

# New Lipid Lowering Medications

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PCSK9 Inhibitors Lipid Medications		
Proprotein convertase subtilisin/kexin type 9		
	Alirocumab (Profluent)	Evolocumab (Repatha)
<b>FDA-approved indications</b>	<ul style="list-style-type: none"> <li>Primary hyperlipidemia (HLD)</li> <li>Homozygous familial hypercholesterolemia (HoFH)</li> <li>Secondary prevention of cardiac events</li> </ul>	
<b>Dosing</b>	<ul style="list-style-type: none"> <li><b>HoFH:</b> 150 mg SC q2 weeks</li> <li><b>HLD or secondary cardiac prevention:</b> 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</li> </ul>	<ul style="list-style-type: none"> <li><b>HoFH:</b> 420 mg SC q4 weeks; may increase to 420 mg q2 weeks if meaningful response not achieved in 12 weeks</li> <li><b>HLD or secondary cardiac prevention:</b> 140 mg q2 weeks or 420 mg q4 weeks</li> </ul>
<b>Dosage forms</b>	<ul style="list-style-type: none"> <li>Auto-injector 75 mg/mL or 150 mg/mL</li> </ul>	<ul style="list-style-type: none"> <li>Repatha Sure Click (auto-injector) 140 mg/mL</li> <li>Repatha Pushtronex System (single use infusor with pre-filled cartridge) 420 mg/3.5 mL – administered over 9 minutes</li> </ul>
<b>Storage</b>	<ul style="list-style-type: none"> <li>Store in refrigerator in outer carton until used</li> <li>Once used, keep at room temperature, use within 30 days</li> </ul>	
<b>Injection clinical pearls</b>	<ul style="list-style-type: none"> <li>Do not shake or warm with water</li> <li>Administer by SC injection into thigh, abdomen, or upper arm</li> <li>Rotate injection site with each injection</li> </ul>	
<b>Drug interactions</b>	<ul style="list-style-type: none"> <li>No known significant interactions</li> </ul>	
<b>Monitoring parameters</b>	<ul style="list-style-type: none"> <li>Lipid panel before initiating therapy, 4-12 weeks after initiating, and q3-12 months thereafter</li> </ul>	
<b>Side effects</b>	<ul style="list-style-type: none"> <li>Injection site reaction (4-17%)</li> <li>Hypersensitivity reaction (9%)</li> <li>Influenza (6%)</li> <li>Myalgia (4-6%)</li> <li>Diarrhea (5%)</li> </ul>	<ul style="list-style-type: none"> <li>Nasopharyngitis (6-11%)</li> <li>Upper respiratory tract infection (9%)</li> <li>Diabetes mellitus (9%)</li> <li>Influenza (8-9%)</li> <li>Injection site reaction (6%)</li> <li>Myalgia (4%)</li> </ul>

## Adenosine Triphosphate-citrate Lyase - ACL Inhibitor

Indicated for adults with heterozygous familial 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	180 mg	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.
	Bempedoic acid/ezetimibe (Nexlizet)	180 mg /10mg		

\*indicates medication is available in generic form.

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# 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. The mineralocorticoid receptor antagonist blocks the effects of aldosterone and reduces the risk of kidney function decline as well as heart failure.

Class / Action	Generic / Trade Name	Daily Dose	Frequency	Considerations
<b>Nonsteroidal, selective mineralcorticoid antagonist.</b> Blocks mineralcorticoid receptor mediated sodium reabsorption and mineralcorticoid overactivation in epithelial (for example kidneys) and nonepithelial (for example heart, blood vessels) tissues.	<b>Finerenone / Kerendia</b>	<b>10-20 mg</b>	<b>Once daily</b>	Monitor potassium 4 weeks after initiation or dose adjustment (although impact on potassium is much less than non-selective mineralcorticoid antagonists like spironolactone). Since medication is a CYP3A4 substrate, avoid taking with other strong cyp3A4 inhibitors. Avoid grapefruit or grapefruit juice. May take with or without food.

