New Lipid Lowering Medications

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PCSK9 Inhibitors Lipid Medications

Proprotein convertase subtilisin/kexin type 9

	Alirocumab (Profluent)	Evolocumab (Repatha)
FDA-approved indications	Primary hyperlipidemia (HLD) • Homozygous familial hypercholesterolemia (HoFH) • Secondary prevention of cardiac events	
Dosing	• **HoFH**: 150 mg SC q2 weeks • **HLD or secondary cardiac prevention**: 75 mg SC q2 weeks or 300 mg SC q4 weeks; if adequate LDL response not achieved, may increase to max of 150 mg q2 weeks	• **HoFH**: 420 mg SC q4 weeks; may increase to 420 mg q2 weeks if meaningful response not achieved in 12 weeks • **HLD or secondary cardiac prevention**: 140 mg q2 weeks or 420 mg q4 weeks
Dosage forms	• Auto-injector 75 mg/mL or 150 mg/mL	• Repatha Sure Click (auto-injector) 140 mg/mL • Repatha Pushtronex System (single use infusor with pre-filled cartridge) 420 mg/3.5 mL – administered over 9 minutes
Storage	• Store in refrigerator in outer carton until used • Once used, keep at room temperature, use within 30 days	
Injection clinical pearls	• Do not shake or warm with water • Administer by SC injection into thigh, abdomen, or upper arm • Rotate injection site with each injection	
Drug interactions	• No known significant interactions	
Monitoring parameters	• Lipid panel before initiating therapy, 4-12 weeks after initiating, and q3-12 months thereafter	
Side effects	• Injection site reaction (4-17%) • Hypersensitivity reaction (9%) • Influenza (6%) • Myalgia (4-6%) • Diarrhea (5%)	• Nasopharyngitis (6-11%) • Upper respiratory tract infection (9%) • Diabetes mellitus (9%) • Influenza (8-9%) • Injection site reaction (6%) • Myalgia (4%)

Adenosine Triphosphate-citrate Lyase - ACL Inhibitor

Indicated for adults with heterozygous familiar hypercholesterolemia or established ASCVD who require additional LDL lowering. Use with maximally tolerated statins for further LDL reduction. Available in a combination pill with ezetimibe. The effects on CV morbidity and mortality have not yet been determined.

Class / Action	Generic / Trade Name	Daily Dose	Frequency	Considerations
Lowers LDL cholesterol by inhibiting production in the liver.	**Bempedoic acid / Nexletol** **Bempedoic acid/ezetimibe (Nexlizet)**	**180 mg** **180 mg /10mg**	**Once daily**	May increase uric acid levels- use caution in gout. May take with or without food. No dose adjustment for renal or hepatic impairment.

**indicates medication is available in generic form.*

New nonsteroidal MRAs for Type 2 and Chronic Kidney Disease

Nonsteroidal Selective Mineralcorticoid Antagonist

Indicated for people with chronic kidney disease (CKD) associated with Type 2 diabetes. Reduces the risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks, and hospitalization for heart failure in adults with chronic kidney disease associated with type 2 diabetes.

Class / Action	Generic / Trade Name	Daily Dose	Frequency	Considerations
Nonsteroidal, selective mineralcorticoid antagonist. Blocks mineralcorticoid receptor mediated sodium reabsorption and mineralcorticoid overactivation in epithelial (for example kidneys) and nonepithelial (for example heart, blood vessels) tissues.	**Finerenone / Kerendia**	**10-20 mg**	**Once daily**	Monitor potassium 4 weeks after initiation or dose adjustment (although impact on potassium is much less than non-slective mineralcorticoid antagonists like spironolactone). Since CYP3A4 substrate, avoid taking with strong cype3A4 inhibitors; avoid grapefruit or grapefruit juice. May take with or without food.

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Antihypertensive Medications

ACE and ARBs are preferred therapy if experiencing hypertension and albuminuria – If B/P not at goal with either of these agents, add a diuretic or other class. Do not use during pregnancy or in persons w/ renal or hepatic dysfunction. Start w/ low dose, gradually increase. If one class is not tolerated, the other should be substituted. For those treated with an ACE inhibitor, angiotensin receptor blocker, or diuretic, serum creatinine/estimated glomerular filtration rate and serum potassium levels should be monitored at least annually. ADA Standards CV Disease Risk Management

