

Pharmacotherapy for Cardiovascular Diseases in Primary Care

VA/DoD Medications Used in the Management of Cardiovascular Diseases in Primary Care			
DRUG ^a	ORAL DOSE	POTENTIAL SIDE EFFECTS	PRECAUTIONS/CONTRAINDICATIONS/COMMENTS
ANTIPLATELET/ANTICOAGULANT			
Aspirin ^b	UA/MI 160 mg-325 mg (1 st dose) Chronic 81 mg-325 mg qd	<ul style="list-style-type: none"> • GI intolerance: dyspepsia, nausea, GI bleeding, heartburn • Bronchospasm: prominent in patients with a history of asthma and nasal polyps • Tinnitus • Thrombocytopenia 	<ul style="list-style-type: none"> • ASA hypersensitivity: bronchospasm, angioedema, and anaphylaxis • Active, severe bleeding • Clopidogrel should be used in patients who are unable to take ASA
Clopidogrel ^{b,c,d}	NSTE-ACS 300 mg oral load then 75 mg qd for at least 1 month & up to 9 months with elective PCI Post stent 300 mg oral load then 75 mg qd at least 1 month & up to 12 months Non acute conditions 75 mg qd May be given with aspirin (81-325 mg) unless aspirin is contraindicated or not tolerated	<ul style="list-style-type: none"> • Thrombotic thrombocytopenic purpura rarely reported (sometimes after less than 2 weeks exposure) • Bleeding • GI intolerance: diarrhea • Clopidogrel increases risk of major bleeding (i.e., requiring transfusion of ≥ 2 units) when combined with ASA 	<ul style="list-style-type: none"> • History of bleeding diathesis • Chest pain without ECG changes in whom etiology of chest pain is unlikely to be ischemic in origin • Known hypersensitivity to ticlopidine, due to cross reactivity or any component of the product • Known hypersensitivity to clopidogrel or any component of the product • Active pathological bleeding (GI bleeding and intracranial hemorrhage) • Withhold clopidogrel for 5-7 days prior to elective CABG or other major surgical intervention
Warfarin ^{b,c}	Prevent systemic embolization: INR 2-3 Prevent recurrent MI within first 3 months: INR 2.5-3.5	<ul style="list-style-type: none"> • Bleeding (e.g., GU/GI) • Skin necrosis 	<ul style="list-style-type: none"> • Pregnancy • Hemophilia • Cerebrovascular hemorrhage • History of warfarin induced skin necrosis • Vitamin K may decrease anticoagulant response; patient should be instructed on importance of consistent dietary intake of vitamin K
CARDIOVASCULAR			
ACE Inhibitors			
Captopril ^{b,c} Enalapril ^b Fosinopril ^b Lisinopril ^{b,c} Ramipril ^{b,c,d}	12.5–150 mg/day (divided bid-tid) 2.5–20 mg/day (divided qd-bid) 5–40 mg qd 2.5–40 mg qd 2.5–10 mg/day (divided qd-bid; qd for prevention of cardiovascular events)	<ul style="list-style-type: none"> • Hypotension, hyperkalemia, acute renal impairment, angioedema, cough • Monitor K⁺ and renal function 	<ul style="list-style-type: none"> • Avoid in 2nd and 3rd trimesters of pregnancy due to possible fetal and neonatal morbidity and death • Hypersensitivity • Bilateral renal artery stenosis • Renal failure; use ACEI with caution in patients sCr >3.0 mg/dL • Take captopril 1 hr prior to food ingestion • Concomitant therapy with K⁺-sparing diuretics and/or K⁺ supplements may result in hyperkalemia

