

# Pharmacotherapy for Type 2 Diabetes Mellitus (T2DM) 2025 A VA Clinician's Summary



U.S. Department of Veterans Affairs

Veterans Health Administration PBM Academic Detailing Services

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A VA Clinician's Summary



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# Key messages

Use a SGLT2 inhibitor in patients with T2DM with ASCVD, HF, and/or CKD4	
Consider continuous glucose monitoring in Veterans with diabetes who are on daily insulin	
to achieve individualized glycemic management targets and/or avoid hypoglycemia	

# Pharmacotherapy approach for type 2 diabetes

**SGLT2 inhibitors** and **GLP-1 RAs** are beneficial across multiple clinical conditions, including treatment of type 2 diabetes mellitus (T2DM), atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), and chronic kidney disease (CKD). **The efficacy of these agents extends beyond their glucose lowering effects.**<sup>1,2</sup>

# SGLT2 inhibitors

**SGLT2 inhibitors are first-line agents for patients with ASCVD and T2DM, HF, and/or CKD.**<sup>1,2</sup> Benefits are not related to glucose lowering and should be used regardless of HbA1c level. Considerations for selecting SGLT2 inhibitors:

Empagliflozin and canagliflozin lower major adverse cardiovascular events, including myocardial infarction, stroke, and cardiovascular death in patients with ASCVD and T2DM.<sup>3-13</sup>



- Empagliflozin, dapagliflozin, and sotagliflozin reduce the risk of hospitalization for heart failure or cardiovascular death in patients with heart failure with reduced, mid-range, or preserved ejection fraction (HFrEF, HFmEF, HFpEF).<sup>13-19</sup>
- Empagliflozin, canagliflozin, and dapagliflozin reduce the risk of worsening renal function (worsening eGFR, end-stage kidney disease, or renal death).<sup>6-13,20-23</sup>

# **GLP-1** RAs

**GLP-1 RAs are alternatives to SGLT2 inhibitors.** For ASCVD, the benefits are comparable between the drug classes. Renal benefits are more limited for GLP-1 RAs and costs are higher. Considerations for selecting GLP-1 RA<sup>1,2</sup>:

- Lower rates of major adverse cardiovascular events including myocardial infarction, stroke, and cardiovascular death in patients with ASCVD using injectable semaglutide, liraglutide, and dulaglutide.<sup>11-15,24-32</sup>
- A lack of evidence in lowering HF risk (neutral outcome) or decreasing HF hospitalizations.<sup>11–16</sup> GLP-1 RA (injectable semaglutide) improved quality of life in HF with preserved ejection fraction (HFpEF) and obesity.<sup>33</sup>
- Tirzepatide, a GIP/GLP-1 RA, lowers risk of a composite death from cardiovascular causes or worsening heart failure in patients with HFpEF and obesity.<sup>34</sup>
- Injectable semaglutide reduces risk of worsening renal function,<sup>12</sup> while liraglutide and dulaglutide reduce albuminuria.<sup>11,13,32</sup>
- A greater potential for weight loss than SGLT2 inhibitors.<sup>1,2</sup> Weight loss can benefit glycemic control, may improve MASLD, and reduce medication burden.



Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality in patients with diabetes.<sup>2</sup>

#### Figure 1. SGLT2 inhibitor and GLP-1 RA's role in therapy for cardiorenal benefits<sup>\*1,13</sup>

ASCVD	<ul> <li>Use SGLT2 Inhibitor (empagliflozin) in T2DM and ASCVD or high risk of ASCVD</li> <li>If a SGLT2 inhibitor cannot be used, use a GLP-1 RA (injectable semaglutide)</li> </ul>
HF	<ul> <li>Use SGLT2 inhibitor (empagliflozin) in addition to other GDMT for HFrEF, HFmEF, or HFpEF in patients with and without T2DM</li> <li>GLP-1 RA (injectable semaglutide) improved quality of life in HFpEF and obesity; evidence does not show reduction in hospitalizations or mortality</li> </ul>
CKD	<ul> <li>Use SGLT2 inhibitor (empagliflozin) in T2DM and CKD. In those without T2DM, use SGLT2 inhibitor if eGFR ≥ 20 ml/min/1.73 m<sup>2</sup> and uACR &gt; 200 mg/g, or eGFR 20-45 ml/min/1.73 m<sup>2</sup> and uACR &lt; 200 mg/g</li> <li>Use with maximally tolerated doses of ACE I or ARB</li> <li>If SGLT2 inhibitor cannot be used in patients with T2DM and CKD, use GLP-1 RA</li> </ul>