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
ACE Inhibitors Angiotensin Converting Enzyme **Action -** Block the conversion of AT-I to AT-II. Also stimulates release of nitric oxide causing vasodilation.	benazepril / Lotensin†	10 – 40 mg	1 x a day	Try to take same time each day. Effects seen w/in 1 hr of admin, max effects in 6 hrs. **Side effects**: Can cause cough (due to increased bradykinin) – can try different med in same class. Also can cause fatigue, dizziness, hypotension. **†**These meds are also available as a combo w/ low dose HCTZ (hydrochlorothiazide). **‡**These meds are also available as a combo w/ CCB (calcium channel blocker) usually amlodipine
	captopril /Capoten*†	12.5 - 100 mg	2-3 x a day	
	Enalopril/ Vasotec*†	2.5 - 40 mg	1-2 x a day	
	Fosinopil / Monopril†	10- 40 mg	1 x a day	
	Lisinopril *† Prinivil Zestril	 10 – 40 mg 10 - 40 mg		
	Ramipril / Altace*†	2.5 – 10 mg		
	Moexipril / Univasc†	3.75 - 15 mg		
	Perindopril/Aceon‡ Perindopril/ Indapamide combo (Coversyl)	2-16 mg 2 - 8 mg 0.625 - 2.5 mg		
	Quinapril /Accupril†	5 – 40 mg		
	Trandolapril/ Mavik Trandolapril/ Verapamil combo (TARKA)	1.0 – 4 mg 1-4 mg 180 to 240 mg		
ARBs -Angiotensin Receptor Blockers **Action -**Block AT-I receptor which reduces aldosterone secretion and vasoconstriction	Azilsartan/Edarbi Azilsartan/ Chlorthalidone combo (Edarbyclor)	40 - 80 mg 40 mg 12.5 - 25 mg	1 x daily	Try to take same time each day **Side effects**- Can cause dizziness, drowsiness, diarrhea, hyperkalemia, hypotension**.** **†**These meds are also available as a combo w/ low dose HCTZ (hydrochlorothiazide). **‡**These meds are also available as a combo w/ CCB (calcium channel blocker) usually amlodipine
	Candesartan/Atacand†	8 – 32 mg		
	Eprosartan/Teveten†	400 - 600 mg		
	Irbesartan/ Avapro†	75 – 300 mg		
	Losartan / Cozaar*†	25 – 100 mg		
	Olmesartan / Benicar†‡ Tribenzor (triple combo)	20 – 40 mg		
	Telmisartan / Micardis	20 – 80 mg		
	Valsartan / Diovan†‡ Exforge HCT (triple combo) Valsartan/ Nebivolol combo (Byvalson)	80 – 320 mg 80 mg 5 mg		

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Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
DRIs - Direct Renin Inhibitors -	Aliskiren / Tekturna†	150 – 160 mg	1 x daily	Generally well tolerated. †These meds are also available as a combo w/ low dose HCTZ (hydrochlorothiazide).

Beta Blockers are commonly prescribed as an add-on to other B/P meds for people with DM. Beta Blockers are beneficial for persons w/ concurrent cardiac problems and prevention of recurrent MI and heart failure. Caution in DM since Beta Blockers can cause hyperglycemia and mask hypoglycemia induced tachycardia (but do not block hypoglycemia related dizziness and sweating). Monitor B/P, heart rate, lipids and glucose.

Beta Blockers *β1- Selective* **Action:** Blockade β1 receptors & reduce cardiac output & kidney renin activation.g	Acebutolol / Sectral*	200 – 800 mg	2 x daily	Side Effects: Usually CNS related including sedation, dizziness, lightheaded . Watch for bradycardia, hypotension, depression and sexual dysfunction. Check heart rate each visit, adjust dose if HR <50. Can cause heart block – review package insert for drug-drug interactions. Watch for exercise intolerance. When stopping beta blockers, taper dose gradually. Use cautiously at lowest dose. †These meds are also available as a combo w/ low dose HCTZ (hydrochlorothiazide).
	Atenolol / Tenormin*	25 – 100 mg	1 x daily	
	Atenolol with Chlorthalidone/ Tenoretic	50 -100 mg 25 mg	1 x daily 1 x daily	
	Betaxolol / Kerlone	5 – 10 mg	2 x daily	
	Bisoprolol/ Zebeta†	2.5 – 10 mg		
	Metoprolol tartate/Lopressor*†	25 – 100 mg	1 x daily	
	Metoprolol succinate / Toprol XL	25 - 100 mg		
	Nebivolol/Bystolic	5 to 40 mg		
	Nebivolol with Valsartan/ Byvalson	5 mg 80 mg		
Beta Blockers *Non Selective* **Action**: Blockades β1 & β2	Nadolol / Corgard*	40 - 120 mg	1 x daily	
	Nadolol with Bendroflumethiazide	40-80 mg 5 mg		
	Penbutolol / Levatol	10 - 40 mg	1 x daily	
	Pindolol / Visken	10 – 40 mg	2 x daily	
	Propanolol / Inderal*	40 – 160 mg	2 x daily	
	Inderal LA (extended)	60 – 180 mg	1 x daily	
	Timolol / Blocadren*	10 – 60 mg	2 x daily	
Combined α- and β- Blockers	Corvedilol / Coreg	6.25 – 50 mg	2 x daily	Same precautions as beta blockers.
	Coreg CR	20 – 80 mg	1 x daily	
	Labetalol / Normodyne*	100 – 2400 mg	2 x daily	

