and the treating physician concludes that the patient has coronary disease.

EVALUATION

After the diagnosis of CCD has been established by one or more of the clinical scenarios as listed above and the patient is started on guideline-directed management and therapy (GDMT), it is important to evaluate for a change in symptoms or a change in functional capacity. Patients with CCD should be followed at least annually or more frequently as clinically indicated for any worsening or new symptoms or functional capacity. Assess for clinical heart failure, reassess left ventricular ejection fraction (LVEF), or both. Furthermore, during clinical follow-up, assess for adherence to and adequacy of lifestyle and medical interventions, as well as monitor for complications of CCD and its treatments.

HISTORY

Conduct a history including both personal and family, paying particular attention to the following:

- **Symptoms:** Recognizing a change in symptoms or a decrease in functional capacity may indicate that further cardiovascular diagnostic evaluation is needed.
 - Assess each patient for new, persistent, or worsening chest pain. Refer to the [Acute Chest Pain Care Guide](#) for patients who present with acute changes in symptoms.
 - Assess for heart failure symptoms, such as dyspnea on exertion or bilateral lower extremity edema. Refer to the [Heart Failure Care Guide](#) for more details.
 - While classic symptoms like chest pain, shortness of breath, and fatigue are common, CCD presentation can vary. Atypical presentations, particularly in women and patients with diabetes (DM), may include upper back pain, nausea, and jaw discomfort.

HEALTH EQUITY ALERT

Ischemic heart disease represents the leading cause of death in women, who experience relatively worse outcomes compared to men. This is due to sex-specific differences from biological factors, as well as gender-specific differences from broader social, environmental, and community factors. There exists a knowledge gap regarding these differences in presentation, risk factors, pathophysiology, and response to treatment, which contributes to cardiovascular outcome disparities. In addition to traditional risk factors, sex-specific risk factors include autoimmune disease, pregnancy, menopause, and depression.

Evaluation, cont'd

- **Personal:** Smoking, diet, regular physical activity, impaired glucose tolerance, metabolic syndrome, DM, obesity, HTN, dyslipidemia, cardiovascular or cerebrovascular events, CKD, Non-Alcoholic Fatty Liver Disease (NAFLD)/ Non-Alcoholic Steatohepatitis (NASH), autoimmune/inflammatory disease (e.g., lupus, rheumatoid arthritis, psoriasis), hepatitis C, history of pancreatitis, medications that alter lipids (e.g., steroids, retinoids, HIV antiretroviral therapy (ART), post transplantation antirejection medications).
 - Evidence supports the association between ASCVD and mental health issues. Depression is an independent risk factor as well as more prevalent in patients with ASCVD. Also, schizophrenia, bipolar disorder, anxiety, and post-traumatic stress disorder have been found to increase the risk for ASCVD. Care coordination and collaboration with mental health is very important.
 - Evidence supports the association between infections in the mouth, such as periodontal disease, and ASCVD. Periodontal organisms have been identified in atheromas and may cause injury directly to epithelium and partially activate the inflammatory response seen with atherosclerosis. Referral for a comprehensive dental exam should occur as part of newly diagnosed ASCVD and routine dental checkups are recommended.
- **Family:** Cardiovascular disease (CVD), HTN, dyslipidemia
- Identify **medical conditions** that increase the patient's risk of future ASCVD events:

• Prediabetes/impaired glucose tolerance	• Diabetes mellitus	• Autoimmune diseases
• Metabolic syndrome	• Hypertension	• Hepatitis C
• Overweight/obesity	• NAFLD/NASH	• HIV
• Medications (e.g., steroids, retinoids, ART, antirejection medications, etc.)	• Prior cardiovascular events	• Prior cerebrovascular events
- **Social determinants of health:** Traditional risk factors, such as age, family history, and the medical conditions listed above, are often assessed for patients with CCD. However, also consider factors like socioeconomic status, access to healthy food prior to incarceration, access to health care prior to incarceration, and social support, as these can significantly impact cardiovascular health.

PHYSICAL EXAM

Complete comprehensive physical exam, paying particular attention to the following:

- Height, weight, BMI, waist circumference, blood pressure, jugular venous pressure (JVP), cardiac evaluation, peripheral and carotid pulses, vascular bruits
- Consider screening for mental health, such as depression and anxiety

LABS

Order the following initial labs:

- Complete blood count (CBC)
- Comprehensive metabolic panel (CMP)
- Lipid Panel, which includes total cholesterol, HDL-C, triglycerides (TG), LDL-C, and calculated non-high-density lipoprotein cholesterol (non-HDL-C)
- Thyroid-stimulating hormone (TSH)
- Urine toxicology (utox), as clinically indicated.
- Hemoglobin A1c (A1c) if diabetes status is unknown.

DIAGNOSTIC STUDIES

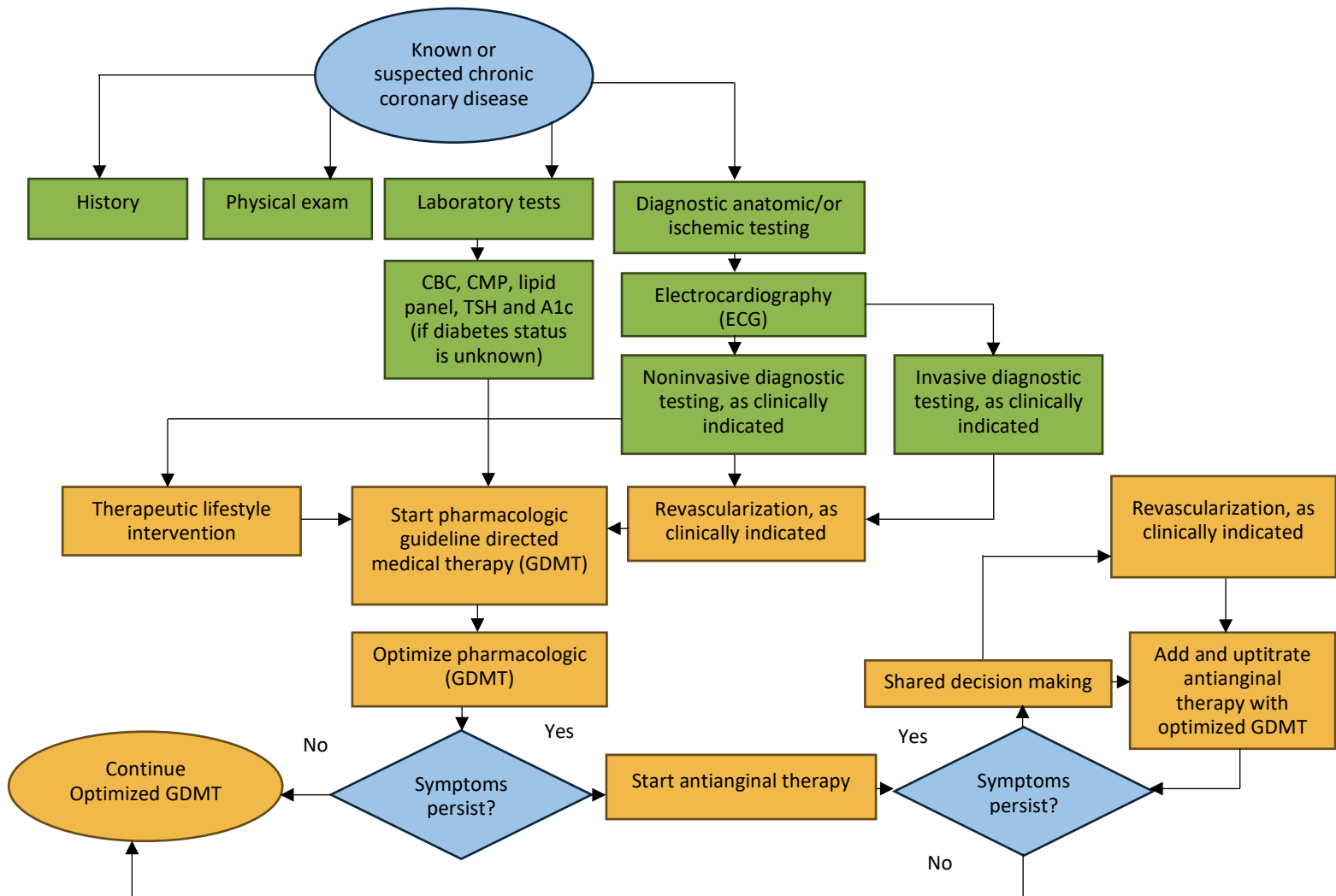
The selection of diagnostic studies depends on a patient's presentation and risk profile.

- Baseline resting 12-lead electrocardiogram (ECG) resting.
- Consider noninvasive or invasive diagnostic testing, such as an exercise or dobutamine stress echocardiogram.
- Consider a transthoracic echocardiogram (TTE) as clinically indicated.
- For patients with CCD comanaged by cardiology, coronary angiography may be recommended as clinically indicated.

DOCUMENTATION

Patients with chronic coronary disease may be documented in the electronic health record system (EHRS) as "chronic ischemic heart disease" (ICD-10 I25) or one of the subcategories of "chronic ischemic heart disease".

EVALUATION ALGORITHM



TREATMENT

THERAPEUTIC LIFESTYLE

Lifestyle management is the cornerstone of CCD treatment, which aims to reduce major adverse cardiovascular events (MACE) and improve overall health. Managing patients with CCD begins with implementation of lifestyle changes including nutrition therapy, physical activity, smoking cessation, and assessment of sleep issues, as well as managing stress, monitoring mood symptoms, abstinence from drugs, and engagement in substance use disorder services and mental health services, if clinically indicated.

REVASCULARIZATION PROCEDURES

Coronary angiography may demonstrate significant atherosclerosis, and revascularization may be recommended by cardiology. Depending on the coronary anatomy, valvular anatomy, comorbidities, and other patient factors, cardiology may recommend either percutaneous coronary intervention (PCI) usually with stent implantation or coronary artery bypass graft (CABG). These procedures are performed at a higher level of care (HLOC) and may necessitate Co management with cardiothoracic surgery.

ANTIPLATELET THERAPY AND ORAL ANTICOAGULANTS

The use of aspirin for secondary ASCVD prevention is well established for reduction of MACE. The following section will guide medication management for patients with CCD who require another antiplatelet and/or oral anticoagulation. Keep in mind that drug-eluting stent (DES) is more commonly used in preference to bare metal stent (BMS) in patients undergoing PCI to prevent restenosis, MI, or acute stent thrombosis. Since there is a limited role for the use of BMS, this section focuses on antiplatelet therapy for patients with DES.

Treatment, cont'd

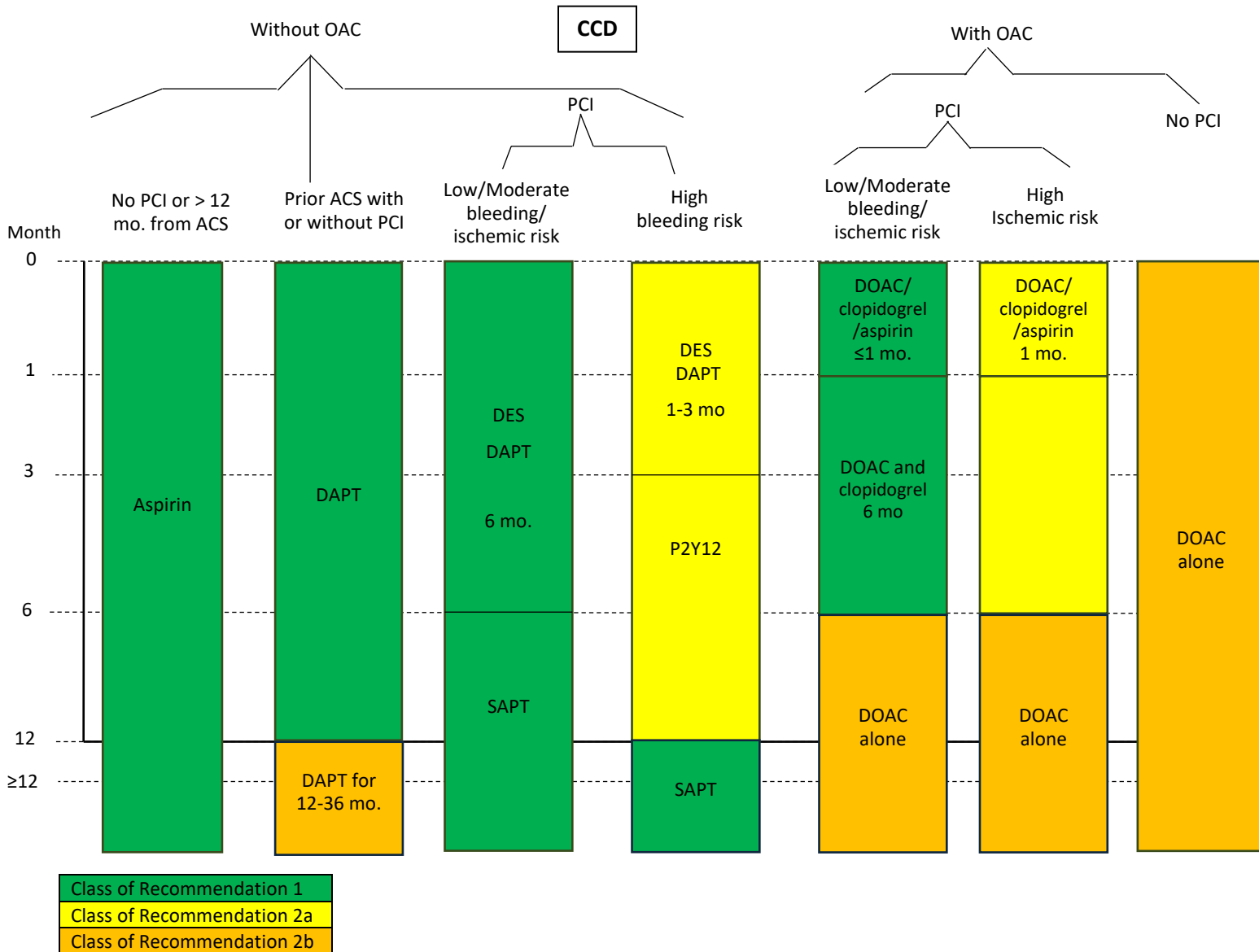
Antiplatelet Therapy without Oral Anticoagulation

Clinical Indication	Antiplatelet Strategies
Patient with CCD without indication for therapeutic oral anticoagulation.	Prescribe low dose aspirin 81 mg daily. In patients without PCI-related indication, recent ACS or MI, or CABG-related indication, the addition of clopidogrel to aspirin is not useful to reduce MACE.
Patient with CCD without indication for therapeutic oral anticoagulation and without indication for dual antiplatelet therapy (DAPT) with high risk of recurrent ischemic events, but low-to-moderate bleeding risk.	Consider adding low-dose rivaroxaban 2.5 mg twice day to low-dose aspirin 81mg daily.
Patient with CCD who was treated with percutaneous coronary intervention (PCI) with low-to-moderate bleeding risk.	DAPT consisting of aspirin and clopidogrel is recommended for the first 6 months following PCI, followed by single antiplatelet therapy (SAPT), usually aspirin. Specialty referral to cardiology is advised, especially if alternative antiplatelets are recommended.
Patient with CCD who was treated with PCI with high bleeding risk.	DAPT can be prescribed for 1-3 months, followed by clopidogrel or another P2Y12 inhibitor monotherapy for at least 12 months. Specialty referral to cardiology is advised, especially if alternative antiplatelets are recommended.
Patient with CCD who had a previous MI with low bleeding risk.	Extended DAPT, which is defined as DAPT longer than 12 months and up to 3 years. After completion of extended DAPT, prescribe SAPT, usually aspirin. Specialty referral to cardiology is advised. AND If patient has no history of stroke, transient ischemic attack (TIA), or intracranial hemorrhage (ICH), vorapaxar may be added to aspirin. Specialty referral to cardiology is advised.
Patient with CCD who was treated with coronary artery bypass graft (CABG).	DAPT for 6-12 months after CABG. Specialty referral to cardiology is advised.
Patients with CCD and previous stroke, TIA, or ICH.	Avoid prasugrel. AND Avoid vorapaxar
All patients with CCD.	Avoid chronic nonsteroidal anti-inflammatory drugs (NSAIDs).
All patient on DAPT.	Prescribe proton pump inhibitor (PPI), such as pantoprazole, to reduce gastrointestinal bleeding risk. Avoid prescribing omeprazole with clopidogrel.