\*Before starting a SGLT2 inhibitor, ensure eGFR  $\geq$  20 mL/min/1.73 m<sup>2</sup> and continue until ESRD/dialysis. ASCVD: established cardiovascular disease (acute coronary syndrome, myocardial infarction [MI], stable or unstable angina, peripheral artery disease, stroke, or any revascularization procedure). High risk indicators of ASCVD: age  $\geq$  55 years with  $\geq$  2 risk factors (obesity, hypertension, smoking, dyslipidemia, or albuminuria). HF: includes HFrEF, HFmEF, HFpEF. CKD: eGFR < 60 mL/min/1.73 m<sup>2</sup> or uACR  $\geq$  30 mg/g.

# Metformin

Metformin continues to be a mainstay of diabetes therapy and has been used for decades. It has proven efficacy in lowering HbA1c, does not cause hypoglycemia or weight gain, and is cost effective.<sup>1,2,35-37</sup>

- Safe to initiate with eGFR > 45 mL/min/1.73m<sup>2</sup> and does not cause renal dysfunction.
- May continue at a reduced dose of up to 1000 mg/day in patients with eGFR 30-45 mL/ min/1.73m<sup>2</sup>.
- Titrate dose slowly, take with food, and consider using a sustained action formulation to reduce or prevent GI side effects. SA formulation has a lower rate of GI side effects (9.2% vs 19.8%) and lower rate of diarrhea (13.5% vs 3.1%) than IR formulation.
- Important to use shared decision-making to consider re-challenging with metformin in patients with a history of GI intolerance, particularly if due to rapid titration, higher dose, taking on an empty stomach, or using the IR formulation.

## Use a shared decision-making approach to determine optimal pharmacotherapy

Consider cardiorenal benefits when choosing therapy in Veterans with type 2 diabetes9-31

In Veterans with T2DM, use a SGLT2 inhibitor first for patients with ASCVD, HF, or CKD and add metformin if additional glycemic control is needed. Metformin is beneficial for glycemic control and may reduce cardiovascular mortality and progression to ESRD. Consider combination empagliflozin/metformin tablets for patients taking both agents. If a sulfonylurea or DPP-4 inhibitor is being used in a patient with ASCVD, HF, or CKD, consider replacing the sulfonylurea or DPP-4 inhibitor with a SGLT2 inhibitor when HbA1c is in target range. In cases where HbA1c is not controlled, then add a SGLT2 inhibitor to existing therapy.



#### Figure 2. Cardiac and renal benefits

MACE composite: major adverse cardiovascular events (nonfatal stroke, nonfatal MI, and cardiovascular death); HF composite: cardiovascular (CV) death and HF hospitalization; Kidney composite: end stage renal disease, eGFR < 10-15 mL/min/1.73 m<sup>2</sup>, or death from renal/CV causes. For ASCVD, use SGLT2 inhibitors **empagliflozin** or canagliflozin, and GLP-1 RA injectable semaglutide, liraglutide, or dulaglutide. For HF, use SGLT2 inhibitors **empagliflozin**, dapagliflozin, or sotagliflozin. For CKD, use SGLT2 inhibitors **empagliflozin**, canagliflozin, or dapagliflozin and GLP-1 RA injectable semaglutide (other GLP-1 RAs reduce albuminuria). (**Bolded** = formulary agent). DPP4-I = dipeptidyl peptidase 4 inhibitor. Negative numbers indicate a reduction in risk, therefore provide cardiorenal benefits.

After addressing the cardiorenal benefits of medications, further adjustments are made based on whether further hemoglobin A1c lowering is needed. In patients who are overweight or obese, it is beneficial to consider medications that are weight neutral or may promote weight loss.