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Angiotensin II Receptor Blockers^{d,e} Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan	4-32 mg/day (divided qd-bid) 400-800 mg/day (divided qd-bid) 75-300 mg qd 25-100 mg/day (divided qd-bid) 5-40 mg qd 20-80 mg qd 80-320 mg qd	<ul style="list-style-type: none"> Hypotension, hyperkalemia, acute renal impairment, angioedema, dyspnea Less incidence of cough than ACEIs Monitor K⁺ and renal function 	<ul style="list-style-type: none"> Avoid in 2nd and 3rd trimesters of pregnancy due to possible fetal and neonatal morbidity and death Hypersensitivity Bilateral renal artery stenosis Renal failure Alternative to ACEIs in patients who cannot tolerate ACEIs Concomitant therapy with K⁺-sparing diuretics and/or K⁺ supplements may result in hyperkalemia Losartan/valsartan reported to ↑ reabsorption of lithium; monitor levels and for signs of toxicity Telmisartan may ↑ peak and trough digoxin levels by 49% and 20%, respectively; monitor trough digoxin levels at steady-state
β-Blockers Propranolol ^b Atenolol ^{b,c} Metoprolol IR ^{b,c} Metoprolol XL ^{b,d} Alpha-beta blocker Carvedilol ^{b,d}	IR: 40-480 mg/day (divided qd-bid) SR: 80-160 mg qd 25mg-100 mg qd (may require 200 mg qd for angina) 50-300 mg/day (divided qd-bid) (6.25-100 mg bid for HF) 50-400 mg qd (12.5-200 mg qd for HF) 3.125-25mg bid (patients ≥ 85kg may be titrated to 50mg bid with caution)	<ul style="list-style-type: none"> Bradycardia, hypotension, fatigue, insomnia, depression, sexual dysfunction, cold extremities, masking of hypoglycemia, nightmares/vivid dreams Wheezing and dyspnea seen with larger doses 	<ul style="list-style-type: none"> Sinus bradycardia SBP < 90mmHg 2nd or 3rd degree heart block Cardiogenic shock Severe bronchospastic disease Sick sinus syndrome Overt, decompensated HF May cause growth retardation in 1st trimester Discontinue with slow taper over 1 wk Verapamil/diltiazem may potentiate pharmacologic effects of β-blockers; additive effects on cardiac conduction Adjust dose of atenolol in chronic kidney disease
Calcium Channel Blockers Diltiazem IR ^{b,c} Diltiazem SR ^{b,c} Verapamil IR ^{b,c} Verapamil SR ^{b,c} Dihydropyridines Amlodipine ^{b,d} Felodipine ^{b,d} Nifedipine SR ^{b,c}	90-360 mg/day (divided tid-qid) 120-540 mg qd 120-360 mg/day (divided bid-tid) 120-480 mg/day (divided qd-bid) 2.5-10 mg qd 2.5-10 mg qd 30-120 mg qd (manufacturer max=90 mg qd)	<ul style="list-style-type: none"> Verapamil may cause constipation DHPs may cause ankle edema, dizziness, flushing, headache 	<ul style="list-style-type: none"> CCBs should be used with caution in patients with HF Diltiazem & verapamil may decrease heart rate, cause heart block and/or are contraindicated in AV node dysfunction (2nd or 3rd degree heart block), systolic HF and decreased LV function Use all CCBs with caution in patients with liver dysfunction; use diltiazem & verapamil with caution in patients with impaired kidney function Verapamil/diltiazem may potentiate pharmacologic effects of β-blockers; additive effects on cardiac conduction Short-acting nifedipine should be avoided due to its potential to precipitate acute and life-threatening hypotension
Diuretics Furosemide ^{b,c} (primarily for HF) Chlorthalidone Hydrochlorothiazide ^{b,c} HCTZ/Triamterene ^{b,c} Spironolactone ^{b,c} (primarily for HF)	20-400 mg/day (consider dividing bid if dose > 160 mg/day) 12.5-25 mg qd (max=50 mg/day) 12.5-25 mg qd (max=50 mg/day) 25/37.5-50 mg/75mg qd 12.5-25 mg qd (max 50 mg qd, use with caution due to hyperkalemia)	<ul style="list-style-type: none"> Hypokalemia, hyperuricemia, hypochloremic alkalosis, dilutional hyponatremia Spironolactone: hyperkalemia, gynecomastia, GI intolerance, hyperchloremic metabolic acidosis 	<ul style="list-style-type: none"> Monitor potassium levels for diuretic induced hypokalemia K⁺-sparing diuretics, K⁺ supplements may cause ↑ K⁺ Diuretic-induced hyperuricemia does not require treatment in the absence of gout or kidney stones Thiazide diuretics may ↑ TC and ↑ TG, although these effects may be transient Thiazide diuretics may ↑ lithium reabsorption; ↓ lithium dose by 50%
Centrally Acting Clonidine Tablet ^{b,c} Clonidine Patch ^b Methyldopa ^b	0.1-0.8 mg/day (divided bid-tid) (max can be up to 2.4 mg/d) 0.1-0.6 mg patch weekly 500 mg-3g/day (divided bid-qid doses)	<ul style="list-style-type: none"> Drowsiness, dry mouth May exacerbate depression 	<ul style="list-style-type: none"> Taper dose to discontinue Clonidine patches are costly but may be useful in selected patients. Full effect of clonidine patch may not be evident until several days after it is first placed