Antiplatelet Therapy with Therapeutic Direct Oral Anticoagulation (DOAC)

Clinical Indication	Antiplatelet with Oral Anticoagulation Strategies
Patient with CCD with indication for therapeutic oral anticoagulation.	Direct oral anticoagulation (DOAC) monotherapy may be considered if there is no acute indication for concomitant antiplatelet therapy.
Patient with CCD who was treated with elective PCI with low to moderate bleeding risk.	DAPT for 1-4 weeks, followed by clopidogrel for 6 months, in addition to therapeutic anticoagulation therapy. OR For patients with low thrombotic risk, consider discontinuing SAPT 1 year after PCI, and continue with DOAC alone. Specialty referral to cardiology is advised, especially if alternative antiplatelets are recommended.
Patient with CCD who was treated with PCI with high thrombotic risk and low bleeding risk.	DAPT for 1 month, followed by clopidogrel for 6 months, in addition to therapeutic anticoagulation therapy. Specialty referral to cardiology is advised, especially if alternative antiplatelets are recommended.

ANTIPLATELET THERAPY ALGORITHM



ACS indicated acute coronary syndrome; ASA, aspirin; CCD, chronic coronary disease; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; DOAC, direct oral anticoagulant; MI, myocardial; OAC, oral anticoagulants; PCI, percutaneous coronary intervention; SAPT, single antiplatelet therapy. This figure does not encompass all recommendations for antiplatelet therapy, so please reference the preceding tables to identify the most applicable recommendations by clinical scenario.

REDUCING RISK OF CARDIOVASCULAR EVENTS

In patients with CCD, angiotensin-converting enzyme inhibitors (ACEi) or angiotensin-receptor blockers (ARB) can reduce cardiovascular event, particularly in high-risk patients with CCD, who have LVEF ≤40%, comorbid diabetes, comorbid hypertension, and/or comorbid CKD.

Beta blockers are indicated in patients with CCD who have a previous MI, angina, history of or current LVEF ≤50%, arrhythmias, or uncontrolled or resistant hypertension despite other maximally tolerated antihypertensive medications. In the absence of these clinical indications, the use of beta blocker therapy is not beneficial in reducing MACE.

The addition of colchicine 0.5 mg daily for secondary prevention may be considered to reduce recurrent ASCVD events. Colchicine is contraindicated with concurrent use of strong CYP3A4 inhibitors or P-gp inhibitors, so drug-drug interactions should be checked before initiating colchicine. Colchicine is also contraindicated in patients with pre-existing blood dyscrasias, chronic kidney disease, and severe hepatic impairment. Given these limitations and colchicine’s narrow therapeutic index, there is a need for a highly individualized approach for patients who remain at very high risk despite maximally tolerated GDMT. Specialty referral to cardiology is advised if colchicine is considered.

Treatment cont'd

LIPID MANAGEMENT

Statins (HMG-CoA reductase inhibitors) should be used as first-line cholesterol-lowering therapy, unless contraindicated. However, considerable residual risk often persists even after aggressive statin monotherapy for secondary prevention among patients with CCD. In patients with CCD, high-intensity statin therapy is recommended with the aim of achieving a $\geq 50\%$ reduction in LDL-C (low density lipoprotein cholesterol) levels to reduce the risk of major adverse cardiovascular events (MACE).

In patients with CCD in whom high-intensity statin therapy is contraindicated or not tolerated, moderate-intensity statin therapy is recommended with the aim of achieving 30% to 49% reduction in LDL-C levels to reduce the risk of MACE.

	High-intensity	Moderate-intensity	Low-intensity
LDL-C Lowering *	$\geq 50\%$	30-49%	$< 30\%$
First-line Statins	Atorvastatin 40 – 80 mg Rosuvastatin 20 – 40 mg	Atorvastatin 10 – 20 mg Rosuvastatin 5 – 10 mg Pravastatin 40 – 80 mg	Pravastatin 10 – 20 mg
Other Statins		Simvastatin 20 – 40 mg Lovastatin 40 – 80 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 2 – 4 mg	Simvastatin 10 mg Lovastatin 20 mg Fluvastatin 20 – 40 mg Pitavastatin 1 mg

* Percentage reductions are estimates from data across large populations. Individual responses to therapy varied in randomized controlled trials.

Statin Contraindications: For majority of patients, statins are safe, however:

- Patients with active hepatic disease or unexplained persistent elevations in aminotransferase levels.
- Pregnancy and breastfeeding because of effects on the cholesterol pathway.

Statin-Associated Side Effects: For most patients, statins are safe and well-tolerated. However, statin-associated side effects (SASE) may occur in a significant subset of statin-treated patients, which are discussed in detail on pages 33-34.

- **Statin-associated muscle symptoms (SAMS):** Most frequent SASE
- **New onset DM:** More frequent if associated with BMI ≥ 30 , FBS ≥ 100 mg/dL, or A1c $\geq 6\%$.
- **Hepatic dysfunction:** Transaminase elevation 3x ULN – Infrequent.

Ezetimibe is the most used non-statin agent. It lowers LDL-C levels by 18% to 20% and has a low incidence of side effects.

- Recommended in combination with statin therapy in patients who do not meet LDL-C goals (threshold levels) with dietary modification and maximally tolerated statin therapy.
- Ezetimibe may also be used in situations of statin-associated muscle symptoms. Combination therapy with statins is relatively safe.
- Furthermore, patients with CCD who are considered very high risk (see table below) with LDL-C level ≥ 70 mg/dL despite maximally tolerated statin therapy, **ezetimibe** can be considered to further reduce the risk of MACE.

PCSK9 monoclonal antibodies (PCSK9 mAb) are powerful LDL-lowering drugs. PCSK9 mAbs (previously referred to as PCSK9 inhibitors or PCSK9i) bind to PCSK9 proteins and increase the number of LDL receptors available to clear circulating LDL-C. There are 2 FDA approved PCSK9 mAbs: alirocumab (Praluent®) and evolocumab (Repatha®). They generally are well-tolerated, but long-term safety reduction requires continued research. PCSK9 mAbs, when used alone or in combination with other lipid-lowering therapy, are administered subcutaneously every 2-4 weeks and are non-formulary.

If LDL-C level remains ≥ 70 mg/dL or non-high-density lipoprotein cholesterol (non-HDL-C) level ≥ 100 mg/dL despite maximally tolerated statin and **ezetimibe**, a PCSK9 monoclonal antibody (PCSK9 mAb) can be beneficial to further reduce the risk of MACE.

Treatment cont'd

Adenosine-triphosphate citrate lyase (ACL) inhibitors are a newer class of LDL-lowering drugs. The FDA approved bempedoic acid (Nexleto[®]) and bempedoic acid with ezetimibe (Nexlizet[®]). Bempedoic acid is administered orally and activated by an enzyme present in liver cells, but not muscle cells. Therefore, bempedoic acid has been considered a possible advantage in patients with statin-associated muscle symptoms. This medication should be prescribed and managed by a specialist.

Inclisiran* (Leqvio[®]) is an **antilipemic small interfering ribonucleic acid (siRNA)** targeting PCSK9, one of the newest LDL-lowering drugs. It is administered by subcutaneous injection every 6 months and is non-formulary. This medication should be prescribed and managed by a specialist.

If lipid lowering therapy is still insufficient to achieve LDL <70 mg/dL, then it may be reasonable to add bempedoic acid or inclisiran (in place of PCSK9 mAb).

Very High-Risk* ASCVD Group	
Major ASCVD Events	High-Risk Conditions
Recent ACS within the past 12 months.	Age ≥ 65 y
History of MI other than recent ACS.	Heterozygous FH
History of ischemic stroke.	History of prior CABG or PCI outside of major ASCVD events.
Symptomatic PAD (history of claudication with ABI < 0.85 or previous revascularization or amputation).	DM
	HTN
	CKD (eGFR 15-59 mL/min)
	Current smoking.
	Persistently elevated LDL-C ≥ 100 mg/dL despite maximally tolerated statin therapy and ezetimibe.
	History of CHF.

* Very high-risk: a history of multiple major ASCVD events or 1 major ASCVD event with multiple high-risk conditions.

CHF = congestive heart failure

CKD = chronic kidney disease

eGFR = estimated glomerular filtration rate

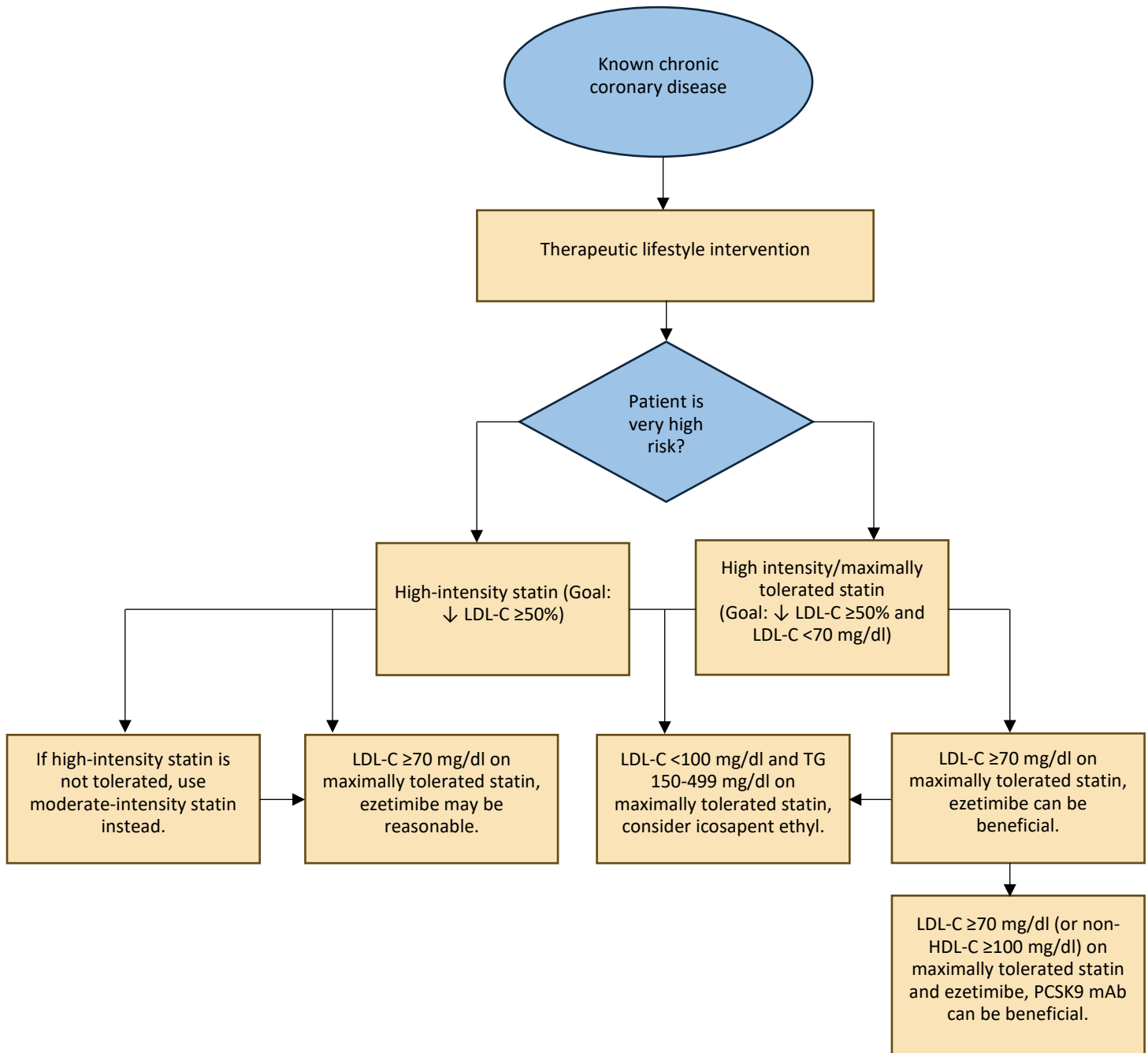
MI = myocardial infarction

In patients with CCD on maximally tolerated statin therapy with LDL-C <100 mg/dL and persistent fasting triglyceride (TG) level of 150 to 499 mg/dL, **icosapent ethyl** may be considered to further reduce the risk of MACE and cardiovascular death. It can be used with maximally tolerated statin therapy to lower the risk of cardiovascular events (myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization) in adults with persistent hypertriglyceridemia who have clinical ASCVD or who have diabetes mellitus and two or more other cardiovascular risk factors for heart disease. Additionally, Vascepa[™], which contains only eicosapentaenoic acid (EPA), does not increase LDL-C levels.

The addition of **niacin**, **fenofibrate**, or dietary supplements containing omega-3 fatty acids to statin therapy are not beneficial in reducing cardiovascular risk.

For more information, please refer to the [Dyslipidemia Care Guide](#). See the medication tables below with CCHCS formulary agents for statin and non-statin therapy (See pages 32-35).

LIPID-LOWERING THERAPY ALGORITHM



BLOOD PRESSURE MANAGEMENT

In patients with CCD and comorbid hypertension, the blood pressure target is <130/<80 mmHg to reduce cardiovascular events and all-cause death. In addition to nonpharmacologic strategies that emphasize therapeutic lifestyle intervention, GDMT angiotensin-converting enzyme inhibitors (ACEi) or angiotensin-receptor blockers (ARB) are recommended as first-line therapy to reduce cardiovascular events.

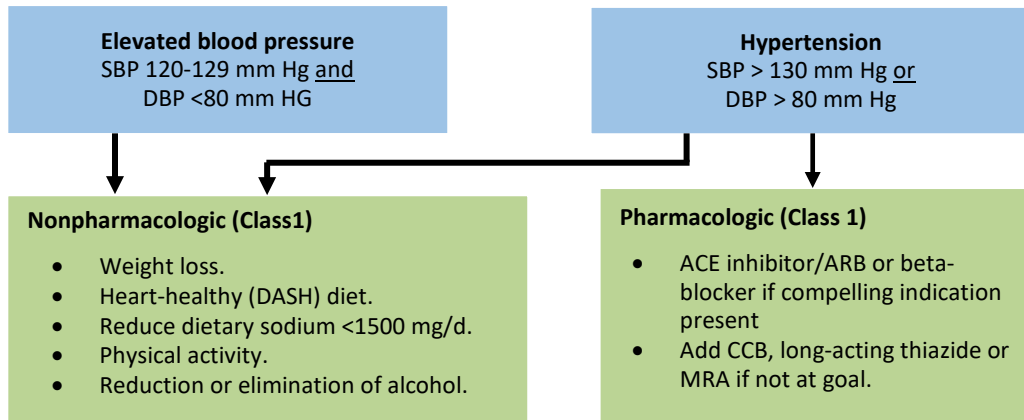
Beta-blockers can be first-line therapy, if there is another clinical indication for use, such as recent MI, angina, LVEF ≤50%, or arrhythmias.

Additional antihypertensive medications, such as dihydropyridine calcium channel blockers, long-acting thiazide diuretics, and/or mineralocorticoid receptor antagonists, can be added to reach the blood pressure target of <130/<80 mm Hg.

For more information, please refer to the [Hypertension Care Guide](#)

Treatment cont'd

BLOOD PRESSURE THERAPY ALGORITHM



ANTIANGINAL THERAPY

For patients with CCD that have chronic angina syndromes, they may present with angina or ischemic equivalents, such as dyspnea or arm pain with exertion. However, some patients, particularly women and patients with DM, may present with angina symptoms of upper back pain, nausea, and jaw discomfort. Chronic stable angina varies by age, sex, race, ethnicity, and geographic region. It is important to assess the severity and frequency of angina symptoms as well as functional capacity to guide management. For patients with new, worsening, or more frequent angina symptoms, specialty referral to cardiology is advised. For patients who present with acute chest pain, HLOC may be required. Please refer to the [Acute Chest Pain Care Guide](#) for more information.