#### Figure 3. Medications are added or adjusted based on Veteran health needs and goals<sup>1,2</sup>

If further hemoglobin A1c lowering is needed, select based on ability to lower A1c:



If weight loss is needed with BMI  $\ge$  27 kg/m<sup>2</sup>, select based on ability of the medication to promote weight loss:



\*Use caution in elderly due to risk of hypoglycemia. <sup>†</sup>See VA PBM Formulary for criteria for use. https://www.va.gov/formularyadvisor/. See Table 1 for more details. HbA1c lowering: very high > 1.5%, high 1–1.5%, intermediate 0.5–1%. Weight loss: very high/high: 6–30 lb loss, intermediate: 3–5 lb loss, neutral: 2 lb or less loss or gain, mild to moderate gain: 3–8 lb.



### Type 2 diabetes and liver disease

Metabolic dysfunction-associated steatotic liver disease (MASLD) is caused by excess fat in the liver. T2DM is the most impactful risk factor for development of MASLD, liver fibrosis, and liver cancer. Screening patients with metabolic risk factors (e.g., insulin resistance, obesity, or T2DM) for MASLD may identify those with metabolic dysfunction-associated steatohepatitis (MASH). Early identification of MASLD or MASH allows for interventions that may prevent future hepatic complications.

#### Figure 4. Metabolic dysfunction associated liver disease<sup>1,37</sup>



\*FIB-4 = Fibrosis-4 Index is a noninvasive test to assess for liver fibrosis using age, AST, ALT, platelet count: **Online Calculator**. FIB-4 is less accurate if age < 35 or  $\ge$  65 years. Recheck FIB-4 in patients with Type 2 diabetes every 1–2 years.



Lifestyle modification to promote and sustain weight loss (e.g., hypocaloric diet, plant-based diet, physical activity) may help reverse and eliminate MASLD. Consider a GLP-1 RA or pioglitazone for treatment of MASH in patients with T2DM.<sup>37</sup>

# **Initiating insulin**

When deciding to start insulin in a Veteran, it is important to consider the following factors:

- Consider GLP-1 RA before insulin if inadequate glycemic control on two or more oral medications. If HbA1c > 10% and/or having signs of catabolism, consider insulin before GLP-1 RA.<sup>1,2</sup>
- Cognitive function, visual acuity, and ability to detect hypoglycemia
- Willingness to do injections
- Concerns for weight gain
- Use motivational interviewing. Ask the Veteran: "How do you feel about taking insulin? What are your thoughts about how this will fit into your lifestyle? Will using insulin have implications for employment or military service?" Avoid punitive statements about insulin or imply that the patient has "failed". Diabetes is a progressive disease.

# **Insulin selection**

#### Basal insulin<sup>1,2</sup>

Basal insulins include NPH, glargine, and degludec.

- Start with a basal insulin and one injection daily at bedtime.
- NPH can cause more hypoglycemia than glargine, making glargine the preferred initial basal insulin.<sup>38-40</sup> Insulin glargine-yfgn (Semglee<sup>®</sup>) is a biosimilar to insulin glargine (Lantus<sup>®</sup>). See ADS Biologics/Biosimilar SharePoint for more information.
- Glargine 300 units/mL (or U300) is a concentrated version of glargine 100 units/mL (or U100). Glargine 300 units/mL and insulin degludec have a longer duration of action than glargine 100 units/mL (over 24 hours). Both are associated with less nocturnal and less severe hypoglycemia compared to glargine 100 units/mL. In patients with recurrent hypoglycemia, despite dosage adjustments, consider a trial of insulin glargine 300 units/mL. If hypoglycemia continues, consider switching to insulin degludec.<sup>41</sup> See criteria for use: https://www.va.gov/formularyadvisor/.

#### Figure 5. Using basal insulin<sup>\*1,2</sup>



\*Individualize insulin regimen based on Veteran-specific factors and glucose measurements.

#### Prandial (mealtime) insulin<sup>1,2</sup>

Prandial insulins include aspart, glulisine, lispro, and regular.