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Peripherally Acting Reserpine ^b	0.05-0.25 mg qd	<ul style="list-style-type: none"> Sedation, nightmares, tremors, nasal congestion, activation of peptic ulcer May exacerbate depression 	<ul style="list-style-type: none"> Active PUD, ulcerative colitis, history gallstones Depression with suicidal tendencies May cause a hypertensive reaction when initiated in patients on a MAOI
Vasodilators Minoxidil ^b Hydralazine ^{b,c}	5-40 mg/day (divided qd-bid) (max=100 mg/day) 30-200 mg/day (divided bid-qid)	<ul style="list-style-type: none"> Hypertrichosis, edema, and pericardial effusions with minoxidil Headache, edema and SLE (dose-related) with hydralazine 	<ul style="list-style-type: none"> Direct-acting vasodilators do not reduce LV hypertrophy Should be used with a diuretic and β-blockers to reduce edema and reflex tachycardia Hydralazine used in combination with ISDN for HF
Alpha-blockers Doxazosin ^{b,d} Prazosin ^{b,d} Terazosin ^{b,d}	1-4 mg qd (max=16 mg/d) 1-15 mg/day (divided bid-tid) (max=20 mg/d) 1-5 mg qd (max=20 mg/d)	<ul style="list-style-type: none"> First-dose syncope, dizziness Tachyphylaxis 	<ul style="list-style-type: none"> Initiate at low doses (1 mg) with 1st dose given at bedtime to avoid syncope
Nitrates Nitroglycerin SL tab ^{b,c} or spray ^c ISDN ^{b,c} ISDN ER ISMN conventional ISMN ER ^b Nitroglycerin patch ^b Nitroglycerin ointment ^b	0.4 mg tab (or 1-2 sprays) SL at time of chest pain (or prophylaxis), q 5 min up to 3 doses 10-120 mg (divided bid-tid) (up to 160 mg used in combination w/hydralazine for HF) 40 mg bid 10-20 mg bid 30-120 mg qd 2.5-20 mg/24 hrs topically qd (remove at hs) 1/2-5 inches topically q 8 hrs	<ul style="list-style-type: none"> Persistent transient headache (may be severe) Postural hypotension, syncope Transient flushing Allergic contact dermatitis is rare with topical preparations 	<ul style="list-style-type: none"> Allow nitrate-free interval of 10-12 hours to prevent tolerance (e.g., dose tid at 7am, 12pm, 5pm) Use with caution in SBP < 90 mmHg Contraindicated in conjunction with sildenafil Contraindicated in severe anemia Use with caution in patients with increased intracranial pressure Avoid nitrates with right ventricular infarction
Digoxin Digoxin ^{b,c}	0.0625-0.375 mg qd (usual dose 0.125-0.25 mg qd to achieve goal of 0.5-1.0 ng/ml)	<ul style="list-style-type: none"> Signs of toxicity include nausea, confusion, abdominal pain, diarrhea, visual disturbances, arrhythmias, bradycardia, fatigue, anorexia, headache 	<ul style="list-style-type: none"> Avoid in hypertrophic obstructive cardiomyopathy Caution with AV block, ventricular arrhythmias Verapamil/diltiazem may \uparrow digoxin levels 20-70% Telmisartan may \uparrow peak and trough digoxin levels by 49% and 20%, respectively; monitor trough digoxin levels at steady-state Diuretics may induce hypokalemia which may \uparrow risk of digitalis toxicity
LIPID-LOWERING			
Statins Atorvastatin ^d Fluvastatin ^{b,d} Lovastatin ^b Pravastatin ^d Simvastatin ^{b,c}	10-80 mg qd 20-80 mg/day (divided qpm-bid) XL 80mg qpm 10-80 mg qpm with food (80 mg given as 40 mg bid) 10-80 mg qpm 5-80 mg qpm	<ul style="list-style-type: none"> Abdominal pain, constipation, diarrhea, dyspepsia, nausea, myopathy (<0.2%; 5% in combination with gemfibrozil; 2% in combination with niacin), rhabdomyolysis Increase in LFTs >3 x the upper limit, and CPKs >10 x the upper limit 	<ul style="list-style-type: none"> Hypersensitivity Caution in hepatic disease LFT monitoring is recommended by drug manufacturers - within 3 months of initiation or changing dose, and then periodically Avoid in pregnant/lactating women Caution in severe renal impairment, use lowest dose in moderate renal impairment Evening/bedtime dosing may improve efficacy Increased risk for myopathy when any statin is combined with fibrates or niacin (≥ 1 gm daily). The risk is also increased if combining atorvastatin, lovastatin or simvastatin with potent inhibitors of CYP 3A4 (azole antifungals, macrolide antibiotics, immunosuppressives, protease inhibitors or delavirdine, grapefruit juice, nefazodone, diltiazem, verapamil, or amiodarone).