If a patient remains symptomatic after optimizing GDMT, the addition of beta blocker therapy or calcium channel blocker (CCB) therapy should be considered for angina symptom control. Beta blockers have been considered the first antianginal to use in patients with symptomatic CCD. Alternatively, a long-acting dihydropyridine CCB, such as amlodipine, extended release (ER) nifedipine, or nicardipine, may be considered first-line antianginal therapy if there are contraindications or unacceptable adverse effects with beta blocker therapy. Non-dihydropyridine CCBs, such as verapamil and diltiazem, should be avoided in patients with LVEF $\leq 50\%$ because these medications can further depress LV function. Non-dihydropyridine CCBs should also be used with caution in combination with beta blockers because of bradycardia risk and LV dysfunction.

The addition of a long-acting nitrate to a beta blocker or a CCB improves exercise tolerance, reduces angina frequency, and reduces short-acting nitrate use. Sublingual nitroglycerine or nitroglycerine spray is recommended for immediate short-term relief of angina or equivalent symptoms. In randomized studies, nitroglycerine spray compared with sublingual formulation is more effective and efficient at relieving angina, but with less headache.

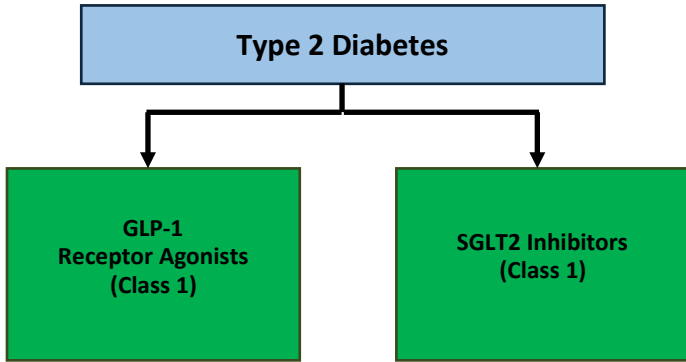
In patients who remain symptomatic despite treatment with beta blockers, CCB, or long-acting nitrate therapies, ranolazine is recommended. Specialty referral to cardiology is advised, if ranolazine is considered to comanage refractory angina.

COMORBID DIABETES

In patients with CCD and comorbid type 2 diabetes, use of either a sodium-glucose cotransporter-2 inhibitor (SGLT2i) or a glucagon-like peptide-1 receptor agonist (GLP-1 RA) with proven cardiovascular benefit (see table below) is recommended to reduce the risk of MACE. The cardiovascular benefits of SGLT2i and GLP-1 RA are not contingent upon hemoglobin A1c lowering. Therefore, initiation can be considered in people with CCD and comorbid type 2 diabetes irrespective of the current hemoglobin A1c.

Treatment cont'd

COMORBID DIABETES TREATMENT ALGORITHM



COMORBID HEART FAILURE

In patients with CCD and comorbid heart failure, use of SGLT2i has proven benefit (see table below), irrespective of diabetes status.

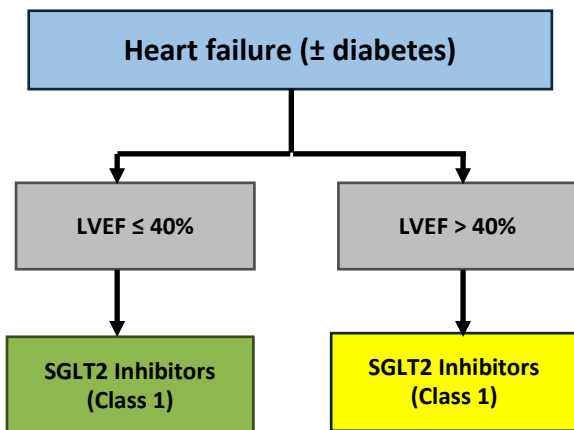
Cardiovascular Benefit		
	Effect on MACE	Heart Failure
SGLT2i	Canagliflozin Empagliflozin	Dapagliflozin (FDA approved HF GDMT) Empagliflozin (FDA approved HF GDMT) Sotagliflozin (FDA approved SGLT2i/SGLT1i) Bexagliflozin Canagliflozin Ertugliflozin
GLP-1 RA	Dulaglutide Liraglutide Semaglutide (SQ)	

Bold = Formulary

FDA = United States Food and Drug Administration

In patients with CCD and LVEF ≤50%, HF GDMT beta blockers are sustained release metoprolol succinate, carvedilol, and bisoprolol. For more information, please refer to the [Heart Failure Care Guide](#).

HEART FAILURE TREATMENT ALGORITHM



Treatment cont'd

TOBACCO USE AND SUBSTANCE USE

In patients with CCD, history of tobacco use should be assessed to identify those who may benefit from patient education, and smoking cessation should be advised for all patients who currently smoke tobacco.

Additionally, use of other substances has adverse cardiovascular effects for patients with CCD.

	Potential Adverse Cardiovascular Effects
Alcohol	<ul style="list-style-type: none"> • Heavy alcohol use and binge drinking associated with increased morbidity and mortality. • May increase serum triglycerides. • Potential drug-drug interactions with cardiovascular therapies.
Cocaine Methamphetamine	<ul style="list-style-type: none"> • Stimulation of the sympathetic nervous system • Platelet activation and aggregation • Increased myocardial oxygen demand. • Can present with cocaine-associated chest pain. • MI risk independent of route of administration
Opioids	<ul style="list-style-type: none"> • Possible association with the risk of MI in chronic use • Potential drug-drug interactions with cardiovascular therapies
Marijuana	<ul style="list-style-type: none"> • Stimulation of the sympathetic nervous system. • Platelet activation. • Endothelial dysfunction. • Carbon monoxide toxicity from smoking and inhalation. • Route of administration may impact toxicity, with edible products associated with fewer acute cardiovascular symptoms.

MENTAL HEALTH

It is estimated that 20% to 40% of patients with CCD have concomitant mental health conditions such as depression and anxiety, and negative psychological states (eg, general distress) are associated with diminished quality of life, atherosclerotic disease progression, and negative effects on cardiovascular risk factors leading to increased MACE. Therefore, targeted discussions and screening for mental health is reasonable for providers to assess and to refer for additional mental health evaluation and management. Furthermore, treatment for mental health conditions with either pharmacologic or nonpharmacologic therapies, or both, is reasonable to improve cardiovascular outcomes. Team-based care has been shown to facilitate behavior change, promotes weight loss, tobacco cessation, and reduces depression.

PATIENT EDUCATION

Patient education empowers patients to make informed decisions about their treatment goals and to manage their condition by understanding:

- Risk factors and how to modify them.
- Importance of healthy lifestyle habits, including diet, exercise, and stress management.
- Medications, their purpose, potential side effects, and proper adherence.
- Diagnostic tests and how these test guide management.
- Procedures, including the benefits, risks, and alternatives to recommended procedures.
- Warning symptoms and signs of worsening angina or potential complications.

Shared decision-making is crucial, and patients should be actively involved in treatment decisions based on their individual needs, preferences, and understanding of the benefits, risks, and alternatives of various treatment options. See [PE-1](#) and [PE-2](#) for details.

Treatment cont'd

Medication Tables

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Cyclooxygenase-1 Inhibitors			
Aspirin (acetylsalicylic acid) Tablet: 81 mg EC, 325 mg, 325 mg EC, 325 mg buffered \$	Usual dose: 81 mg orally once daily. <u>Renal Impairment:</u> Use of low-dose aspirin for primary and secondary prevention of atherosclerotic events in patients with cardiovascular disease is recommended. CrCl less than 10 mL/minute: Avoid analgesic doses. <u>Hepatic Impairment:</u> Avoid with severe hepatic insufficiency.	<u>Adverse reactions:</u> Abdominal pain, dyspepsia, GI ulcer, heartburn, nausea, vomiting, agitation, dizziness, hemorrhage, bronchospasm, tinnitus, angioedema. <u>Drug interactions:</u> <ul style="list-style-type: none"> • Probenecid, cidofovir, ketorolac, abrocitinib, defibrotide, NSAIDs, anticoagulants, antiplatelets, methotrexate, tenofovir, acetazolamide, SSRIs, SNRIs. 	<u>Contraindications:</u> Hypersensitivity to NSAIDs; patients with syndrome of asthma, rhinitis, and nasal polyps, active peptic ulcer disease, severe hepatic impairment. <u>Caution in the following:</u> Patients with platelet and bleeding disorders, dehydration, heavy ethanol use, erosive gastritis.
Platelet Aggregation Inhibitors			
Clopidogrel (Plavix®) Tablet: 75 mg \$	<u>Acute coronary syndrome:</u> 300 mg oral loading dose and then continue at 75 mg once daily (initiating clopidogrel without a loading dose will delay establishment of an antiplatelet effect by several days). <u>Recent MI, recent stroke, or established peripheral arterial disease:</u> 75 mg once daily orally without a loading dose <u>Max dose:</u> 75 mg/day for chronic treatment. <u>Renal Impairment:</u> Experience is limited in patients with severe renal disease or renal failure; use caution. <u>Hepatic Impairment:</u> No dosage adjustment needed.	<u>Adverse reactions:</u> Bleeding, headache, dizziness, rash, abdominal pain, dyspepsia, colitis, hepatitis, thrombotic thrombocytopenic purpura. <u>Drug interactions:</u> <ul style="list-style-type: none"> • Abrocitinib, defibrotide, NSAIDs, anticoagulants, antiplatelets, SSRIs, SNRIs, repaglinide, opioids, rifampin, omeprazole. 	<u>Black Box Warning:</u> Reduced effect on platelet function in patients who are homozygous for nonfunctional alleles of the CYP2C19 gene (i.e., poor metabolizers). Consider another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers. <u>Contraindications:</u> Active bleeding, hypersensitivity to clopidogrel or any component of product. <u>Caution in the following:</u> patients with kidney impairment, CYP2C19 poor metabolizers, history of hypersensitivity or hematologic reaction to other thienopyridines. Premature discontinuation increases risk of cardiovascular events Discontinue 5 days prior to elective surgery that has a major risk of bleeding.

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Platelet Aggregation Inhibitors, cont'd			
Prasugrel (Effient®) Tablet: 5 mg, 10 mg \$	<ul style="list-style-type: none"> Acute coronary syndrome managed by percutaneous coronary intervention: Body weight ≥ 60 kg: 60 mg oral loading dose, then 10 mg orally daily with aspirin (75-325 mg daily). Body weight < 60 kg: 60 mg oral loading dose, then 5 mg orally daily with aspirin (75-325 mg daily). <p>Max dose: 10mg/day for chronic treatment .</p> <p>Geriatric patients: Not recommended in patients age ≥ 75 years except in high-risk situations (history of diabetes mellitus or prior myocardial infarction).</p> <p>Renal Impairment: No dosage adjustment needed; use caution in moderate to severe impairment (patients at higher risk of bleeding).</p> <p>Hepatic Impairment:</p> <ul style="list-style-type: none"> Mild to moderate hepatic impairment (Child-Pugh class A and B): No dosage adjustment necessary Severe hepatic impairment (Child-Pugh class C): Not studied. 	<p><u>Adverse reactions:</u> Bleeding, hypertension, hyperlipidemia, backache, headache, dyspnea, nausea, dizziness, thrombotic thrombocytopenic purpura.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Abrocitinib, defibrotide, NSAIDs, anticoagulants, antiplatelets, SSRIs, SNRIs, opioids. 	<p><u>Black Box Warning:</u> Prasugrel can cause significant and sometimes fatal bleeding. Additional risk factors for bleeding include body weight <60 kg, propensity to bleed, concomitant use of medications that increase the risk of bleeding. Suspect bleeding in any patient who is hypotensive and has recently undergone invasive or surgical procedures.</p> <p><u>Contraindications:</u> active pathological bleed, prior transient ischemic attack or stroke, hypersensitivity to prasugrel or any component of product.</p> <p><u>Caution in the following:</u> hepatic disease, Asian ethnicity, elderly.</p> <ul style="list-style-type: none"> Do not start in patients likely to undergo urgent coronary artery bypass graft surgery. When possible, discontinue at least 7 days prior to any surgery. If possible, manage bleeding without discontinuing prasugrel. Stopping increases the risk of subsequent cardiovascular event.

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Protease-Activated Receptor-1 (PAR-1) Antagonist			
Vorapaxar (Zontivity®) Tablet: 2.08 mg \$\$\$\$\$	<p><u>For the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction or peripheral arterial disease:</u> 2.08 mg orally once daily with aspirin and/or clopidogrel.</p> <p><u>Max dose:</u> 2.08 mg/day.</p> <p><u>Renal Impairment:</u> No dosage adjustment needed.</p> <p><u>Hepatic Impairment:</u></p> <ul style="list-style-type: none"> Mild to moderate hepatic impairment: No dosage adjustment needed. Severe hepatic impairment: Not recommended. 	<p><u>Adverse reactions:</u> Bleeding, anemia, depression, GI bleeding, rash, retinopathy</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Strong CYP3A inhibitors (ketoconazole, itraconazole, posaconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, boceprevir, telaprevir, telithromycin, conivaptan). Strong CYP3A inducers (rifampin, phenytoin, carbamazepine, St. John's Wort). Abrocitinib, defibrotide, NSAIDs, anticoagulants, antiplatelets, SSRIs, SNRIs. 	<p><u>Black Box Warning:</u> Antiplatelet agents increase the risk of bleeding, including intracranial hemorrhage (ICH) and fatal bleeding.</p> <p><u>Contraindications:</u> active pathologic bleeding, history of stroke, transient ischemic attack, or ICH; concomitant use with strong CYP3A inhibitors or inducers.</p> <p><u>Caution in the following:</u> Increased risk of bleeding proportional to underlying bleeding risk, including ICH and fatal bleeding; risk factors include low body weight, older age, and reduced renal or hepatic function.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Direct Factor Xa Inhibitors			
<p>Rivaroxaban (Xarelto®)</p> <p>Tablet: 2.5 mg, 10 mg, 15 mg, 20 mg</p> <p>Administer NA</p> <p>May order as KOP in select cases where the patient would benefit from self-administration</p> <p>\$\$\$\$\$</p>	<p><u>Coronary artery disease:</u> 2.5 mg twice daily; administer in combination with daily low dose aspirin. May consider for use in patients who are at high risk of cardiovascular events and low risk of bleeding if therapeutic anticoagulation is not required for another indication.</p> <p><u>Acute coronary syndrome (after stabilization with initial management) (off label):</u> 2.5 mg twice daily; administer in combination with low dose aspirin plus clopidogrel; continue rivaroxaban for ~1 year. As add-on to clopidogrel (not prasugrel or ticagrelor) and aspirin therapy in patients who are not at high risk of bleeding and do not require chronic therapeutic anticoagulation for another indication; patient preference should also be taken into consideration given the higher risk of bleeding when adding rivaroxaban to dual antiplatelet therapy.</p> <p><u>Renal Impairment:</u> CrCl <15 mL/minute: Avoid use; patients with eGFR <15 mL/minute were excluded from the clinical trial for this indication. Hemodialysis, intermittent (thrice weekly): Not dialyzable: Avoid use. Peritoneal dialysis: Avoid use.</p> <p><u>Hepatic Impairment:</u> Mild impairment (Child-Pugh Class A): No dose adjustment needed, but avoidance of rivaroxaban is recommended for any degree of hepatic disease associated with coagulopathy. Moderate/Severe impairment (Child-Pugh Class B/C): Avoid use.</p>	<p><u>Adverse reactions:</u> Bleeding, muscle cramps, abdominal pain, back pain, dyspepsia, fatigue, pruritus, sinusitis, syncope, insomnia, anxiety, depression, Stevens-Johnson syndrome</p> <ul style="list-style-type: none"> • Increased risk of epidural spinal hematoma with neuroaxial anesthesia or spinal puncture. <p><u>Drug Interactions:</u></p> <ul style="list-style-type: none"> • Avoid with combined P-glycoprotein inhibitor and CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, ritonavir, conivaptan [Vaprisol]) • Increased bleeding risk with anti-platelets, anticoagulants, and thrombolytics. 	<p><u>Black Box Warning:</u> Premature discontinuation increases risk of thrombotic events; epidural or spinal hematomas have occurred in patients treated with rivaroxaban who were receiving neuraxial anesthesia or undergoing spinal puncture.</p> <p><u>Contraindications:</u> Active pathological bleeding, pregnancy or breastfeeding, prosthetic heart valves, moderate-severe hepatic impairment, severe hypersensitivity reaction to rivaroxaban or any component of the formulation.</p> <p><u>Caution in the following:</u> hepatic impairment, renal impairment, older adults.</p> <p>Half-Life: 5-9 hours Monitoring: Renal function prior to initiation of therapy, periodically throughout treatment and more frequently in clinical situations where renal function may decline.</p> <p>Antidote: Andexxa® (recombinant Factor Xa).</p>