- Consider GLP-1 RA before adding prandial insulin if inadequate glycemic control on basal insulin and one or more oral agents.<sup>42</sup>
- Add prandial insulin when coverage is needed for meals. Consider when HbA1c continues to be above goal, basal insulin dose is > 0.5 units/kg, or glucose readings are elevated after meals.
- Rapid acting insulins like aspart, glulisine, and lispro should be administered 0–15 minutes before meals and are preferred to insulin regular due to easier administration.
- Insulin regular should be administered 30 minutes before meals. The longer time of onset and duration may increase hypoglycemia risk.<sup>43</sup>

#### Figure 6. Using prandial insulin



\*Post-prandial glucose or next premeal glucose over target range. Adjust prandial insulin based on patterns.

Consider using a pre-mixed insulin if the Veteran is having difficulty with multiple injections.<sup>1,2,44</sup>

- Insulin aspart protamine/insulin aspart 70/30 (Novolog 70/30) or insulin 70/30 NPH/REG (Novolin 70/30) – Note these are look-alike, sound-alike drugs.
- Need to have regular meal routines and not skip meals.
- Novolog 70/30 is preferred since it is administered 0–15 minutes before mealtime, while Novolin 70/30 is administered 30 minutes before eating.

# Ensure patient adherence before changing therapy.

- ✓ Provide instructions and demonstrate proper technique for insulin and other injectable products.
- ✓ Review all medications to ensure they are being used correctly before considering dose adjustments or changes in therapy.
- See VA Instructional Videos in the Veteran Health Library. How to Give Yourself a Subcutaneous Injection, How to Use Your Insulin Pen, How to Use Your GLP-1 Agonist Pen.

# **Diabetes Self-Management Education and Support (DSMES)**

#### DSMES should be offered:<sup>1,2</sup>

- At diagnosis, annually, or when not meeting treatment goals.
- When complicating factors develop, or transitions in life and care occur.
- VA DSMES Resources: Diabetes Self-Management Education and Support (DSMES) -Nutrition and Food Services (va.gov).

**DSMES considerations:** 

- Emphasize meal planning and lifestyle modifications, assess medication adherence, and optimize dose(s) at every visit. Follow up every 3–6 months to avoid therapeutic inertia.
- Check HbA1c every 3 months and adjust regimen if not in target range.
- Use patient factors and preferences to select medication(s) and glycemic treatment goals.
- Optimize regimen for cardiorenal benefit, weight loss, and reduced hypoglycemia risk.
- Use PCMHI for patients experiencing diabetes distress syndrome or other social stressors.
- Work with a Clinical Pharmacy Practitioner (CPP) to determine an optimal treatment plan.

### **Blood glucose monitoring**

Patients prescribed non-insulin agents:

 Refer to the Pharmacy Benefits Management (PBM): Dispensing guidance for Home Glucose Monitoring Test Strips in Patients with Type 2 Diabetes Who Are Not Receiving Insulin. (intranet)

#### Patients prescribed insulin:

Veterans who require insulin regimens may benefit from continuous glucose monitoring (CGM), which can be offered depending on needs and resources available. Clinicians need to confirm diagnosis of diabetes and chronic insulin requirements and document this in the medical record.



- Clinicians, including staff on PACT teams, should become familiar with viewing and interpreting CGM data.
- Using shared decision making, consider CGM in Veterans requiring chronic insulin to achieve desired glycemic management targets and/or avoid hypoglycemia.
- Ensure patients are provided education. Instructional videos from VA: VA Diabetes Care and Educational Video.
- Glucose monitor and test strips are provided, and quantity of strips is based on the frequency for testing (e.g., calibration of CGM, confirm "high" or "low" readings).
- For more information about patient selection for CGM, refer to Guidance on Patient Selection Criteria for Continuous Glucose Monitors.



Consider continuous glucose monitoring in Veterans with diabetes who are on daily insulin to achieve individualized glycemic management targets and/or avoid hypoglycemia.