Diuretics are often used as adjunct therapy. Obtain baseline B/P, electrolytes, uric acid, glucose and lipids prior to starting and periodically. May require supplementation w/ magnesium and potassium.

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Considerations
Thiazide Diuretics **Action:** cause diuresis and decrease vascular resistance. (Many meds combined with this class)	**Hydrochlorathiazide (HCTZ)*** **HydroDIURIL** **Microzide**	12.5 – 25 mg Most frequently prescribed	1 x daily in am with or w/out food **Side effects**: lyte imbalances; hypokalemia, hypomagnesemia, hyperuricemia, hyperglycemia, hyperlipidemia and hyper/hypocalcemia. S/S include muscle cramps, fatigue, dizziness and cardiac arrhythmias .
	Chlorthalidone / Clorpres*	12.5 – 25 mg	
	Metolazone / Zaroxolyn*	2.5 – 20 mg	
	Indapamide / Lozol*	1.2 – 2.5 mg	

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Considerations
Loop Diuretics (resistant HTN)	Furosemide/Lasix*	20 – 600 mg 2x day	Side Effects as above, but more intense. Need K^+ supplement.
	Torsemide / Demadex*	2.5 – 200 mg 1x day	Used if GFR < 30 or if greater diuresis is needed
	Bumetanide / Bumex*	0.5 – 10 mg 2 x day	

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
Potassium Sparing Diuretics	Amiloride / Midamor	5 – 20 mg	1 x day	Usually combined with thiazide diuretic to balance serum potassium. Alone, they do little to lower BP.
	Triamterene / Dyrenium	37.5 – 75 mg	1 x day	
	Spironolactone / Aldactone*	25 – 100 mg	1-2 x day	
	Eplerenone / Inspra	50 - 100 mg	1 -2 x day	

Calcium Channel Blockers are usually second or third line BP med for diabetes, since they have less impact on CVD. They may also be used for those who can't tolerate ACE or ARB Therapy.

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
Calcium Channel Blocker *Nondihydropyridine* Relaxes coronary blood vessels to decrease heart rate and cardiac output.	**Diltiazem immediate release***	30 – 360 mg	4 x day	**Monitor** BP, heart rate, liver enzymes and cardiac function a baseline and periodically. Take at the same time each day (with meals if possible). Take in evening if experience drowsiness. **Side Effects**: Watch for cardiac conduction abnormalities, bradycardia, CHF and edema. Can cause peripheral edema and constipation. Metabolized through CYP3A4, so review package insert for drug and food interactions (ie grapefruit).
	Diltiazem extended release*			
	Cardizem CD	120 – 480 mg	1 x day	
	Tiazac	120 – 540 mg	1 x day	
	Dilacor, Diltia	180 – 540 mg	1 x day	
	Verapamil immediate release* Calan	80 -320 mg	3 x day	
	Verapamil sustained release* Calan SR, Veralan	120 mg – 480 mg	1 -2 x day	
	Verapamil extended release*			
	Covera-HS	120 – 480 mg	1 x day	
	Verelan PM	100 – 400 mg		
Calcium Channel Blocker – *Dihydropyridine* Causes vasodilation and decreases peripheral vascular resistance.	Amlodipine/Norvasc	2.5 – 10 mg	1 x day	
	Felodipine / Plendil	2.5 – 10 mg	1 x day	
	Isradipine controlled release DynaCirc CR	2.5 – 10 mg	1 x day	
	Nicardipine sustained release / Cardene SR	30 – 60 mg	2 x day	
	Nifedipine long-acting* Adalat CC /Procardia XL	30 – 120 mg	1 x day	
	Nisoldipine / Sular	10 – 40 mg	1 x day	

α1 – Receptor Blockers - Often used for pts with DM & benign prostatic hypertrophy (BPH).