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Treatment cont'd

DRUG CLASS/ MEDICATION	DOSING	ADVERSE EFFECTS / INTERACTIONS*	COMMENTS
RENIN-ANGIOTENSIN SYSTEM INHIBITORS			
<ul style="list-style-type: none"> Black Box Warning: Fetal toxicity, pregnancy category D. When pregnancy is detected, discontinue ACEi as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus. Do not use ACEi and ARB together Less antihypertensive effects in Black than non-Black patients 			
ANGIOTENSIN-CONVERTING ENZYME INHIBITORS (ACEi)			
<p>Enalapril (Vasotec®)</p> <p>Tablet: 2.5 mg, 5mg, 10 mg, 20 mg</p> <p>\$</p>	<p><u>Hypertension:</u> Initially, 5 mg orally once daily; 2.5 mg orally once daily if on diuretic, hypovolemia, hyponatremia, moderate-severe CHF</p> <p><u>Acute coronary syndrome (off-label):</u> Initially, 2.5-5 mg orally daily in 1 or 2 divided doses (depending on initial blood pressure)</p> <p><u>Usual dose:</u> 5-40 mg/day in 1-2 divided doses</p> <p><u>Max:</u> 40 mg/day</p> <p><u>Renal impairment:</u> CrCl ≤ 30 ml/min: Initial dose 2.5 mg once daily HD: 2.5 mg after dialysis, on dialysis days.</p>	<p><u>Adverse reactions:</u> Dizziness, hypotension, headache, fatigue, cough, hyperkalemia, photosensitivity, hyperuricemia, Stevens-Johnson syndrome, head/neck/intestinal angioedema, hepatotoxicity, pancreatitis, increased BUN and SCr</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Potassium-sparing diuretics, potassium supplements, hypoglycemic agents, NSAIDS, ARBs, aliskiren, lithium, azathioprine, allopurinol, pregabalin, trimethoprim, sacubitril. 	<p><u>Contraindications:</u> Pregnancy, idiopathic or hereditary angioedema; angioedema related to treatment with ACEi, hypersensitivity to enalapril or an ACEi, concomitant use with aliskiren in patients with diabetes, concomitant use with sacubitril</p> <p><u>Caution in the following:</u> Renal artery stenosis, moderate-severe renal impairment, older patients, Black, volume depletion, hyponatremia, hypotension, HF, aortic stenosis, hypertrophic cardiomyopathy, CAD, aortic stenosis, cerebrovascular disease, collagen vascular disease.</p> <p>Monitor renal function and potassium levels.</p>
<p>Lisinopril (Prinivil®, Zestril®)</p> <p>Tablet: 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg</p> <p>\$</p>	<p><u>Hypertension:</u> Initially, 10 mg orally once daily; 5 mg orally once daily if on diuretic</p> <p><u>Acute coronary syndrome (off-label):</u> Initially, 2.5-10 mg orally once daily (depending on initial blood pressure)</p> <p><u>Usual dose:</u> 10-40 mg once daily</p> <p><u>Max dose:</u> 80 mg/day</p> <p><u>Renal impairment:</u> CrCl 10-30ml/min: Initial dose 5 mg once daily; max 40 mg/day CrCl < 10 ml/min or HD: Initial dose 2.5 mg once daily; max 40 mg/day.</p>	<p><u>Adverse reactions:</u> Dizziness, hypotension, syncope, headache, URI, cough, fatigue, abdominal pain, photosensitivity, hyperuricemia, head/neck/intestinal angioedema, hyperkalemia, pancreatitis, increased BUN and SCr, Stevens-Johnson syndrome</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Potassium-sparing diuretics, potassium supplements, hypoglycemic agents, NSAIDS, ARBs, aliskiren, lithium, azathioprine, allopurinol, pregabalin, trimethoprim, sacubitril. 	<p><u>Contraindications:</u> Pregnancy, idiopathic or hereditary angioedema; angioedema related to treatment with ACEi, hypersensitivity to lisinopril or another ACEi, concomitant use with aliskiren in patients with diabetes, concomitant use with sacubitril.</p> <p><u>Caution in the following:</u> Aortic stenosis, CVA, hypertrophic cardiomyopathy, ischemic heart disease, renal impairment, renal artery stenosis, collagen vascular disease, cerebrovascular disease, older patients, Black patients.</p> <p>Monitor renal function and potassium levels.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS /INTERACTIONS*	COMMENTS
<p>ANGIOTENSIN RECEPTOR BLOCKERS (ARB) ARBs are as effective as ACEi in hypertension with fewer adverse effects but cost significantly more</p>			
<p>Losartan (Cozaar®) Tablet: 25 mg, 50 mg, 100 mg \$</p>	<p><u>Hypertension:</u> Initially, 50 mg orally once daily; 25 mg orally once daily if on diuretic; increase dose weekly if needed.</p> <p><u>Acute coronary syndrome:</u> Initially, 25-50 mg once daily (depending on initial blood pressure).</p> <p><u>Usual dose:</u> 25-100 mg/day in 1-2 divided doses.</p> <p><u>Max dose:</u> 100 mg/day.</p> <p><u>CHF with reduced EF:</u> Initial dose: 25-50mg.</p> <p><u>Renal impairment:</u> no adjustment needed; in volume depleted patient's initial dose: 25mg/day.</p> <p><u>Hepatic impairment:</u> Initial dose: 25 mg/day.</p>	<p><u>Adverse effects:</u> Angioedema, anaphylaxis, severe hypotension (especially CHF patients), headache, nausea, dizziness, pharyngitis, diarrhea, myalgia, insomnia, fatigue, sinusitis, hyperkalemia, hepatitis, acute renal insufficiency and failure, cough, musculoskeletal pain, chest pain, asthenia, URI symptoms, dyspepsia, rhabdomyolysis.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • NSAIDs, lithium, potassium-sparing diuretics, ACEis, aliskiren (contraindicated in patients with diabetes), MAOIs, potassium, supplements, eplerenone, digoxin, rifampin, fluconazole, phenobarbital, clofarabine, lofexidine. 	<p><u>Contraindications:</u> Hypersensitivity to ARBs, pregnancy, concomitant use with aliskiren in patients with diabetes.</p> <p><u>Caution in the following:</u> HF, hepatic impairment, renal artery stenosis, hyperkalemia, hyponatremia, hypovolemia.</p> <p>Monitor renal function and potassium levels.</p> <p>Unlike ACEis, ARBs are much less likely to cause cough.</p> <p>Less antihypertensive effects in Black than non-Black patients.</p> <p>Recommended use criteria: Documented failure or intolerance to ACEi or for patients already controlled on ARB.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS /INTERACTIONS*	COMMENTS
BETA-BLOCKERS			
<ul style="list-style-type: none"> Black Box Warning: Abrupt discontinuation of any beta-adrenergic blocking agent, particularly in patients with preexisting cardiac disease, can cause myocardial ischemia, myocardial infarction, ventricular arrhythmias, or severe hypertension When discontinuing therapy, beta-blockers should be gradually stopped to avoid rebound hypertension (decrease dose by 50% for 3 days and then another 50% for 3 days) 			
CARDIOSELECTIVE BETA-1 ANTAGONISTS			
Atenolol (Tenormin®) Tablet: 25 mg, 50 mg, 100 mg. \$	<p><u>Hypertension:</u> Initially, 25-50 mg orally once daily; if inadequate response after 1 to 2 weeks, may increase to 100 mg once daily.</p> <p><u>Chronic stable angina:</u> Initially, 50mg orally once daily; increase to 100 mg/day if needed after 7 days.</p> <p><u>Usual dose:</u> 25-100 mg once daily.</p> <p><u>Max dose:</u> 100 mg/day (hypertension), 200 mg/day (angina).</p> <p><u>Renal impairment:</u> CrCl 15 to 35 mL/min: Max dose 50 mg/day CrCl < 15 mL/min: Max dose 25 mg/day.</p>	<p><u>Adverse reactions:</u> Bradycardia, Dizziness, fatigue, depression, nightmares, diarrhea, impotence, cold extremities, hypotension, fatigue, HF, chest pain, heart block, edema, nausea, vertigo, abnormal lipids, supraventricular tachycardia, dyspnea.</p> <p><u>Drug interactions:</u> Amiodarone, dronedarone, verapamil, diltiazem, clonidine, NSAIDs, digoxin, reserpine, disopyramide, MAOIs, anti-diabetic agents, α-blockers.</p>	<p><u>Contraindications:</u> Sinus bradycardia, 2nd or 3rd degree heart block, uncompensated HF, cardiogenic shock, overt cardiac failure, hypersensitivity to atenolol or any component of the product.</p> <p><u>Caution in the following:</u> Renal impairment, bronchospastic disease, conduction abnormality, diabetes, HF, myasthenia gravis, pheochromocytoma, PAD, thyroid disease, anesthesia, and major surgery, older adults, avoid abrupt withdrawal, pregnancy, and lactation.</p> <p>May mask symptoms of hypoglycemia.</p>
Metoprolol Succinate (Toprol-XL®) Tablet (ER): 25 mg, 50 mg, 100 mg, 200 mg. \$	<p><u>Hypertension:</u> Initially, 25-100 mg orally daily; may increase dose at weekly intervals.</p> <p><u>Chronic stable angina:</u> Initially, 100 mg orally daily; may increase dose at weekly intervals.</p> <p><u>Usual dose:</u> 50-200 mg once daily.</p> <p><u>Max dose:</u> 400 mg/day.</p> <p><u>Renal impairment:</u> no adjustment needed, give dose after dialysis.</p> <p><u>Hepatic impairment:</u> start with low doses and titrate gradually.</p>	<p><u>Adverse reactions:</u> CHF, bradycardia, Heart block, fatigue, dizziness, diarrhea, rash, pruritus, depression, sleep disturbances, gangrene, dyspnea, bronchospasm, angina.</p> <p><u>Drug interactions:</u> Celecoxib, ceritinib, clonidine, antidiabetic agents, NSAIDs, verapamil, diltiazem, rifampin, lidocaine, venlafaxine, amiodarone, dronedarone, propafenone, quinidine, fluoxetine, paroxetine, reserpine, MAOIs, α-blockers.</p>	<p><u>Contraindications:</u> Sinus bradycardia; 2nd or 3rd degree heart block; cardiogenic shock; overt HF; sick sinus syndrome (except in patients with a functioning artificial pacemaker); severe peripheral arterial disease, hypersensitivity to metoprolol succinate or any component of the product.</p> <p><u>Caution in the following:</u> HF, PAD, diabetes, thyroid disorder, hepatic impairment, bronchospastic disease, myasthenia gravis, psoriasis, anesthesia, and major surgery, older adults, avoid abrupt withdrawal and pregnancy.</p> <p>May mask symptoms of hypoglycemia.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS /INTERACTIONS*	COMMENTS
BETA-BLOCKERS CONTINUED			
CARDIOSELECTIVE BETA-1 ANTAGONISTS CONTINUED			
Metoprolol Tartrate (Lopressor®) Tablet (IR): 25mg, 50mg, 100mg \$	<p><u>Hypertension; chronic stable angina:</u> Initially, 50 mg orally twice daily; may increase dose at weekly intervals.</p> <p><u>Usual dose:</u> 100-200 mg/day in 2 divided doses with food.</p> <p><u>Max dose:</u> 450 mg/day.</p> <p><u>Renal impairment:</u> No adjustment needed, give dose after dialysis.</p> <p><u>Hepatic impairment:</u> Initiate at low dose and titrate dose slowly.</p>	<p><u>Adverse reactions:</u> Fatigue, dizziness, diarrhea, pruritus, rash, depression, dyspnea, bradycardia, sleep disturbance, nightmares, HF, heart block, gangrene, bronchospasm, photosensitivity.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Amiodarone, dronedarone, verapamil, diltiazem, clonidine, digoxin, MAOIs, reserpine, quinidine, fluoxetine, paroxetine, propafenone, antidiabetic agents, NSAIDs, celecoxib, ceritinib, rifampin, lidocaine, venlafaxine, α-blockers. 	<p><u>Contraindications:</u> Sinus bradycardia; 2nd or 3rd degree heart block; cardiogenic shock; overt HF; sick sinus syndrome (except in patients with a functioning artificial pacemaker); severe PAD, hypersensitivity to metoprolol tartrate or any component of the product.</p> <p><u>Caution in the following:</u> Hepatic impairment, bronchospastic disease, conduction abnormality, diabetes, HF, myasthenia gravis, pheochromocytoma, PAD, psoriasis, psychiatric disease, thyroid disease, history of severe anaphylactic reactions, anesthesia and major surgery, older adults, avoid abrupt withdrawal and pregnancy May mask symptoms of hypoglycemia.</p>
NONSELECTIVE BETA-BLOCKER			
Propranolol (Inderal®) Tablet (IR): 10mg, 20mg, 40mg, 60mg \$ Capsules (ER): 60 mg, 80 mg, 120 mg, 160 mg \$-\$\$	<p><u>Hypertension:</u> <u>IR tab:</u> Initially, 40 mg PO twice daily; increase at 3-7 day intervals.</p> <p><u>ER cap:</u> Initially, 80 mg once daily; increase at 3-7 day intervals.</p> <p>Usual dose: 80-160 mg/day.</p> <p><u>Chronic stable angina:</u> <u>IR tab:</u> Initially, 10-20 mg orally 2-4 times daily; increase at 3-7 day intervals</p> <p><u>ER cap:</u> Initially, 80 mg orally once daily; increase at 3-7 day intervals Usual dose: 80-320 mg/day.</p> <p><u>Max dose:</u> 640 mg/day (hypertension); 320 mg/day (angina)</p> <p><u>Geriatric patients:</u> Initiate at low dose and titrate dose slowly.</p> <p><u>Renal or Hepatic impairment:</u> No adjustment needed.</p>	<p><u>Adverse reactions:</u> Bradycardia, hypotension, fatigue, vivid dreams, nausea, diarrhea, pruritus, rash, bronchospasm, hypersensitivity reactions, impotence, Peyronie's disease, cold extremities, angina, heart block, heart failure, depression, Stevens-Johnson syndrome</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> amiodarone, dronedarone, verapamil, diltiazem, lidocaine, epinephrine, thioridazine, clozapine, fluoxetine, haloperidol, warfarin, digoxin, clonidine, antidiabetic agents, NSAIDs, MAOIs, α-blockers. 	<p><u>Contraindications:</u> Blood pressure < 50/30 mmHg, HR < 80 beats/min, decompensated HF, cardiogenic shock; sinus bradycardia, sick sinus syndrome, or heart block greater than 1st degree (except in patients with a functioning artificial pacemaker); bronchial asthma; pheochromocytoma, hypersensitivity to propranolol or any component of the product, concurrent use with thioridazine.</p> <p><u>Caution in the following:</u> Hepatic or renal impairment, bronchospastic disease, conduction abnormality, diabetes, HF, myasthenia gravis, PAD, psoriasis, psychiatric disease, thyroid disease, older adults, avoid abrupt withdrawal and pregnancy. May mask symptoms of hypoglycemia.</p> <p>Propranolol is often used for mental health indications, so ensure clear communication between primary care and mental health for patients with comorbid conditions.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS / INTERACTIONS*	COMMENTS