Table 1.Pharmacotherapy for type 2 diabetes1-12

S		ering %	CV outcomes				emia	Possible side	
Clas	Medication	n 9 VARIAN Veight VARIAN Veight Outcome change VARIAN Veight Outcome change		Hypoglyc	effects/ considerations				
Biguanide	metformin metformin SA	1–1.5	Possible benefit	*	*	Modest loss (1–2 lb loss)	No	<ul> <li>GI side effects common</li> <li>Monitor eGFR</li> <li>Risk for B12 deficiency</li> <li>Assess continuation if IV contrast is needed</li> </ul>	
tors	<b>empagliflozin</b> canagliflozin	pagliflozin Benefit Benefit Benefit agliflozin		• Genital mycotic infections and UTI are rare events; risk factors are older age, uncontrolled DM, indwelling catheter, prior					
SGLT2 inhibit	dapagliflozin	0 5–1†	Neutral	Benefit	Benefit	diate loss r (3–5 lb loss)	No	<ul> <li>Volume depletion and</li> </ul>	
	ertugliflozin		Neutral	Benefit	Neutral			<ul><li>hypotension</li><li>Euglycemic diabetic</li></ul>	
	sotagliflozin		*	Benefit	*			ketoacidosis (rare)	
	bexagliflozin		*	*	*			<ul> <li>Hold 3-4 days prior to surgery<sup>§</sup></li> </ul>	
GLP-1 receptor agonists	injectable semaglutide <sup>‡</sup> liraglutide dulaglutide		Benefit	Neutral	Benefit	Interme- diate to very high loss (4–9 lb		<ul> <li>Contraindicated in personal or family history of MTC or MEN2</li> <li>Avoid in gastroparesis, high risk of pancreatitis, or gallbladder disease</li> </ul>	
	exenatide lixisenatide oral semaglutide	1–2	Neutral	Neutral	*	loss)	No	<ul> <li>Side effects are dose-related</li> <li>Gl side effects common; reduced by eating smaller meals and stopping before full; avoid spicy foods</li> <li>Renal impairment (if volume depleted due to vomiting)</li> <li>Guidance for use when needing surgery<sup>§</sup></li> <li>Consider for treatment of MASH (not EDA approved)</li> </ul>	

**Formulary medications in bold.** To view VA National Formulary: https://www.va.gov/formularyadvisor/. \*No data available. <sup>†</sup>SGLT2 inhibitors have reduced glucose lower effects with renal impairment. Cardiovascular and renal benefits of SGLT2 inhibition are maintained to an eGFR of 20 mL/min/1.73m<sup>2</sup>. <sup>‡</sup>Semaglutide and tirzepatide show the most weight loss. <sup>§</sup>See VA Periprocedural Management of Diabetes Mellitus Medications and Devices. Green = positive effect; Yellow = neutral effect; Red = negative effect.

Table 1.Pharmacotherapy for type 2 diabetes1-12

S		ering %	CV outcomes		Donal		temia	Possible side effects/ considerations	
Clas	Medication	HbA1c low	ASCVD	HF	outcome	come change			
DPP-4 inhibitors	sitagliptin linagliptin alogliptin saxagliptin	0.5–1	Neutral	Neutral Possible risk	*	Neutral (0–2 lb gain)	No	<ul> <li>Pancreatitis</li> <li>Hypersensitivity reactions</li> <li>Arthralgias</li> <li>Avoid use with GLP-1 RA or GIP/GLP-1</li> </ul>	
GIP/GLP-1 RA	tirzepatide <sup>‡</sup>	2–2.5	*	Benefit	*	Very high loss (18–30 lb loss)	No	<ul> <li>Similar cautions as GLP-1 RA</li> <li>Might decrease efficacy of oral contraceptives, mostly in first 4 weeks, need alternative method</li> <li>FDA approved for obstructive sleep apnea with obesity</li> <li>Consider for treatment of MASH (not FDA approved)</li> </ul>	
Sulfonylureas	<b>glipizide</b> glimepiride glyburide	1–1.5	Neutral	Neutral	Neutral	Mild to moderate gain (4–6 lb gain)	Yes	<ul> <li>Increased risk of hypoglycemia in elderly, renal impairment, poor intake, and/or interaction with some antimicrobials</li> <li>Photosensitivity and skin reactions</li> </ul>	
TZD	<b>pioglitazone</b> rosiglitazone	1–1.5	Possible benefit Possible risk	Increased risk Increased risk	*	Moderate gain (6–7 lb gain)	No	<ul> <li>Do not use in HF or hypervolemia</li> <li>Increased risk of bone fractures</li> <li>Edema</li> <li>Consider pioglitazone for treatment of MASH (not FDA approved)</li> </ul>	
Meglitinide	nateglinide repaglinide	0.7–1.1	Neutral	Neutral	*	Moderate gain (3–8 lb gain)	Yes	<ul> <li>Reduces postprandial glucose more than sulfonylurea</li> <li>Take before each meal, hold if skip meal</li> </ul>	