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LIPID-LOWERING			
Bile Acid Resins			
Colestipol powder ^b	5-30 gm/day (divided qd-tid)	<ul style="list-style-type: none"> Nausea, bloating, constipation, flatulence May ↑ TG 	<ul style="list-style-type: none"> Complete biliary obstruction Caution if active PUD due to GI irritation Best tolerated 2-5 gm bid; usual effective dose 8-10 gm/d Take other medications 1 hr prior or 4 hr after resin
Colestipol tablets ^{b,c}	2-16 gm/day (divided qd-tid)		
Fibrates			
Gemfibrozil ^{b,c}	600 mg bid AC	<ul style="list-style-type: none"> GI symptoms, nausea, vomiting, diarrhea, rash, hepatitis, gallstones, and myositis 	<ul style="list-style-type: none"> Gallbladder disease Monitor ALTs throughout therapy; contraindicated in hepatic disease Reduce dose in modest renal insufficiency; contraindicated in severe renal dysfunction Risk of myopathy with statin Monitor INR; may need to adjust warfarin dosage to prevent bleeding complications
Niacin			
Niacin ER ^{b,c}	500 mg-2 gm qd hs (use titration pack)	<ul style="list-style-type: none"> Flushing, blurred vision, GI distress, itching, headache, hepatotoxicity, hyperglycemia, hyperuricemia 	<ul style="list-style-type: none"> Hepatic disease; persistent elevation of LFTs Monitor ALTs at baseline; 6 weeks after start or dosage change; monitor every 6-12 months thereafter Active PUD Arterial bleeding Causes glucose intolerance; caution in established or borderline DM Decreases urinary secretion of uric acid, caution with gout If CrCl is 10-50 ml/min give 50% of dose; if <10 ml/min give 25% Take with food to avoid flushing or GI upset
Niacin IR ^b	1.5-3 gm/day (divided tid) Start IR 50-100 mg bid-tid, ↑ dose by 300 mg/day per week		

ACEI=angiotensin-converting enzyme inhibitors; ACS=acute coronary syndrome; ALT=alanine aminotransferase; ASA=aspirin; AST=aspartate aminotransferase; AV=atrioventricular; BPH=benign prostatic hyperplasia; CCB=calcium channel blocker; CPK=creatine phosphokinase; CrCl=creatinine clearance; CYP 3A4=cytochrome P450 3A4 isoenzyme; DHP=dihydropyridine; DM=diabetes mellitus; ECG=electrocardiogram; ER=extended release; GI=gastrointestinal; GU=genitourinary; HF=heart failure; HTN=hypertension; INR=internal normalized ratio; IR=immediate release; ISDN=isosorbide dinitrate; ISMN=isosorbide mononitrate; K+=potassium; LFT=liver function tests; LV=left ventricular; MAOI=monoamine oxidase inhibitor; MI=myocardial infarction; NNT=number needed to treat; NYHA=New York Heart Association; PUD=peptic ulcer disease; SBP=systolic blood pressure; sCr=serum creatinine; SL=sublingual; SLE=systemic lupus erythematosus; SR=sustained-release; TC=total cholesterol; TG=triglycerides; UA/MI=unstable angina/myocardial infarction; XL=extended release

^a Partial list

^b VA National Formulary item

^c DoD Basic Core Formulary item

^d VA criteria for use (refer to www.vapbm.org)

^e DoD Place In Therapy (PIT) guide (www.pec.ha.osd.mil)