NONSELECTIVE BETA-BLOCKER/SELECTIVE ALPHA 1 BLOCKER			
<ul style="list-style-type: none"> BLACK BOX WARNING: ABRUPT DISCONTINUATION OF ANY BETA-ADRENERGIC BLOCKING AGENT, PARTICULARLY IN PATIENTS WITH PREEXISTING CARDIAC DISEASE, CAN CAUSE MYOCARDIAL ISCHEMIA, MYOCARDIAL INFARCTION, VENTRICULAR ARRHYTHMIAS, OR SEVERE HYPERTENSION 			
<ul style="list-style-type: none"> WHEN DISCONTINUING THERAPY, BETA BLOCKERS SHOULD BE GRADUALLY STOPPED TO AVOID REBOUND HYPERTENSION (DECREASE DOSE BY 50% FOR 3 DAYS AND THEN ANOTHER 50% FOR 3 DAYS) 			
<p>Carvedilol (Coreg®)</p> <p>Tablet (IR): 3.125 mg, 6.25 mg, 12.5 mg, 25 mg</p> <p>\$</p>	<p><u>Hypertension:</u> Initially, 6.25 mg orally twice daily; may double dose every 7-14 days.</p> <p><u>Chronic stable angina (off-label):</u> Initially, 12.5 mg orally twice daily; increase dose as tolerated to desired effect; usual dose 25-50 mg twice daily.</p> <p><u>Max dose:</u> 50 mg/day (hypertension); 50 mg twice daily (angina).</p> <p><u>Renal impairment:</u> No adjustment needed.</p> <p><u>Hepatic impairment:</u> Severe: Contraindicated.</p>	<p><u>Adverse reactions:</u> Dizziness, fatigue, hypotension, diarrhea, hyperglycemia, asthenia, bradycardia, weight increase, vomiting, nausea, arthralgia, visual disturbances, edema, syncope, angina, anemia, pulmonary edema, elevated hepatic enzymes, CHF, asthma, increased cough, dyspnea, erectile dysfunction, depression, insomnia, Stevens-Johnson syndrome</p> <ul style="list-style-type: none"> Intraoperative floppy iris syndrome has been reported during cataract surgery. <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> rifampin, MAOIs, clonidine, cyclosporine, digoxin, amiodarone, verapamil, diltiazem, antidiabetic agents, quinidine, fluoxetine, paroxetine, propafenone, reserpine, NSAIDs, epinephrine, dronedarone, α1-blockers. 	<p><u>Contraindications:</u> Patients with severe bradycardia (except in patients with a functioning artificial pacemaker), 2nd or 3rd degree AV block, decompensated HF, requiring IV inotropic therapy, sick sinus syndrome, cardiogenic shock, bronchial asthma, severe hepatic impairment, hypersensitivity to carvedilol or any component of the product.</p> <p><u>Caution in the following:</u> AD, Prinzmetal angina, bradycardia, bronchospastic disease, HF, major surgery, diabetes, thyroid disorder, WPW syndrome, psoriasis, pheochromocytoma, renal impairment, hepatic impairment, myasthenia gravis, older adults, avoid abrupt withdrawal, pregnancy, and lactation.</p> <p>May mask symptoms of hypoglycemia.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS / INTERACTIONS*	COMMENTS
<p>NONSELECTIVE BETA-BLOCKER/SELECTIVE ALPHA 1 BLOCKER, CONT'D</p> <ul style="list-style-type: none"> BLACK BOX WARNING: ABRUPT DISCONTINUATION OF ANY BETA-ADRENERGIC BLOCKING AGENT, PARTICULARLY IN PATIENTS WITH PREEXISTING CARDIAC DISEASE, CAN CAUSE MYOCARDIAL ISCHEMIA, MYOCARDIAL INFARCTION, VENTRICULAR ARRHYTHMIAS, OR SEVERE HYPERTENSION WHEN DISCONTINUING THERAPY, BETA BLOCKERS SHOULD BE GRADUALLY STOPPED TO AVOID REBOUND HYPERTENSION (DECREASE DOSE BY 50% FOR 3 DAYS AND THEN ANOTHER 50% FOR 3 DAYS) 			
<p>Labetalol</p> <p>Tablet: 100mg, 200mg, 300mg</p> <p>\$-\$\$\$\$</p>	<p><u>Hypertension:</u> Initially, 100 mg orally twice daily; increase in increments of 100 mg twice daily every 2-3 days if needed</p> <p><u>Usual dose:</u> 200-400 mg twice daily; 100-200 mg twice a day in older adults</p> <p><u>Max dose:</u> 2400 mg/day in 2-3 divided doses</p> <p><u>Renal impairment:</u> No adjustment needed.</p> <p><u>Hepatic impairment:</u> Reduce dose by 50%.</p>	<p><u>Adverse reactions:</u> HF, hyperkalemia, hepatotoxicity, bronchospasm, hypotension, nausea, dizziness, headache, fatigue, nasal congestion, dyspnea, erectile dysfunction, psoriasis</p> <ul style="list-style-type: none"> Intraoperative floppy iris syndrome has been reported during cataract surgery. <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Amiodarone, verapamil, diltiazem, clonidine, dronedarone, halothane, cimetidine, digoxin, antidiabetic agents, nitroglycerin, MAOIs, NSAIDs, imipramine, epinephrine, α-blockers. 	<p><u>Contraindications:</u> Severe bradycardia; heart block > 1st degree (except in patients with a functioning artificial pacemaker); cardiogenic shock; bronchial asthma; uncompensated cardiac failure; conditions associated with severe and prolonged hypotension, hypersensitivity to labetalol or any component of the product.</p> <p><u>Caution in the following:</u> Bronchospastic disease, conduction abnormality, diabetes, HF, hepatic impairment, myasthenia gravis, PAD, pheochromocytoma, psoriasis, psychiatric disease, thyroid disease, latent cardiac insufficiency, older adults, pregnancy avoid abrupt withdrawal</p> <p>May mask symptoms of hypoglycemia</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Colchicine (Lodoco®) Tablet: 0.5 mg \$\$	<p><u>Reduce the risk of myocardial infarction (MI), stroke, coronary revascularization, and cardiovascular death in adult patients with established atherosclerotic disease or with multiple risk factors for cardiovascular disease:</u> 0.5 mg orally once daily.</p> <p><u>Max dose:</u> 0.5 mg/day for prevention of cardiovascular and stroke events.</p> <p><u>Renal Impairment:</u> Avoid use in persons with moderate renal impairment receiving moderate CYP3A4 inhibitors.</p> <p><u>Hepatic Impairment:</u> Avoid use in persons with any degree of hepatic impairment and receiving strong P-gp inhibitors or strong/moderate CYP3A4 inhibitors.</p>	<p><u>Adverse reactions:</u> Myalgia, weakness, numbness, paresthesias, diarrhea, vomiting, abdominal cramping, abdominal pain, thrombocytopenia, leukopenia, pancytopenia.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Strong CYP3A4 inhibitors (atazanavir, clarithromycin, darunavir/ritonavir, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, tipranavir/ritonavir. • Moderate CYP3A4 inhibitors (amprenavir, aprepitant, diltiazem, erythromycin, fluconazole, fosamprenavir, verapamil. • Strong P-gp inhibitors (cyclosporine, ranolazine) • Statins, fibrates, gemfibrozil, digoxin, oral contraceptives. 	<p><u>Contraindications:</u> Renal failure (CrCl < 15 mL/min), severe hepatic impairment, concomitant use with strong CYP3A4 inhibitors or P-gp inducers, patients with pre-existing blood dyscrasias, hypersensitivity to colchicine or components of product.</p> <p><u>Caution in the following:</u> Renal impairment, hepatic impairment, elderly.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS /INTERACTIONS*	COMMENTS
CALCIUM CHANNEL BLOCKERS (CCB)			
DIHYDROPYRIDINES: Higher incidence of peripheral edema than non-dihydropyridines			
Amlodipine (Norvasc®) Tablet: 2.5 mg, 5 mg, 10 mg \$	<p><u>Hypertension:</u> Initially, 5 mg orally once daily; 2.5 mg orally once daily if small, fragile, or older patients; increase dose after 7-14 days if needed.</p> <p><u>Angina:</u> 5-10 mg once daily</p> <p><u>Usual dose:</u> 2.5-10 mg once daily</p> <p><u>Max dose:</u> 10 mg/day</p> <p><u>Renal impairment:</u> No adjustment needed</p> <p><u>Hepatic impairment:</u> initial dose 2.5 mg/day</p>	<p><u>Adverse reactions:</u> Peripheral edema, fatigue, abdominal pain, nausea, somnolence, headache, flushing, dyspnea, palpitations, dizziness, reflex tachycardia, gingival hyperplasia, hypotension-may be acute, nausea, eczema (especially in chronic use or older patients), rash, pruritus.</p> <ul style="list-style-type: none"> Increased angina and/or MI has occurred with initiation or dosage titration, hepatitis, hypersensitivity reactions and erythema multiforme. <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Codeine, methadone, oxycodone, hydrocodone, simvastatin, cyclosporine, tacrolimus, sildenafil, carbamazepine, phenytoin, rifamycins, MAOIs, azole antifungals, macrolide antibiotics, protease inhibitors, dantrolene, diltiazem and verapamil, St. John's Wort, primidone, lofexidine. <p><u>Food Interaction:</u></p> <ul style="list-style-type: none"> Grapefruit juice. Monitor closely with concurrent use. 	<p><u>Contraindications:</u> Hypersensitivity to amlodipine or other dihydropyridines.</p> <p><u>Caution in the following:</u> Use with caution in older adults, CHF, patients with severe aortic stenosis, severe obstructive coronary disease, severe hepatic impairment.</p>
Nifedipine ER (Adalat CC®, Procardia XL®) Tablet (XL): 30 mg, 60 mg, 90 mg Tablet (CC): 30 mg, 60 mg, 90 mg \$\$-\$\$	<p><u>Angina:</u> Initially, 30-60 mg orally once daily; increase dose after 7-14 days if needed.</p> <p><u>Hypertension:</u> Initially, 30-60 mg orally once daily; increase dose after 7-14 days if needed.</p> <p><u>Usual dose:</u> 30-90 mg/day</p> <p><u>Max dose:</u> 120 mg/day (XL) 90 mg/day (CC).</p> <p>CC: Take on an empty stomach; 1 hour before or 2-3 hours after eating.</p> <p><u>Renal impairment:</u> no adjustment needed.</p> <p><u>Hepatic impairment:</u> not studied, use caution</p> <p>Do not cut, crush or chew. Taper dose to D/C.</p>	<p><u>Adverse reactions:</u> Peripheral edema, CHF, palpitations and arrhythmia, pulmonary edema, flushing, reflex tachycardia, nausea, dizziness, headache, nervousness, hypotension, fatigue/weakness, elevated liver enzymes, GI obstruction/ulcers (XL form), cholestasis, Steven-Johnson syndrome, muscle cramps, dyspnea, insomnia, nasal congestion, gingival overgrowth, eczema (especially in chronic use or older adults)</p> <ul style="list-style-type: none"> Increased angina and/or MI has occurred with initiation or dosage titration <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Cyclosporine, tacrolimus, digoxin, clopidogrel, lacosamide, carbamazepine, phenytoin, phenobarbital, rifamycins, MAOIs, azole antifungals, macrolide antibiotics, protease inhibitors, flecainide, nafcillin, rifampin, verapamil, St. John's Wort, lofexidine, dantrolene, secobarbital, butalbital, butabarbital, primidone. <p><u>Food Interactions:</u></p> <ul style="list-style-type: none"> Grapefruit. Do not eat grapefruit or drink grapefruit juice while taking this medication. 	<p><u>Contraindications:</u> Hypersensitivity to nifedipine or other dihydropyridines, galactose intolerance, and IR formulations contraindicated to manage hypertensive crisis and essential HTN</p> <p><u>Caution in the following:</u> HF or severe aortic stenosis, severe left ventricular dysfunction, renal impairment, severe hepatic impairment, hypertrophic cardiomyopathy, concomitant therapy with β-blocker or digoxin, edema, or recent D/C of β-blocker.</p> <p>Avoid ER /XL tabs in patients with stricture/narrowing of GI tract, or GI hypomotility.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS /INTERACTIONS*	COMMENTS
CALCIUM CHANNEL BLOCKERS (CCB)			
Non-Dihydropyridines			
<ul style="list-style-type: none"> • Cause less vasodilation and more cardiac depression than dihydropyridine CCBs; can cause reductions in heart rate & contractility 			
<p>Diltiazem (Cardizem[®], Cardizem CD[®], Dilt CD[®])</p> <p>Tablet (IR): 60 mg, 90 mg</p> <p>Capsule (ER-24hr): 120 mg, 180 mg, 240 mg, 300 mg, 360 mg (NF)</p> <p>\$-\$\$</p>	<p><u>Hypertension:</u> ER-24h cap: Initially, 180-240 mg orally once daily; increase dose after 14 days if needed</p> <p><u>Angina:</u> IR tab: Initially, 30 mg orally 4 times daily; increase dose every 1-2 days if needed ER-24h cap: Initially, 120-180 mg orally once daily; increase dose every 7-14 days if needed</p> <p><u>Usual dose:</u> IR: 180-360 mg/day ER-24h: 120-360 mg/day (hypertension); 240-360 mg/day (angina)</p> <p><u>Max dose:</u> 60 mg/day (IR); 540 mg/day (ER-24h)</p> <p><u>Renal impairment:</u> no adjustment needed</p> <p><u>Hepatic impairment:</u> Consider using lower doses ER cap/tab: Swallow whole. Do not cut, crush, chew, or dissolve.</p>	<p><u>Adverse reactions:</u> Headache, constipation, peripheral edema, fatigue, rhinitis, pharyngitis, dyspepsia, myalgia, dizziness, asthenia, heart block, rash, bradycardia, arrhythmias, syncope, elevated liver enzymes, acute liver injury, hypotension-may be severe, CHF, serious dermatologic conditions, gingival hyperplasia, abnormal dreams, depression, hallucinations, insomnia, nervousness, personality changes</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Flobanserin, eliglustat, lomitapide, simvastatin, lovastatin, atorvastatin, β-blockers, digoxin, amiodarone, lithium, buspirone, carbamazepine, rifampin, phenobarbital, butalbital, butobarbital, pentobarbital, codeine, morphine, fentanyl, hydrocodone, buprenorphine, meperidine, tramadol, methadone, lofexidine, cyclosporine, tacrolimus, theophylline, clonidine, dantrolene, verapamil, felodipine, ergotamine, primidone, colchicine, phenytoin, ranolazine, erythromycin, clarithromycin, MAOIs, antiarrhythmics, protease inhibitors, azole antifungals, amlodipine, flecainide, guanfacine, nafcillin, St. John’s Wort, clopidogrel, lurasidone, thioridazine. 	<p><u>Contraindications:</u> Hypersensitivity to diltiazem, sick sinus syndrome (without pacemaker); 2nd or 3rd degree AV block; severe hypotension (SBP < 90), acute MI and pulmonary congestion, A. fib/flutter associated with accessory bypass tract (IV form), V-Tach (IV form), concomitant use of colchicine, flobanserin, lomitapide, eliglustat. Avoid use in patients with HFrEF, cardiac conduction defects</p> <p><u>Caution in the following:</u> Left ventricular dysfunction, hepatic or renal dysfunction</p> <p>IR tablets not FDA approved for HTN.</p>