**Formulary medications in bold.** To view VA National Formulary: https://www.va.gov/formularyadvisor/. \*No data available. <sup>†</sup>SGLT2 inhibitors have reduced glucose lower effects with renal impairment. Cardiovascular and renal benefits of SGLT2 inhibition are maintained to an eGFR of 20 mL/min/1.73m<sup>2</sup>. <sup>‡</sup>Semaglutide and tirzepatide show the most weight loss. <sup>§</sup>See VA Periprocedural Management of Diabetes Mellitus Medications and Devices. Green = positive effect; Yellow = neutral effect; Red = negative effect.

 Table 2.

 Renal dosing for glucose-lowering medications<sup>1,2,33,45-63</sup>

SS		Ctouting date	Maximum	Action if eGFR (mL/min/1.73m²)				
Cla	Medication	Starting dose	daily dose	> 45 to < 60	> 30 to < 45	> 15 to < 30	< 15 or ESRD	
Biguanide	metformin metformin SA	500 mg daily or BID or 500mg daily (SA)	2,500 mg (IR) 2,000 mg (SA)	Max dose 2,000 mg/day ✔	Max dose 1,000 mg/day* ••	Х	Х	
	bexagliflozin	20 mg daily	20 mg daily	✓	✓	••	Х	
ors⁺	canagliflozin	100 mg daily	300 mg daily	100mg max ••	100mg max ••	100mg max to 25 mL/min ••	Х	
inhibi	dapagliflozin	5 mg daily	10 mg daily	✓	~	✓ 25 mL/min	Х	
<b>SGLT2</b>	empagliflozin	10 mg daily	25 mg daily	~	~	✓ 20 mL/min	Х	
	ertugliflozin	5 mg daily	15 mg daily	✓	••	X	Х	
	sotagliflozin	200 mg daily	400 mg daily	√	√	••	Х	
	dulaglutide	0.75 mg weekly	4.5 mg weekly	√	~	1	Limited data	
sts	exenatide	10 mcg BID	20 mcg BID	√	✓	X	Х	
goni	exenatide XR	2 mg weekly	2 mg weekly	✓	Х	Х	Х	
ptor ag	liraglutide	0.6 mg weekly	1.8 mg weekly	√	~	✓	Limited data ••	
rec	lixisenatide	10 mcg daily	20 mcg daily	✓	√	X	X	
GLP-1	injectable semaglutide	0.25 mg weekly	2 mg weekly	✓	~	✓	Limited data	
	oral semaglutide	3 mg daily	14 mg daily	✓	~	✓	Limited data	
GIP/GLP-1 RA	tirzepatide	2.5 mg weekly	15 mg weekly	~	~	~	Limited data ••	
ırs	alogliptin	25 mg daily	25 mg daily	12.5 mg/day <sup>‡</sup>	12.5 mg/day <sup>‡</sup>	6.25 mg/day <sup>‡</sup>	6.25 mg/day <sup>‡</sup>	
ibito	linagliptin	5 mg daily	5 mg daily	✓	√	✓	✓	
P-4 inhi	saxagliptin	2.5–5 mg daily	5 mg daily	√	2.5 mg/day ••	2.5 mg/day ••	2.5 mg/day ••	
DP	sitagliptin	100 mg daily	100 mg daily	√	50 mg/day ••	25 mg/day ••	25 mg/day ••	