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
α1 – Receptor Blockers Vasodilation	Doxazoxin/Cardura*	1 – 8 mg	1 x day	Take at hs and low dose to reduce risk of postural hypotension/syncope.
	Prazosin / Minipress*	2 – 20 mg	2 - 3 day	
	Terazosin/ Hytrin*	1 – 10 mg	1 – 2 day	

α2 agonists- Not usually first line due to side effects. Effective in pts w/ renal disease, since does not compromise renal function.

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
α2 agonists – Centrally act to block influence of norepinephrine on the heart and lower B/P	Clonidine / Catapres*	0.1 to 0.8 mg	2 x day	Administer w/ diuretic. Side effects: sedation, dry mouth, bradycardia orthostatic hypotension, impotence. Do not stop abruptly, can cause hypertensive crisis.
	Methyldopa / Aldomet*	250 – 1000 mg	2-3 x day	

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Neuropathy Medication for Diabetes

Prevention – Maintain glycemic control; quit smoking, alcohol reduction, exercise.

Pathogenetically Oriented Therapy

- Alpha lipoic acid 600 – 1,800 mg a day

Prescription Therapy:

1st line – Tricyclic Antidepressants (Amitriptyline, Nortriptyline, Desipramine)

- Calcium Channel Modulators (Gabapentin, Pregabalin)
- Serotonin Norepinephrine Reuptake Inhibitors (SNRI – Venlafaxine, Duloxetine)

2nd Line - Topical Capsaicin Cream for localized pain – Apply 2-4 x daily for up to 8 wks

- Opioids (Tramadol, Oxycodone)

Reasons for Treatment Failure

- Dose too low
- Inadequate trial – requires 2-8 weeks of treatment to observe symptom reduction
- Pt expecting elimination of symptoms – only reduces symptoms by about 50%
- Incorrect diagnosis: If in doubt, refer to neurologist
- If patient does not respond or has adverse effects, change medication class
- In patient has some but inadequate relief, raise the dose and consider adding or changing meds.

References: Ziegler, D. Painful diabetic neuropathy. Diabetes Care 2009; 32 (Supp 2): S414-S419

Class	Generic / Trade Name	Usual Daily Dose Range	Comments	Side Effects/ Caution
1st Line Agents **Tricyclic Antidepressants TCA** Improves neuropathy and depression	Amitriptyline / Elavil	25 – 100 mg* Avg dose 75mg	Usually 1st choice	Take 1 hour before sleep. Side effects; dry mouth, tiredness, orthostatic hypotension. **Caution**: not for pts w/ unstable angina (<6 mo), MI, heart failure, conduction system disorder.
	Nortriptyline / Pamelor	25 - 150 mg* (for burning mouth)	Less sedating and anticholinergic	
	Desipramine / Norpramine	25 – 150 mg* *Increase by 25mg weekly till pain relieved		
Calcium Channel Modulators	Gabapentin/ Neurontin	100 - 1,200mg TID	Improves insomnia, fewer drug interactions	Sedation, dizziness, peripheral edema, wt gain **Caution**; CHF, suicide risk, seizure disorder.
	Pregabalin / Lyrica *FDA approved for neuropathy treatment	50 - 200mg TID		
Serotonin Norepinephrine Reuptake Inhibitor SNRI	Duloxetine / Cymbalta *FDA approved for neuropathy treatment	60 mg daily Start at 30 mg	Improves depression, insomnia	Nausea, sedation, HTN, constipation, dizziness, dry mouth, blurred vision. **Caution**: adjust dose for renal insufficiency, do not stop abruptly, taper dose.
	Venlafaxine/ Effexor	75 - 225 mg daily		
2nd Line Agents Opioids	Weak opioids Tramadol / Ultram	50 – 400 mg	Sedation, nausea, constipation (always prescribe stool softener) **Caution:** abuse, suicide risk, short acting opioids not recommended for long term tx, can develop tolerance	
	Strong opioids Oxycodone	10 – 100 mg		
Local Treatment	Capsaicin Cream (0.025%) Apply 2-4 x daily for up to 8 wks			
Other choices	If above medications not effective, contraindicated or intolerable consider: Buproprion/Wellbutrin Paroxetine / Paxil Citalopram / Celexa Topiramate / Topamax Topical Lidocaine (for localized pain).			

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