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## Cholesterol Medications

### LDL Lowering Medications

Class / Action	Generic / Trade Name	Usual Daily Dose Range	LDL % Lowering	Considerations
<b>“Statins”</b> HMG- CoA Reductase Inhibitors  Inhibits enzyme that converts HMG-CoA to mevalonate - limits cholesterol production	Atorvastatin / Lipitor*	10 – 80 mg	20- 60	Lowers TGs 7-30% Raise HDL 5-15% Take at night. <b>Side effects:</b> weakness, muscle pain, elevated glucose levels. Review package insert for specific dosing adjustments based on drug, food interactions (ie grapefruit).
	Fluvastatin / Lescol* Lescol XL	20 – 80 mg 80 mg	20- 35	
	Lovastatin* Mevacor Altoprev XL	20 - 80 mg 10 - 60 mg	20- 45	
	Pravastatin / Pravachol*	10 - 80 mg	20- 45	
	Rosuvastatin / Crestor	5 – 40 mg	20- 60	
	Simvastatin / Zocor*	20 – 80 mg	20- 55	
	Pitavastatin / Livalo	2 – 4 mg		
Bile Acid Sequestrants <b>Action:</b> Bind to bile acids in intestine, decreasing cholesterol production. Secondary action – raise HDL	Cholestyramine/ Questran*	4 to 16 g per day powder – 1 scoop 4g	Lower LDL by 15-30%	May raise TG levels. Raise HDL 3-5%.  Avoid taking in same timeframe w/ other meds – may affect absorption (see package insert). Side effects: GI in nature
	Colesevelam / Welchol <b>Lowers A1c 0.5%</b>	3.75 x 1 daily 1.875 x 2 daily (625mg tablets)		
	Colestipol / Colestid	2 - 16 gms per day tabs Powder – 1 scoop = 5g 5 to 20 gm per day Mix w/ fluid		
Cholesterol Absorption Inhibitors	Ezetimibe / Zetia	10 mg – 1x daily	15-20%	Usually used in combo w/statin. Headache, rash.
Plant Stenols	Benecol	3 servings daily	14%	Well tolerated
Plant Sterols	Take Control	2 servings daily	17%	

### Triglyceride Lowering / HDL Raising Medications

If TG > 500, lower TG first, then reduce LDL.

Class / Action	Generic / Trade	Usual Daily Dose Range	Lowers TG	Considerations
<b>Fibrates or Fibric Acids</b> Reduces liver lipogenesis	Fenofibrate/ Tricor Multiple brand formulations	48-145 mg 1x daily Please refer to individual package insert for dosing	<b>20-50%</b>	Lowers LDL 5-20% Raise HDL 10-20% GI side effects, myopathy Avoid w/ severe renal or hepatic disease
	Gemfibrozil / Lopid*	600mg 2x daily		
<b>Nicotinic Acid</b> Raise HDL/Lower TG Inhibits mobilization of free fatty acid	Niacin (immediate release)*	1.5- 3 gms	20-50%	Raise HDL 15-35% Flushing, hyperglycemia, hepatotoxicity – monitor liver enzymes. Can take w/aspirin to < flushing
	NiaSpan (extended release) Niacin (sustained release)	1-2 gms		
<b>Omega 3 Fatty Acid</b>	Omega 3 Acid/ Lovaza	4 gm a day	45%	Raise HDL 9% - Primary use for TG > 500

### Combination Medications

<b>Vytorin</b>	Zetia + Simvastatin	Observe precautions of each component drug		
<b>Juvisync</b>	discontinued			

\*indicates medication is available in generic form.

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

<sup>†</sup>indicates medication is available in generic form.

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
<b>DRIs - Direct Renin Inhibitors -</b>	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.

<b>Beta Blockers</b> <i>β1- Selective</i> <b>Action:</b> 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	1 x daily	
	Metoprolol tartate/Lopressor*†	25 – 100 mg		
	Metoprolol succinate / Toprol XL	25 - 100 mg		
Nebivolol/Bystolic	5 to 40 mg			
Nebivolol with Valsartan/ Byvalson	5 mg 80 mg			
<b>Beta Blockers</b> <i>Non Selective</i> <b>Action:</b> 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	
	Propranolol / Inderal* Inderal LA (extended)	40 – 160 mg 60 – 180 mg	2 x daily 1 x daily	
Timolol / Blocadren*	10 – 60 mg	2 x daily		
<b>Combined α- and β- Blockers</b>	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
<b>Thiazide Diuretics</b> <b>Action:</b> cause diuresis and decrease vascular resistance. (Many meds combined with this class)	<b>Hydrochlorothiazide (HCTZ)*</b> HydroDIURIL Microzide	12.5 – 25 mg Most frequently prescribed	1 x daily in am with or w/out food <b>Side effects:</b> 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	

\*indicates medication is available in generic form.