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Treatment cont'd

DRUG CLASS /MEDICATION	DOSING	ADVERSE EFFECTS /INTERACTIONS*	COMMENTS
CALCIUM CHANNEL BLOCKERS (CCB)			
Non-Dihydropyridines			
<ul style="list-style-type: none"> • Cause less vasodilation and more cardiac depression than dihydropyridine CCBs; can cause reductions in heart rate & contractility 			
<p>Verapamil (Calan®, Calan-SR®, Isoptin SR®)</p> <p>Tablet: IR: 40 mg, 80 mg, 120 mg</p> <p>ER (12hr): 120 mg, 180 mg, 240 mg.</p> <p>§</p>	<p><u>Angina:</u> IR tab: 80-120 mg orally 3 times daily; may titrate at daily or weekly intervals based on response 8 hours after dosing</p> <p><u>Hypertension:</u> IR tab: Initial, 80 mg orally 3 times daily; titrate based on response; no evidence of added effect with doses > 360 mg/day ER (12hr) tab: Initial, 180 mg orally once daily; may titrate dose up to 240 mg every 12 hours at weekly intervals based on response 24 hours after dosing.</p> <p><u>Dose adjustments:</u> Geriatric or small stature (initial): 40mg 3 times daily (IR), 120 mg daily (ER-12hr)</p> <p><u>Max dose:</u> IR, ER (12hr): 480 mg/day</p> <p><u>Renal impairment:</u> No dosage adjustment needed.</p> <p><u>Hepatic impairment:</u> Severe: Reduce initial verapamil dose to about 33% of the usual starting dose.</p>	<p><u>Adverse reactions:</u> Constipation, dizziness, nausea, hypotension, headache, edema, CHF, fatigue, dyspnea, bradycardia, AV block, rash, flushing, insomnia, confusion, sleep disorder</p> <p><u>Drug Interactions:</u></p> <ul style="list-style-type: none"> • erythromycin, ritonavir, rifampin, ivabradine, statins, antihypertensive agents, antiarrhythmic agents, digoxin, lithium, carbamazepine, phenobarbital, cyclosporine, theophylline, telithromycin, clonidine, sirolimus, temsirolimus, everolimus. 	<p><u>Contraindications:</u> Severe left ventricular dysfunction, hypotension (SBP < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker), second-or third-degree AV block (except in patients with a functioning artificial ventricular pacemaker), atrial flutter or atrial fibrillation and an accessory bypass tract (e.g., Wolff-Parkinson-White, Lown-Ganong-Levine syndromes), hypersensitivity to verapamil or component of product..</p> <p><u>Caution in the following:</u> Liver disease, hypertrophic cardiomyopathy or idiopathic hypertrophic subaortic stenosis, neuromuscular disease, GI obstruction or ileus, fecal impaction, or pre-existing constipation, gastroesophageal reflux disease (GERD) or hiatal hernia associated with reflux esophagitis</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
NITRATES			
Isosorbide mononitrate (Imdur®) Tablet (ER): 30 mg, 60 mg, 120 mg \$	<u>Angina, prevention:</u> Initially, 30 or 60 mg orally once daily; may increase after several days up to a maintenance dosage of 60 to 120 mg once daily <u>Max dose:</u> 240 mg/day, rarely needed <u>Renal Impairment:</u> No dosage adjustment needed <u>Hepatic Impairment:</u> No dosage adjustment needed	<u>Adverse reactions:</u> dizziness, Headache, fatigue, xerostomia, weakness, vomiting, visual impairment, vertigo, hypotension, insomnia, depression, confusion, anxiety, emotion lability, <u>Drug interactions:</u> <ul style="list-style-type: none"> Phosphodiesterase (PDE-5) inhibitors (sildenafil, tadalafil, vardenafil, avanafil), riociguat, rilmenidine, rosiglitazone, blood pressure lowering agents 	<u>Contraindications:</u> Hypersensitivity to isosorbide mononitrate, other nitrates or nitrites, or component of product; concurrent use with PDE-5 inhibitors or riociguat; anemia <u>Caution in the following:</u> Recent myocardial infarction, hypertrophic cardiomyopathy, hypotension, increased intracranial pressure (e.g., recent head trauma or intracranial bleeding), closed-angle glaucoma
Isosorbide dinitrate (Sorbitrate®, Isordil®) Tablet (IR): 10 mg, 20 mg, 30 mg, 40 mg \$\$	<u>Angina, prevention:</u> Initial, 5 to 20 mg orally 2 to 3 times daily; maintenance, 10 to 40 mg 2 to 3 times daily, some patients may require higher doses. <u>Note:</u> A daily dose-free interval of at least 14 hours is recommended to minimize tolerance. <u>Max dose:</u> 480 mg/day. <u>Renal Impairment:</u> No dosage adjustment needed. <u>Hepatic Impairment:</u> No dosage adjustments provided in the manufacturer's labeling; use with caution.	<u>Adverse reactions:</u> dizziness, Headache, hypotension, nausea, xerostomia, vomiting, tolerance, syncope <u>Drug interactions:</u> <ul style="list-style-type: none"> Phosphodiesterase (PDE-5) inhibitors (sildenafil, tadalafil, vardenafil, avanafil), riociguat, rosiglitazone. 	<u>Contraindications:</u> Hypersensitivity to isosorbide dinitrate or component of product, concurrent use with PDE-5 inhibitors or riociguat, anemia, closed-angle glaucoma. <u>Caution in the following:</u> Recent myocardial infarction, hypertrophic cardiomyopathy, hypotension, increased intracranial pressure (e.g., recent head trauma or intracranial bleeding).

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
NITRATES, CONT'D			
<p>Nitroglycerin (Nitrostat®, Nitro-Bid®, Nitro-Dur®)</p> <p>Tablet (SL): 0.3 mg, 0.4 mg, 0.6 mg</p> <p>Topical ointment: 2%</p> <p>Transdermal patch: 0.2 mg/hr, 0.4 mg/hr, 0.6 mg/hr</p> <p>\$\$-\$\$\$</p>	<p><u>Angina, prevention:</u> SL tab: 0.3 to 0.4 mg sublingually 5-10 min prior to activities that may provoke angina Topical ointment: Initially, apply 7.5 mg (½ inch) topically twice daily every 6 hours; may double dose in persons tolerating but failing to respond. Max: 30 mg/dose.</p> <p><u>Transdermal patch:</u> Initially 0.2 to 0.4 mg/hour transdermally for 12 to 14 hours daily with a 10 to 12 hours daily patch-off period. Adjust dose based on symptoms and adverse effects. Dose range: 0.1 to 0.8 mg/hour.</p> <p>NOTE: Use a nitrate-free interval of 10 to 12 hours/day to minimize the risk of tolerance for topical ointment or transdermal patch.</p> <p><u>Renal Impairment:</u> No dosage adjustment needed.</p> <p><u>Hepatic Impairment:</u> No dosage adjustments provided in the manufacturer's labeling; use with caution.</p>	<p><u>Adverse reactions:</u> headache, nausea, vertigo, dizziness, syncope, orthostatic hypotension, hypotension, paresthesias.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Phosphodiesterase (PDE-5) inhibitors (sildenafil, tadalafil, vardenafil, avanafil), riociguat, rosiglitazone, ergotamine, blood pressure lowering agents, apomorphine. 	<p><u>Contraindications:</u> Hypersensitivity to nitroglycerin, other nitrates or nitrites, or any component of the product; concurrent use with PDE-5 inhibitors or riociguat; acute circulatory failure or shock; early myocardial infarction (SL only); increased intracranial pressure; severe anemia.</p> <p><u>Caution in the following:</u> Aortic stenosis, mitral stenosis, dehydration, hypovolemia, hepatic disease, hypotension, recent myocardial infarction.</p>