**Formulary medications in bold.** Green (✓): no adjustment needed; Yellow (••): dose reduction, limited data, or use with caution; Red (X): avoid or contraindicated. \*Do not start metformin at eGFR 30–45 ml/min but can continue at 1,000 mg daily. <sup>†</sup>SGLT2 inhibitors have reduced effect in lowering glucose levels with renal impairment. Cardiovascular and renal benefits of SGLT2 inhibition are maintained to an eGFR of 20 mL/min/1.73 m<sup>2</sup>. <sup>‡</sup>Renal dosing of alogliptin based on creatinine clearance not eGFR.

 Table 2.

 Renal dosing for glucose-lowering medications<sup>1,2,33,45-63</sup>

SSE	Modication		Maximum	Action if eGFR (mL/min/1.73m <sup>2</sup> )			
ບັ	medication	Starting dose	daily dose	> 45 to < 60	> 30 to < 45	> 15 to < 30	< 15 or ESRD
as	glipizide	5 mg 2.5 mg in elderly	40 mg (IR) 20 mg (XR)	2.5 mg/day, slow titration	2.5 mg/day, slow titration	••	••
Sulfonylure	glimepiride	1 – 2 mg	8 mg	1 mg/day, slow titration ••	••	••	х
	glyburide	2.5 mg daily Avoid in elderly	20 mg daily or 10 mg BID	х	х	х	х
TZD	pioglitazone	15 – 30 mg daily	45 mg daily	√	✓	√	√
	rosiglitazone	4 mg daily	8 mg daily	4	4	✓	√

**Formulary medications in bold.** Green (✓): no adjustment needed; Yellow (••): dose reduction, limited data, or use with caution; Red (X): avoid or contraindicated. \*Do not start metformin at eGFR 30–45 ml/min but can continue at 1,000 mg daily. <sup>†</sup>SGLT2 inhibitors have reduced effect in lowering glucose levels with renal impairment. Cardiovascular and renal benefits of SGLT2 inhibition are maintained to an eGFR of 20 mL/min/1.73 m<sup>2</sup>. <sup>‡</sup>Renal dosing of alogliptin based on creatinine clearance not eGFR.

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### Abbreviations

ACE: angiotensin converting enzyme	<b>kg:</b> kilogram				
ARB: angiotensin II receptor blocker	lb: pound				
ASCVD: atherosclerotic cardiovascular disease	m <sup>2</sup> : meters squared				
BID: twice daily	mcg: microgram				
CKD: chronic kidney disease	MASH: metabolic dysfunction-associated				
DPP-4 I: dipeptidyl peptidase-4 inhibitor	steatohepatitis (formerly known as NASH)				
eGFR: estimated glomerular filtration rate	MASLD: metabolic dysfunction associated steatotic liver				
FDA: Food and Drug Administration					
FPG: fasting plasma glucose	MEN2: multiple endocrine neoplasia syndrome type 2				
GI: gastrointestinal	<b>mg:</b> milligram				
GIP RA: glucose-dependent insulinotropic	min: minute				
polypeptide receptor agonist	mL: milliliter				
GLP-1 RA: glucagon-like peptide 1 receptor agonist	MTC: medullary thyroid carcinoma				
HbA1c: hemoglobin A1c	NPH: isophane suspension of human insulin				
HF: heart failure	PACT: primary care aligned care team				
HFrEF: heart failure with reduced ejection fraction	PCMHI: Primary Care-Mental Health Integration				
HFmEF: heart failure with mid-range ejection fraction	REG: regular insulin				
HFpEF: heart failure with preserved ejection fraction	SA: sustained action				
HTN: hypertension	SGLT2: sodium-glucose cotransporter 2				
inj: injectable	T2DM: Type 2 diabetes mellitus				
IR: immediate release	TZD: thiazolidinediones				
IV: intravenous	uACR: urine albumin-creatinine ratio				
kPa: kilopascal	UTI: urinary tract infection				

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