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Considerations	
<b>Loop Diuretics</b> (resistant HTN)	Furosemide/Lasix*	20 – 600 mg 2x day	Side Effects as above, but more intense. Need K <sup>+</sup> supplement.	
	Torsemide / Demadex*	2.5 – 200 mg 1x day		
	Bumetanide / Bumex*	0.5 – 10 mg 2 x day	Used if GFR < 30 or if greater diuresis is needed	
<b>Potassium Sparing Diuretics</b>	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	
<b>Calcium Channel Blocker</b> <i>Nondihydropyridine</i> Relaxes coronary blood vessels to decrease heart rate and cardiac output.	<b>Diltiazem immediate release*</b>	30 – 360 mg	4 x day	<b>Monitor</b> 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.  <b>Side Effects:</b> 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).	
	<b>Diltiazem extended release*</b>				
	Cardizem CD	120 – 480 mg	1 x day		
	Tiazac	120 – 540 mg	1 x day		
	Dilacor, Diltia	180 – 540 mg	1 x day		
	<b>Verapamil immediate release*</b>				
	Calan	80 -320 mg	3 x day		
<b>Calcium Channel Blocker –</b> <i>Dihydropyridine</i> Causes vasodilation and decreases peripheral vascular resistance.	<b>Verapamil sustained release*</b>				
	Calan SR, Veralan	120 mg – 480 mg	1 -2 x day		
	<b>Verapamil extended release*</b>				
	Covera-HS	120 – 480 mg	1 x day		
	Verelan PM	100 – 400 mg	1 x day		
	<b>Amlodipine/Norvasc</b>	2.5 – 10 mg	1 x day		
<b>Calcium Channel Blocker –</b> <i>Dihydropyridine</i> Causes vasodilation and decreases peripheral vascular resistance.	<b>Felodipine / Plendil</b>	2.5 – 10 mg	1 x day		
	<b>Isradipine controlled release DynaCirc CR</b>	2.5 – 10 mg	1 x day		
	<b>Nicardipine sustained release / Cardene SR</b>	30 – 60 mg	2 x day		
	<b>Nifedipine long-acting* Adalat CC /Procardia XL</b>	30 – 120 mg	1 x day		
	<b>Nisoldipine / Sular</b>	10 – 40 mg	1 x day		

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

<b>α1 – Receptor Blockers</b> Vasodilation	Doxazosin/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.

<b>α2 agonists –</b> 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	

\*indicates medication is available in generic form.



## 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:

**1<sup>st</sup> line** – Tricyclic Antidepressants (Amitriptyline, Nortriptyline, Desipramine)

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

**2<sup>nd</sup> 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
<b>1<sup>st</sup> Line Agents</b>  <b>Tricyclic Antidepressants</b> <b>TCA</b> Improves neuropathy and depression	Amitriptyline / Elavil	25 – 100 mg* Avg dose 75mg	Usually 1 <sup>st</sup> choice	Take 1 hour before sleep. Side effects; dry mouth, tiredness, orthostatic hypotension. <b>Caution:</b> 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		
<b>Calcium Channel Modulators</b>	Gabapentin/ Neurontin	100 - 1,200mg TID	Improves insomnia, fewer drug interactions	Sedation, dizziness, peripheral edema, wt gain <b>Caution;</b> CHF, suicide risk, seizure disorder.
	Pregabalin / Lyrica *FDA approved for neuropathy treatment	50 - 200mg TID		
<b>Serotonin Norepinephrine Reuptake Inhibitor</b> <b>SNRI</b>	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. <b>Caution:</b> adjust dose for renal insufficiency, do not stop abruptly, taper dose.
	Venlafaxine/ Effexor	75 - 225 mg daily		
<b>2<sup>nd</sup> Line Agents</b> <b>Opioids</b>	Weak opioids Tramadol / Ultram	50 – 400 mg	Sedation, nausea, constipation (always prescribe stool softener) <b>Caution:</b> abuse, suicide risk, short acting opioids not recommended for long term tx, can develop tolerance	
	Strong opioids Oxycodone	10 – 100 mg		
<b>Local Treatment</b>	Capsaicin Cream (0.025%) Apply 2-4 x daily for up to 8 wks			
<b>Other choices</b>	If above medications not effective, contraindicated or intolerable consider: Bupropion/Wellbutrin      Paroxetine / Paxil      Citalopram / Celexa Topiramate / Topamax      Topical Lidocaine (for localized pain).			

\*indicates medication is available in generic form.