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MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
NITRATES, CONT'D			
<p>Nitroglycerin (Nitrostat®, Nitro-Bid®, Nitro-Dur®)</p> <p>Tablet (SL): 0.3 mg, 0.4 mg, 0.6 mg</p> <p>Injectable: 5 mg/mL</p> <p>\$\$</p>	<p><u>Angina, acute:</u> SL tab: 0.3 to 0.6 mg sublingually at onset; repeat every 5 min if angina persists; may administer up to 3 tablets in a 15-minute period.</p> <p><u>Angina, not responsive to SL nitroglycerin and beta-blockers:</u> IV: Initially, 5 to 10 mcg/min with continuous cardiac monitoring; titrate as needed to relieve angina symptoms in increments of 5 mcg/min every 5-10 min up to 20 mcg/min; if angina persists at a dose of 20 mcg/min, may increase by 10 to 20 mcg/min every 3-5 minutes to a maximum dose of 400 mcg/min.</p> <p><u>Renal Impairment:</u> No dosage adjustment needed.</p> <p><u>Hepatic Impairment:</u> No dosage adjustments provided in the manufacturer's labeling; use with caution.</p>	<p><u>Adverse reactions:</u> headache, nausea, vertigo, dizziness, syncope, orthostatic hypotension, hypotension, paresthesias.</p> <p><u>Drug interactions:</u> phosphodiesterase (PDE-5) inhibitors (sildenafil, tadalafil, vardenafil, avanafil), riociguat, rosiglitazone, ergotamine, blood pressure lowering agents, apomorphine.</p>	<p><u>Contraindications:</u> hypersensitivity to nitroglycerin, other nitrates or nitrites, or any component of the product; concurrent use with PDE-5 inhibitors or riociguat; acute circulatory failure or shock; early myocardial infarction (SL only); increased intracranial pressure; severe anemia</p> <p>Additional contraindications for IV product: Constrictive pericarditis; increased intracranial pressure; pericardial tamponade; restrictive cardiomyopathy.</p> <p><u>Caution in the following:</u> aortic stenosis, mitral stenosis, dehydration, hypovolemia, hepatic disease, hypotension, recent myocardial infarction.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Ranolazine (Ranexa®) Tablet: 500 mg, 1000 mg \$	<p><u>Chronic Angina:</u> Initially 500 mg orally twice daily; may increase to 1,000 mg twice daily if needed</p> <p><u>Max dose:</u> 2,000 mg/day.</p> <p><u>Dosage adjustment:</u> Concurrent moderate CYP3A inhibitors: max dose 500 mg twice daily.</p> <p><u>Renal Impairment:</u></p> <ul style="list-style-type: none"> • CrCl < 60 mL/min: Use caution, monitor renal function after initiation and periodically. • CrCl ≤ 30 mL/min: Initially 500 mg once daily; maximum: 500 mg twice daily • Discontinue if acute renal failure develops. <p><u>Hepatic Impairment:</u> No dosage adjustments provided in the manufacturer's labeling. Use is contraindicated with hepatic cirrhosis.</p>	<p><u>Adverse Reactions:</u> dizziness, headache, constipation, asthenia, nausea, xerostomia, vomiting, vertigo, tinnitus, syncope, hypotension, prolonged QT interval, confusion.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Strong CYP3A inducers (ketoconazole, itraconazole, clarithromycin, nefazodone, nelfinavir, ritonavir, indinavir, saquinavir) • CYP3A inducers (rifampin, rifabutin, rifapentine, phenobarbital, phenytoin, carbamazepine, St John's wort) • Moderate CYP3A inhibitors (diltiazem, verapamil, erythromycin, fluconazole, and grapefruit juice or grapefruit-containing products) • Simvastatin, lovastatin cyclosporine, tacrolimus, sirolimus, digoxin, TCAs, antipsychotics, metformin. 	<p><u>Contraindications:</u> liver cirrhosis, concurrent use with strong CYP3A inhibitors or CYP3A inducers.</p> <p><u>Caution in the following:</u> hepatic impairment, renal impairment, patients ≥75 years of age.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
HMG CoA Reductase inhibitors (statins) - Risk of skeletal muscle effects (e.g., myopathy, rhabdomyolysis) increases with higher doses and concomitant use of certain drugs. Predisposing factors include age > 65, biological female at birth, uncontrolled hypothyroidism, and renal impairment			
<p>Atorvastatin (Lipitor®)</p> <p>Tablet: 10 mg, 20 mg, 40 mg, 80 mg</p> <p>\$</p>	<p>Usual dose: 10-80 mg orally once daily.</p> <p><u>MODERATE-INTENSITY</u> 30% to < 50% reduction in LDL:10-20 mg orally once daily.</p> <p><u>HIGH-INTENSITY</u> ≥ 50% reduction in LDL: 80 mg orally once daily; 40 mg orally once daily if 80 mg not tolerated.</p> <p><u>Dose adjustments:</u> <u>Max dose 20 mg/day:</u> concomitant use with clarithromycin, erythromycin, itraconazole, ketoconazole, voriconazole, saquinavir plus ritonavir, darunavir plus ritonavir, fosamprenavir, atazanavir plus ritonavir, elbasvir/grazoprevir</p> <p><u>Max dose 40 mg/day:</u> concomitant use with nelfinavir.</p> <p><u>Renal Impairment:</u> No adjustment needed.</p> <p><u>Hepatic Impairment:</u> Contraindicated inactive liver disease or unexplained/ persistent transaminase elevations.</p>	<p><u>Adverse Reactions:</u> myopathy, rhabdomyolysis, elevated liver enzymes, diarrhea, arthralgia, myalgia, nasopharyngitis, nausea, dyspepsia, urinary tract infection, insomnia, rhabdomyolysis.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Contraindicated with cyclosporine, posaconazole, certain HIV protease inhibitors (tipranavir plus ritonavir), glecaprevir/pibrentasvir. • Use caution and lowest dose necessary with HIV protease inhibitor (lopinavir plus ritonavir) • Use caution with niacin, fibrates (avoid gemfibrozil if possible). • Use caution with digoxin, oral contraceptives, warfarin, colchicine. • Consider temporarily suspending use while the patient is on daptomycin 	<p>CCHCS PREFERRED AGENT</p> <p><u>Contraindications:</u> hypersensitivity to atorvastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevations of serum transaminases, pregnancy, breast-feeding, concomitant use with certain HIV protease inhibitors (tipranavir plus ritonavir), glecaprevir/pibrentasvir, cyclosporine.</p> <p><u>Caution in the following:</u> heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, preexisting amyotrophic lateral sclerosis (ALS), the elderly.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
<p>HMG CoA Reductase inhibitors (statins) - Risk of skeletal muscle effects (e.g., myopathy, rhabdomyolysis) increases with higher doses and concomitant use of certain drugs. Predisposing factors include age > 65, biological female at birth, uncontrolled hypothyroidism, and renal impairment</p>			
<p>Rosuvastatin (Crestor®)</p> <p>Tablet: 5 mg, 10 mg, 20 mg, 40 mg</p> <p>\$</p>	<p>Usual dose: 5-40 mg orally once daily</p> <p><u>MODERATE-INTENSITY</u> 30% to < 50% LDL reduction: 5-10 mg orally once daily.</p> <p><u>HIGH-INTENSITY</u> ≥ 50% LDL reduction: 20-40 mg orally once daily.</p> <p><u>Dose adjustments:</u> <u>Asian patients:</u> consider lower starting (5 mg/day) and maximum doses.</p> <p><u>Max dose 5 mg/day:</u> concomitant use with cyclosporine.</p> <p><u>Max dose 10 mg/day:</u> concomitant use with lopinavir plus ritonavir, atazanavir plus ritonavir, elbasvir/grazoprevir, glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, gemfibrozil.</p> <p><u>Renal Impairment:</u> CrCl < 30 mL/min (not on hemodialysis): Initial dose: 5 mg/day; Max dose 10 mg/day Rosuvastatin levels in hemodialysis patients are about 50% higher than in normal renal function.</p> <p><u>Hepatic Impairment:</u> Contraindicated inactive liver disease or unexplained/persistent transaminase elevations</p>	<p><u>Adverse Reactions:</u> myopathy, rhabdomyolysis, elevated liver enzymes, diarrhea, arthralgia, myalgia, headache, dizziness, constipation, nausea, dyspepsia, rash, rhabdomyolysis</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Contraindicated with sofosbuvir/velpatasvir/voxilaprevir, lasmiditan • Rosuvastatin may be less likely to interact with other drugs. • Use caution with niacin, fibrates(avoid gemfibrozil if possible). • Use caution with protease inhibitor/ritonavir combinations, warfarin, colchicine • Consider temporarily suspending use while patient is on daptomycin. 	<p><u>Contraindications:</u> hypersensitivity to rosuvastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevations of serum transaminases, pregnancy, breast-feeding, concomitant use with sofosbuvir/velpatasvir/voxilaprevir, Lasmiditan.</p> <p><u>Caution in the following:</u> patients of Asian descent, heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, preexisting amyotrophic lateral sclerosis (ALS), the elderly.</p> <p>For Asian patients, consider 5 mg/day starting dose.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
<p>HMG CoA Reductase inhibitors (statins) - Risk of skeletal muscle effects (e.g., myopathy, rhabdomyolysis) increases with higher doses and concomitant use of certain drugs. Predisposing factors include age >65, biological female at birth, uncontrolled hypothyroidism, and renal impairment</p>			
<p>Pravastatin (Pravachol®)</p> <p>Tablet: 10 mg, 20 mg, 40 mg</p> <p>\$</p>	<p>Usual dose: 20-80 mg orally once daily.</p> <p><u>MODERATE-INTENSITY</u> 30% to < 50% reduction in LDL: 40-80 mg orally once daily.</p> <p>Dose adjustments: <u>Max dose 20 mg/day:</u> concomitant use with cyclosporine.</p> <p><u>Max dose 40 mg/day:</u> concomitant use with clarithromycin, sofosbuvir/ velpatasvir/voxilaprevir</p> <p><u>Reduce dose by 50%:</u> concomitant use with glecaprevir/pibrentasvir</p> <p><u>Renal Impairment:</u> Severe renalimpairment (CrCl < 30 mL/min): Initial dose: 10 mg/day.</p> <p><u>Hepatic Impairment:</u> Contraindicated inactive liver disease or unexplained/ persistent transaminase elevations.</p>	<p><u>Adverse Reactions:</u> Myopathy, rhabdomyolysis, elevated liver enzymes, diarrhea, constipation, nausea, vomiting, musculoskeletalpain, myalgia, rash, headache, dizziness, cough, rhinitis, upper respiratory infection</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Pravastatin may be less likely to interact with other drugs. • Use caution with niacin, fibrates (avoid gemfibrozil) • Consider dose reduction with niacin dose ≥ 1000 mg/day. • Consider temporarily suspending use while the patient is on daptomycin. 	<p><u>Contraindications:</u> Hypersensitivity to pravastatin or any component of the formulation, active liver disease (including cholestasis, hepatic encephalopathy, hepatitis, and jaundice), unexplained/persistent elevation serum transaminases, pregnancy, breast-feeding.</p> <p><u>Caution in the following:</u> heavy alcohol use (alcoholism), history of liver disease/renal impairment, uncontrolled hypothyroidism, sepsis or severe infection, uncontrolled seizure disorder, recent stroke or transient ischemic attack, electrolyte imbalance, preexisting amyotrophic lateral sclerosis (ALS), the elderly.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
<p>Ezetimibe use may be considered in patients who do not meet cholesterol treatment goals with dietary modification and maximally tolerated statin therapy. 2018 Guideline on the Management of Blood Cholesterol from the ACC/American Heart Association Task Force found no proof that adding a non-statin to a statin prevents ASCVD events in patients without clinical ASCVD.</p>			
<p>Ezetimibe (Zetia®)</p> <p>Tablet: 10 mg</p> <p>\$</p>	<p>Dose: 10 mg orally once daily.</p> <p><u>Renal Impairment:</u> No dose adjustment needed.</p> <p><u>Hepatic Impairment:</u> Mild hepatic impairment: No dose adjustment needed. Moderate to severe hepatic impairment: Not recommended.</p>	<p><u>Adverse Reactions:</u> diarrhea, abdominal pain, myalgia, arthralgia, back pain, fatigue, cough, sinusitis, pharyngitis, upper respiratory infection, hepatitis, elevated hepatic enzymes, rhabdomyolysis, anaphylaxis, pruritus, depression, Stevens-Johnson syndrome</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Use caution with fibrates (avoid gemfibrozil), cyclosporine, warfarin, antacids, bile acid sequestrants. 	<p><u>Contraindications:</u> hypersensitivity to ezetimibe or any component of the formulation, concomitant use with statin in patients with active hepatic disease or unexplained persistent elevations in serum transaminases; pregnancy and breastfeeding (when used with a statin).</p> <p><u>Caution in the following:</u> hepatic impairment (use not recommended in moderate or severe impairment), renal impairment, concomitant use with statins, concomitant use with fibrates, pregnancy, breast-feeding, the elderly.</p> <p><u>Use Recommendations:</u> For the addition of Ezetimibe see “Memorandum—Ezetimibe” located on Pharmacy Lifeline page under Memos tab. Pharmacy Lifeline.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
<p>Prescription Omega-3 Polyunsaturated Fatty Acid (PUFA) - Recommended as therapy for persistent hypertriglyceridemia. Nonprescription fish oil products, or marine-derived omega-3 fatty acid preparations, are classified as dietary supplements and are not interchangeable with prescription omega-3 PUFAs.</p>			
<p>Icosapent ethyl (Vascepa®)</p> <p>Tablet: 0.5 gm, 1 gm</p> <p>\$\$\$\$</p>	<p><u>Treatment of persistent fasting hypertriglyceridemia:</u> 2 g orally BID with meals.</p> <p><u>Severe hypertriglyceridemia:</u> 2 g orally BID with meals.</p> <p><u>Renal Impairment:</u> No dose adjustment provided in the manufacturer's labeling (has not been studied). Eicosapentaenoic acid is not renally eliminated.</p> <p><u>Hepatic Impairment:</u> No dose adjustment provided in the manufacturer's labeling (has not been studied).</p>	<p><u>Adverse Reactions:</u> hemorrhage including major hemorrhage, atrial fibrillation/flutter, peripheral edema, gout, musculoskeletal pain, constipation.</p> <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Agents with antiplatelet properties (e.g., P2Y12 inhibitors, NSAIDs, SSRIs, etc.): Omega-3 fatty acids may enhance the antiplatelet effect these agents. • Anticoagulants: Omega-3 fatty acids may enhance anticoagulant effects • Ibrutinib: Omega-3 fatty acids may enhance the antiplatelet effects. 	<p>Recommended Use Criteria: Patient already on icosapent ethyl/Vascepa® upon Reception Center arrival; or prescribed/recommended by consulting cardiologist for clinical ASCVD diagnosis or diabetes with additional cardiovascular risk factors, on statin therapy, LDL-C <100 mg/dL, and triglycerides (TG) ≥150 mg/dL.</p> <p><u>Contraindications:</u> hypersensitivity to icosapent ethyl or any component of formulation.</p> <p><u>Caution in the following:</u> bleeding risk, atrial fibrillation/flutter, fish allergy, hypersensitivity, diabetes, hypothyroidism, hepatic impairment, excessive alcohol intake, breastfeeding.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Sodium-glucose co-transporter 2 inhibitors			
<p>Empagliflozin (Jardiance®)</p> <p>Tablet: 10 mg, 25 mg</p> <p>\$\$\$\$\$</p>	<p><u>Heart failure:</u> 10 mg orally once daily</p> <p><u>Reduction of the risk of CV death in persons with T2DM and established CV disease:</u> 10 mg orally once daily; may increase to 25 mg once daily if additional glycemic control needed.</p> <p><u>Max dose:</u> 25 mg/day.</p> <p><u>Renal Impairment:</u> T2DM:</p> <ul style="list-style-type: none"> eGFR ≥ 30 mL/min: No dosage adjustment needed. eGFR 20-29 mL/min: Not recommended for glycemic control. However, guidelines recommend use in all persons with T2DM and CKD for CV and renal protection regardless of glycemia or presence of albuminuria; may be continued at 10 mg daily if eGFR declines after initiation. eGFR < 20 mL/min: Do not initiate; may continue if eGFR declines after initiation unless not tolerated or renal replacement therapy is initiated . <p>HF:</p> <ul style="list-style-type: none"> eGFR ≥ 20 mL/min: No dosage adjustment needed. eGFR < 20 mL/min: Insufficient data to determine dosing recommendations. <p><u>Hepatic Impairment:</u> No dosage adjustment needed.</p>	<p><u>Adverse reactions:</u> dehydration, hypotension, urinary frequency, urinary tract infections, including urosepsis and pyelonephritis, balanitis, vaginitis, endocrinopathies, hypoglycemia, hypercholesterolemia, polydipsia.</p> <ul style="list-style-type: none"> Intravascular volume contraction. Symptomatic hypotension can occur after initiating empagliflozin. Patients with pre-existing hypercholesterolemia. Monitor LDL-C. Dose-related increases in LDL Geriatric patients > 75 years old experienced an ↑ incidence of S/E. <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> Major: chloroquines Moderate: beta blockers, thiazides, ACEI and ARBs, estrogens, progestins and androgens, HIV “avir” medications, atypical antipsychotics, calcium channel blockers, lithium, corticosteroids, loop diuretics. 	<p><u>Contraindications:</u> history of serious hypersensitivity reaction to empagliflozin; severe renal impairment (eGFR less than 20 mL/min), ESRD/dialysis.</p> <p><u>Caution in the following:</u> history of genital fungal infection, including vaginitis or balanitis, and in uncircumcised males. Patients at the risk of acute kidney injury, include those with dehydration or hypovolemia, particularly in patients with impaired renal function (i.e., eGFR 45 to 60 mL/min), the elderly, patients receiving diuretics, or patients with low systolic blood pressure.</p> <p>Serious hypersensitivity reactions or anaphylaxis, including angioedema, have been reported in patients receiving empagliflozin.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Glucagon-like peptide-1 receptor agonist			
<p>Semaglutide (SQ) (Ozempic®)</p> <p>Injection soln: 0.25 mg, 0.5 mg, 1 mg, 2 mg</p> <p>(Wegovy®)</p> <p>Injection soln: 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, 2.4 mg</p> <p>\$\$\$\$\$</p>	<p><u>Reduction of risk of MACE in adults with T2DM and established cardiovascular disease:</u> Initially, 0.25 mg subcutaneously once weekly x 4 weeks, then 0.5 mg once weekly; may increase to 1 mg weekly after 4 weeks on 0.5 mg/week and 2 mg weekly after 4 weeks on 1 mg/week if additional glycemic control is needed.</p> <p><u>Reduction of risk of MACE in adults with established CV disease and who are obese or overweight:</u> Initially, 0.25 mg subcutaneously once weekly x 4 weeks, then 0.5 mg weekly x 4 weeks, then 1 mg weekly x 4 weeks, then 1.7 mg weekly x 4 weeks; maintenance dose of 2.4 mg (recommended) or 1.7 mg once weekly.</p> <p><u>Max dose:</u> 2 mg/week (T2DM), 2.4 mg/week (obesity)</p> <p><u>Renal Impairment:</u> No dosage adjustment needed.</p> <p><u>Hepatic impairment:</u> No dosage adjustment needed.</p>	<p>Adverse reactions: nausea, diarrhea, constipation, vomiting, abdominal pain, decreased appetite, dyspepsia, fatigue, anxiety</p> <ul style="list-style-type: none"> • Serious but less common: pancreatitis, acute kidney injury, retinopathy, cholelithiasis, AV block, angioedema, anaphylactoid reactions. • Note: Suicidal behavior and suicidal ideation have been reported in clinical trials with other incretin mimetics. Monitor for the emergence or worsening of depression, suicidal thoughts or behavior, and any unusual changes in moods or behaviors. Discontinue semaglutide in patients who develop suicidal thoughts or behaviors. Avoid in patients with a history of suicidal attempts or active suicidal ideation. <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Chloroquine, hydroxychloroquine, sulfonylureas, insulin delay in gastric emptying and potential to reduce the rate of absorption of concomitantly administered oral medications. • When initiating dulaglutide, consider reducing the dose of concomitantly administered insulin secretagogues (e.g., sulfonylureas) or insulin to reduce the risk of hypoglycemia. 	<p><u>Black Box Warning:</u> Semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in animal studies. Relevance in humans has not been determined.</p> <p><u>Contraindications:</u> personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2; serious hypersensitivity reaction to semaglutide or any components.</p> <p><u>Caution in the following:</u> Concomitant use with insulin secretagogues (e.g., sulfonylureas) or insulin; history of pancreatitis, diabetic retinopathy, gall bladder disease, cholelithiasis, renal impairment, hepatic impairment.</p> <p>When using concomitantly with insulin, administer as separate injections.</p> <p>Never mix them together. The two injections may be injected in the same body region, but the injections should not be adjacent to each other.</p>

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Treatment cont'd

MEDICATION	DOSING	ADVERSE EFFECTS DRUG INTERACTIONS	COMMENTS
Glucagon-like peptide-1 receptor agonist			
<p>Dulaglutide (Trulicity®)</p> <p>Injection soln: 0.75 mg/0.5 mL, 1.5 mg/0.5 mL, 3 mg/ 0.5 mL, 4.5 mg/0.5 mL</p> <p>\$\$\$\$\$</p>	<p><u>Reduction of cardiovascular mortality due to MACE in persons with T2DM with established CV disease or multiple CV risk factors:</u> Initially, 0.75 mg subcutaneously once weekly; increase dose to 1.5 mg for additional glycemic control; may further increase the dose by 1.5 mg/week after at least 4 weeks if additional glycemic control is needed.</p> <p><u>Max dose:</u> 4.5 mg weekly</p> <p>If a dose is missed, administer the missed dose as soon as possible if there are at least 3 days (72 hours) until the next scheduled dose.</p> <p>Inject subcutaneously in the abdomen, thigh, or upper arm.</p> <p>Rotate injection sites with each dose.</p> <p><u>Renal impairment:</u> No dose adjustment. Use with caution in patients with ESRD.</p> <p><u>Hepatic impairment:</u> No dose adjustments. Use with caution.</p>	<p><u>Adverse reactions:</u> nausea, diarrhea, constipation, vomiting, abdominal pain, decreased appetite, dyspepsia, fatigue.</p> <ul style="list-style-type: none"> • Serious but less common: pancreatitis, acute kidney injury, retinopathy, cholelithiasis, AV block, angioedema, anaphylactoid reactions. • <u>Note:</u> Suicidal behavior and suicidal ideation have been reported in clinical trials with other incretin mimetics. Monitor patients receiving dulaglutide for the emergence or worsening of depression, suicidal thoughts or behavior, and any unusual changes in moods or behaviors. <p><u>Drug interactions:</u></p> <ul style="list-style-type: none"> • Chloroquine, hydroxychloroquine, sulfonyleureas, insulin; dose-dependent delay in gastric emptying and potential to reduce the rate of absorption of concomitantly administered oral medications. • When initiating dulaglutide, consider reducing the dose of concomitantly administered insulin secretagogues (e.g., sulfonyleureas) or insulin to reduce the risk of hypoglycemia. 	<p><u>Black Box Warning:</u> Dulaglutide causes a dose-related and treatment duration dependent increase in incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure in animal studies. Relevance in humans has not been determined.</p> <p><u>Contraindications:</u> personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2; serious hypersensitivity reaction to dulaglutide or any components</p> <ul style="list-style-type: none"> • Not recommended in patients with preexisting severe GI disease, including severe gastroparesis. <p><u>Caution in the following:</u> Concomitant use with insulin secretagogues (e.g., sulfonyleureas) or insulin; history of pancreatitis, diabetic retinopathy, renal impairment, hepatic impairment, gall bladder disease, cholelithiasis.</p> <p>When using dulaglutide concomitantly with insulin, administer as separate injections.</p> <p>Never mix them together. The two injections may be injected in the same body region, but the injections should not be adjacent to each other.</p>

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MONITORING OVERVIEW

Regular follow-up is essential to long-term monitoring of symptoms, medication effectiveness, and potential complications.

CHANGE IN SYMPTOMS, FUNCTIONAL CAPACITY, OR EJECTION FRACTION

If a patient with CCD has an acute change in symptoms, please refer to the Acute Chest Pain Care Guide. For a patient with CCD who have a more gradual change in their symptoms or functional capacity, clinicians should intensify GDMT first, since GDMT optimization reduces major adverse cardiovascular events (MACE). If symptoms or functional capacity do not improve with intensification of GDMT, referral to a specialist is recommended for ischemia workup that will be useful to detect the presence and extent of ischemia, estimate the risk of MACE, and guide medical decision making. Imaging should be considered among patients with new-onset or persistent stable chest pain. For patients with CCD and frequent angina or severe stress-induced ischemia, angiography with possible revascularization may be recommended by the specialist to improve anginal symptoms, even though there is no reduction in MACE. Finally, in patients with CCD with clinical heart failure, newly reduced LVEF, or both, referral to a specialist is recommended for invasive coronary angiography (ICA) to assess coronary anatomy and guide potential revascularization.

