



# Metformin

Product	Dosing	eGFR Dose Adjustment
Metformin	500mg once or twice daily, titrate weekly to 1000mg twice daily	eGFR 45-60 ml/min: monitor kidney function closely eGFR 30-45: Max dose 500mg twice daily, use caution initiating new therapy eGFR <30: use contraindicated
Adverse Effects:		
<ul style="list-style-type: none"> <li>Diarrhea, gas/bloating, nausea/vomiting, reflux</li> </ul>		
Pearls		
<ul style="list-style-type: none"> <li>Typically considered first line treatment and often used in combination with other classes</li> <li>Using extended-release product can decrease lower GI adverse effects, but does not decrease bloating/reflux. Take all metformin with food to minimize.</li> <li>Use caution when selecting ER products-some formulations (Glumetza) may be more expensive</li> <li>Monitor B12-can cause deficiency</li> </ul>		

# GLP-1 Receptor Agonists

Product	Dosing	eGFR Dose Adjustment
Exenatide (Byetta®)	5 mcg BID given 1 hour before meal, may titrate to 10 mcg BID after 4 weeks (Max dose 20 mcg/day)	CrCl <30 ml/min: Do not use
Exenatide ER (Bydureon®)	2mg once weekly (no titration)	eGFR <45 ml/min: Do not use
<b>Dulaglutide (Trulicity®)</b>	0.75mg weekly x 4-8 weeks, may increase dose no more often than every 4 weeks (Max dose 4.5mg)	none
<b>Liraglutide (Victoza®)</b>	0.6 mg daily x 1 week then increase to 1.2 mg (minimally effective dose). May increase up to 1.8mg after 1 week	none
<b>Semaglutide (Ozempic®)</b>	0.25 mg x 4 weeks, then increase to 0.5 mg weekly (minimally effective dose). May increase to next pen strength no more often than every 4 weeks (Max dose 2 mg)	none
Semaglutide (Rybelsus®)	3 mg daily x 4 weeks, then increase to 7mg (minimally effective dose). May increase to 14mg daily after 30 days (Max dose 14mg daily)	none
Tirzepatide (Mounjaro®)	2.5 mg weekly x 4 weeks, then increase to 5mg weekly (minimally effective dose). May increase in 2.5mg/week increments every 4 weeks to max 15mg/week.	none
(GLP-1/GIP agonist, CV trials in progress)		
Adverse Effects:		
<ul style="list-style-type: none"> <li>Nausea, vomiting, diarrhea</li> <li>black box warning against use in patients with family history of medullary thyroid cancer or multiple endocrine neoplasia-2</li> </ul>		
Pearls:		
<ul style="list-style-type: none"> <li>Eating smaller meals with lower fat content (avoid greasy foods) increases GI tolerability</li> <li>Be sure to optimize dosing beyond starting doses after 4 weeks. Continue to increase dose every 4 weeks if BG remain above goals</li> <li>May require lower doses of insulin to avoid hypoglycemia</li> <li>Discontinue if pancreatitis is suspected</li> <li>Avoid use with DPP-4 (no added glucose benefit with increased cost)</li> </ul>		

\*Bolded products have proven CVD benefit

## SGLT-2 Inhibitors

Product	Dosing	eGFR Dose Adjustment	Additional Benefits in Co-morbidities
Canagliflozin (Invokana®)	100mg daily 300mg daily	eGFR 45-60 ml/min: 100mg/d  eGFR <45 ml/min + >300 mg/d urine albumin: 100mg/d  eGFR <45 ml/min + <300 mg/d urine albumin: do not use	<ul style="list-style-type: none"> <li>Decrease HF hospitalization</li> <li>Reduction in CKD Progression</li> <li>Cardiovascular endpoints</li> </ul>
Dapagliflozin (Farxiga®)	5mg daily 10mg daily	eGFR 25-45 ml/min: recommend against use for DM, however safe to continue for diabetic kidney disease or HF	<ul style="list-style-type: none"> <li>Decrease HF hospitalization</li> <li>Reduction in CKD Progression</li> </ul>
Empagliflozin (Jardiance®)	10mg daily 25mg daily	Discontinue if eGFR <30 ml/min (safely used in HF in eGFR>20)	<ul style="list-style-type: none"> <li>Decrease HF hospitalization</li> <li>Reduction in CKD Progression</li> <li>Cardiovascular endpoints</li> </ul>
Ertugliflozin (Steglatro®)	5mg daily 15mg daily	Discontinue if eGFR <60 ml/min	<ul style="list-style-type: none"> <li>Decrease HF hospitalization</li> </ul>
<b>Adverse Effects:</b> <ul style="list-style-type: none"> <li>Genital mycotic infections, urinary tract infections, hypotension, volume depletion</li> </ul> <b>Pearls:</b> <ul style="list-style-type: none"> <li>Encourage appropriate hygiene and hydration to minimize adverse effects</li> <li>May need dose reduction in other diuretic therapies</li> <li>Discontinue 3-4 days prior to surgery or any prolonged fasting state (minimize euglycemic DKA)</li> </ul>			

## DPP-4 Inhibitors

Product	Dosing	eGFR Dose Adjustment
Alogliptin (Nesina®)	25mg daily	CrCl ≥30-60: 12.5mg daily CrCl <30: 6.25mg daily
Linagliptin (Tradjenta®)	5mg daily	None
Saxagliptin (Onglyza®)	5mg daily	eGFR <45: 2.5mg daily
Sitagliptin (Januvia®)	100mg daily	eGFR ≥30-45: 50mg daily eGFR <30: 25mg daily
<b>Adverse Effects:</b> <ul style="list-style-type: none"> <li>Nasopharyngitis, pancreatitis (rare)</li> </ul> <b>Pearls:</b> <ul style="list-style-type: none"> <li>Less A1c lowering and no added CV or renal benefit seen with other classes</li> <li>Starting at max dose is recommended (titration not necessary)</li> <li>Avoid use with GLP-1 agonist (no added glucose control at increased cost)</li> <li>Saxagliptin associated with increased hospitalizations for HF in patients with CV disease or CV risk factors</li> </ul>		