Routine periodic anatomic or ischemic testing without a change in clinical or functional status is not recommended for risk stratification or to guide therapeutic decision-making in patients with CCD.

ANTIPLATELET THERAPY AND ORAL ANTICOAGULANTS

During follow up appointments, continue to weigh the benefits, risks, and alternatives of continued antiplatelet and/or anticoagulant therapy. Review the patient's medication list for drug-drug interactions (DDI), as well as use of NSAIDs at each visit. Inquire about easy bleeding or easy bruising and check the patient's weight as each visit. Order CBC and CMP every 6 months. For more information about anticoagulation, please refer to the [Anticoagulation Care Guide](#).

ANTIANGINAL THERAPY

After antianginal therapy is started, assess the severity and frequency of angina symptoms as well as functional capacity to guide management. Inquire about dizziness, lightheadedness, palpitations, shortness of breath, wheezing, fatigue, bilateral lower extremity edema, or other potential side effects of beta blocker therapy or CCB. Check the patient's heart rate and blood pressure, as well as a cardiac exam and a pulmonary exam at each visit. For patients with new, worsening, or more frequent angina symptoms, specialty referral to cardiology is advised. For patients who present with acute chest pain, HLOC may be required. Please refer to the [Acute Chest Pain Care Guide](#) for more information.

If a patient remains symptomatic after initiating antianginal therapy with either a beta blocker or a CCB, consider dose escalation to relieve angina symptoms or the addition of a long-acting nitrate to initial antianginal therapy. If a patient develops adverse effects from beta blocker therapy, switching to CCB may be indicated. Specialty referral to cardiology is advised for patients who have refractory angina despite GDMT and escalating antianginal therapy or for patients who require revascularization.

In patients with CCD who were initiated on beta blocker therapy for previous MI without current angina, LVEF $\leq 50\%$, arrhythmias, or uncontrolled hypertension, it may be reasonable to reassess the indication for long-term (>1 year) use of beta blocker therapy.

Beta blocker therapy should not be withdrawn abruptly but gradually tapered to avoid acute tachycardia, hypertension, exacerbations of angina, and/or ischemia. Warn patients against interruption or discontinuation of beta blocker therapy. When discontinuing chronically administered beta blocker therapy, gradually reduce the dosage over a period of 1 to 2 weeks and carefully monitor the patient. If angina markedly worsens or acute ischemia develops, reinstate beta blocker, at least temporarily, and take other measures appropriate for the management of unstable angina. For patients who present with acute chest pain, HLOC may be required. Please refer to the [Acute Chest Pain Care Guide](#) for more information.

Monitoring cont'd

LIPID MANAGEMENT

Once lipid-lowering drug therapy has started, check patient's fasting lipids:

- 1-3 months after starting treatment.
- 1-3 months after dose adjustment until within the therapeutic range.

Once patient has reached the appropriate/optimal lipid levels:

- Check fasting lipids every 12 months, unless there are adherence problems or other reasons for more frequent testing every 3 months, such as changes in therapy.

Measure total creatinine kinase levels (total CK) in patients with statin-associated muscle symptoms and/or objective muscle weakness. Measure transaminases (AST, ALT), total bilirubin, and alkaline phosphatase if there are symptoms suggesting hepatotoxicity. In patients with chronic, stable liver disease, including non-alcoholic fatty liver disease (NAFLD), check a baseline measurement of transaminases (AST, ALT), total bilirubin, and alkaline phosphatase, then schedule monitoring labs. An asymptomatic increase in transaminases more than 3 times the upper limit of normal is an infrequent statin-associated side effect that often resolved with dose reduction or rechallenge with an alternative statin. Severe statin-associated hepatotoxicity is rare and not impacted by routine monitoring of transaminases. Total CK and transaminase levels should NOT be routinely measured given the unlikely impact on clinical outcomes and the lack of established cost effectiveness. Total CK and transaminase levels should NOT be routinely measured given the unlikely impact on clinical outcomes and the lack of established cost effectiveness. For more information on lipid management, please refer to the [Dyslipidemia Care Guide](#).

BLOOD PRESSURE MANAGEMENT

Appropriate follow-up and monitoring enable assessment of adherence and response to therapy, help identify adverse responses to therapy and target organ damage and allow assessment of progress toward treatment goals. Patients with CCD on a new or adjusted antihypertensive regimen should have monthly follow-up until BP control is achieved, which is defined as a BP target of <130/80 mmHg. One BP is controlled, a patient with CCD should follow up every 3-6 months.

Monitoring involves:

- Repeat BP measurement to assess response to therapy.
- Detection of orthostatic hypotension in older patients or those with postural symptoms
- Identification of white coat effect
- Documentation of adherence to therapy or drug-associated side effects
- Documentation of adverse effects
- Reinforcement of therapeutic lifestyle intervention and medication adherence
- Adjustment of medication dosage, if clinically indicated. For example, in patients with CCD who were initiated on beta blocker therapy for previous MI without a history of or current angina, LVEF \leq 50%, arrhythmias, or uncontrolled hypertension, it may be reasonable to reassess the indication for long-term (>1 year) use of beta blocker therapy.
- Laboratory testing, such as CMP for electrolytes, renal function, and other assessment for target organ damage

If the patient presents with symptoms and/or signs of target organ damage, such as acute chest pain or worsening/more frequent angina symptoms, in the setting of SBP \geq 180 mmHg or DBP \geq 120 mmHg, consider transferring patient to HLOC. For more information on acute chest pain, please refer to the [Acute Chest Pain Care Guide](#). For more information on hypertension, please refer to the [Hypertension Care Guide](#).

PATIENT ADHERENCE

Despite the well-documented benefits from GDMT as detailed above, patient adherence to therapy is frequently challenged by adverse effects, so it is important to discuss these with each patient prior to prescribing. Ongoing communication is integral to patient care, as is regular monitoring to check for adherence, adequacy of response, new symptoms, and reaffirmation of benefit.

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Patient Education/Self-Management

Coronary Artery Disease

What You Should Know

What is coronary artery disease? (Also called “coronary heart disease”)

- Coronary artery disease is a condition that puts you at risk for heart attack and other forms of heart disease.
- In people who have coronary artery disease, the arteries that supply blood to the heart get clogged with fatty deposits.

What are the symptoms of coronary artery disease?

Many people have no symptoms. For those who do, the most common symptoms usually with exercise. They can include:

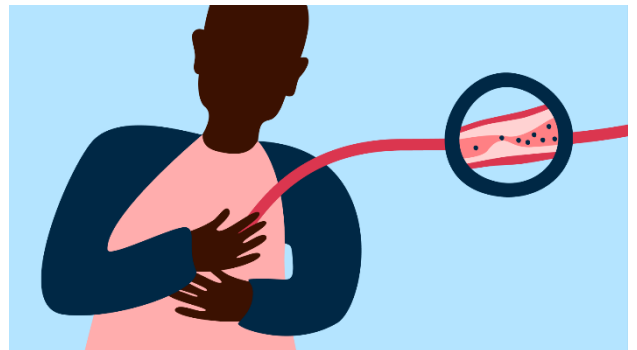
- Pain, pressure, or discomfort in the center of the chest – This type of chest pain called "angina."
- Pain, tingling, or discomfort in other parts of the upper body – This might include the arms, back, neck, jaw, or stomach.
- Feeling short of breath.



What are the symptoms of a heart attack?

The first symptom of coronary artery disease can be a heart attack. That's why it is so important to know how to spot a heart attack. The symptoms of a heart attack can include:

- Pain, pressure, or discomfort in the center of the chest
- Pain, tingling, or discomfort in other parts of the upper body, including the arms, back, neck, jaw, or stomach.
- Shortness of breath
- Nausea, vomiting, burping, or heartburn
- Sweating or cold, clammy skin
- Racing or uneven heartbeat
- Feeling dizzy or lightheaded



Contact your health care team IMMEDIATELY if you have these symptoms concerning for a heart attack.

Is there a test for coronary artery disease?

Your health care provider may check your lipids/cholesterol level, other blood tests, and one or more of the following tests:

- Electrocardiogram (“ECG”): This test measures the electrical activity of your heart
- Stress test: This is also called an exercise test. For this test, you may be asked to run or walk on a treadmill while you also have an ECG. Exercise increases the heart’s need for blood. This test checks if the heart is getting enough blood. If you cannot walk or run, a different type of stress test can be done with a medicine that makes your heart pump faster.
- Echocardiogram: This test uses sound waves to create an image of your heart as it beats
- Cardiac catheterization (“cardiac cath”): During this test, the heart doctor puts a thin tube into a blood vessel in your leg or arm. Then, they move the tube to your heart. Next, the doctor puts a dye that show on x-ray. This part of the test is called “coronary angiography”. It shows whether any of the arteries of your heart are clogged.



How is coronary artery disease treated?

The main treatments for coronary artery disease are:

Lifestyle changes to lower your risk of heart attack:

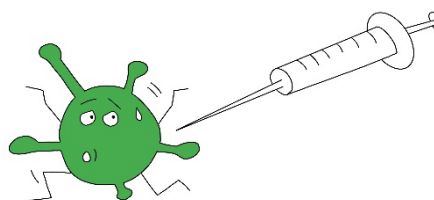
- Exercise
- Lose weight if you are overweight or obese.
- Stop smoking.
- Eat more vegetables and fruits.
- Reduce fat in your diet. Limit meat, milk, eggs, butter, cheese, packaged food, and snack items like cookies, crackers, or chips.



Medicines to treat coronary artery disease are very important. Some medicines lower your risk of heart attack and can help you live longer. Take your medications every day, as instructed. You should also get blood tests recommended by your provider to make sure the medicines are at the best dose for your body.

Your provider may prescribe:

- Medicines called “statins”, which lower cholesterol
- Medicines to lower blood pressure
- Aspirin or other medicines to prevent blood clots.
- Medicines to relieve chest pain or “angina” caused by coronary artery disease, such as “beta blockers”, “calcium channel blockers”, “nitrates”, or others.
- Medicines to treat diabetes if you have diabetes.
- Medicines to treat heart failure if you have heart failure.



Your provider may send you to a heart doctor, who may recommend stenting to open the vessels of the heart or “bypass surgery” to re-route blood around a clogged artery, if needed.

You should also get a flu vaccine every year because this lowers the risk of death. Other recommended vaccines to lower the risk of death are the coronavirus disease 2019 (COVID-19) vaccine and a pneumococcal vaccine. Ask your primary care provider if you’re due to get these vaccines.

Educación/Autogestión del Paciente

Enfermedad coronaria

Lo que debe saber

¿Qué es la enfermedad coronaria? (También conocida como "cardiopatía isquémica")

- La enfermedad coronaria es una condición que le pone en riesgo de sufrir un infarto y otras enfermedades del corazón.
- Las personas que padecen enfermedad coronaria tienen las arterias encargadas de llevar la sangre al corazón obstruidas por depósitos de grasa.

¿Cuáles son los síntomas de la enfermedad coronaria?

Muchas personas no experimentan síntomas. Pero aquellas que sí, generalmente los presentan cuando se ejercitan. Entre los síntomas más comunes encontramos:

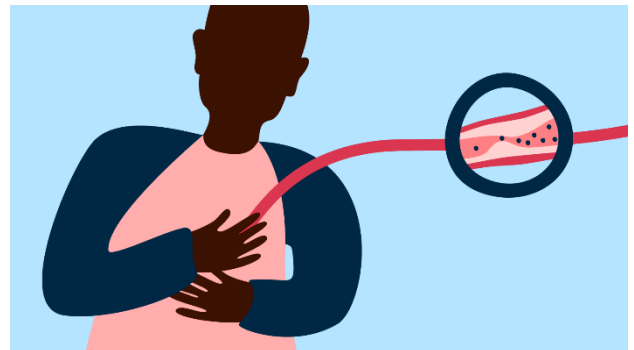
- Dolor, presión o molestia en el centro del pecho: este tipo de dolor de pecho se conoce como "angina."
- Dolor, hormigueo o molestia en otras partes de la parte superior del cuerpo: incluyendo los brazos, la espalda, el cuello, la mandíbula y el estómago.
- Falta de aliento.



¿Cuáles son los síntomas de un infarto?

El primer síntoma de enfermedad coronaria puede ser un infarto. Por ello es muy importante saber cómo detectar un infarto. Entre los síntomas de infarto tenemos:

- Dolor, presión o molestia en el centro del pecho
- Dolor, hormigueo o molestia en otras partes de la parte superior del cuerpo, incluyendo los brazos, la espalda, el cuello, la mandíbula o el estómago.
- Falta de aliento
- Náuseas, vómito, eructos o acidez estomacal
- Sudoración o escalofríos, piel sudorosa
- Ritmo cardíaco acelerado o irregular
- Sensación de mareo o posible desmayo



Si presenta estos síntomas relacionados con un infarto, contacte INMEDIATAMENTE a su equipo de atención médica.

¿Existe algún análisis para detectar la enfermedad coronaria?

Su proveedor de atención médica podría revisar sus niveles de triglicéridos o colesterol, entre otras pruebas sanguíneas, y ordenar uno o más de las siguientes pruebas:

- Electrocardiograma ("ECG"): En esta prueba se mide la actividad eléctrica de su corazón
- Prueba de estrés: También se le conoce como prueba de esfuerzo. En esta prueba se le podría pedir que corra o camine en una caminadora al mismo tiempo que se le hace un ECG. El ejercicio aumenta la demanda de sangre por parte del corazón. Este estudio confirma si el corazón está recibiendo suficiente sangre. Si no puede caminar o correr, se le podría hacer otro tipo de prueba de estrés con un medicamento que hace que su corazón bombee más rápido.
- Ecocardiograma: Esta prueba emplea ondas acústicas para crear una imagen de su corazón mientras está latiendo
- Cateterismo cardíaco ("catéter arterial"): Durante esta prueba, el cardiólogo le coloca un tubo delgado dentro de un vaso sanguíneo de su brazo o pierna. Después, se mueve el tubo hacia su corazón. A continuación, el doctor introduce un medio de contraste para rayos x. Esta parte del estudio se llama "angiografía coronaria". Nos muestra si alguna de las arterias de su corazón está obstruida.



¿Cuál es el tratamiento de la enfermedad coronaria?

Los principales tratamientos para la enfermedad coronaria son los siguientes:

Cambios en el estilo de vida para disminuir su riesgo de infarto:

- Ejercitarse
- Perder peso, si tiene sobrepeso y obesidad.
- Dejar de fumar.
- Comer más frutas y vegetales.
- Cambiar a una dieta baja en grasas. Limitar el consumo de carne, leche, huevos, mantequilla, queso, alimentos procesados y botanas como galletas, crackers y papitas.



Las medicinas para el tratamiento de la enfermedad coronaria son muy importantes. Algunos medicamentos disminuyen su riesgo de sufrir un infarto y pueden ayudarle a tener una vida más larga. Tome sus medicinas todos los días, tal y como se le indique. También debe hacerse los análisis de sangre recomendados por su médico para asegurar que las medicinas se están administrando en la dosis correcta para su organismo. Su médico podría recetarle:

- Medicamentos llamados "estatinas", cuya función es bajar el colesterol
- Medicamentos para bajar la presión arterial
- Aspirina u otros medicamentos para prevenir la formación de coágulos sanguíneos.
- Medicamentos para aliviar el dolor de pecho o "angina" causado por la enfermedad coronaria, tales como "beta bloqueadores", "inhibidores de los canales de calcio", "nitratos", entre otros.
- Medicamentos para el tratamiento de la diabetes, si la padece.
- Medicamentos para el tratamiento de la insuficiencia cardíaca, si la padece.

De ser necesario, su proveedor podría enviarle con un cardiólogo, quien podría recomendarle un stent (endoprótesis) para abrir los vasos sanguíneos del corazón, o una "cirugía de bypass" para desviar el flujo sanguíneo por encima de una arteria obstruida.

También debe aplicarse la vacuna de la gripe cada año, ya que esta disminuye su riesgo de muerte. Otras vacunas recomendadas para disminuir su riesgo de muerte son la vacuna para la enfermedad por coronavirus 2019 (COVID-19) y una vacuna antineumocócica. Pregunte a su proveedor de atención primaria si es momento de que le administren esas vacunas.

