Latest Pharmacologic Therapy for the Treatment of Type 2 Diabetes
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Clinical Associate Professor of Medicine
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Associate Professor, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell

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Associate Professor, Division of Diabetes, Endocrinology and Metabolism,
The University of Nebraska Medical Center, VA Nebraska-Western Iowa Health Care System
Objectives

• Evaluate the importance of glycemic control in preventing complications in type 2 diabetes
• Describe the new drug classes and treatment options for treating type 2 diabetes
• Discuss the uses of Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors and Glucagon-Like Peptide 1 (GLP-1) Receptor Agonists in high cardiovascular risk
• Individualize type 2 diabetes regimens in different clinical settings

Wexler DJ. Presented at ADA 29: June 12-16, 2020
Diabetes Mellitus is associated with an increased risk of both micro- and macrovascular disease

<table>
<thead>
<tr>
<th>Microvascular Disease</th>
<th>Macrovascular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinopathy</td>
<td>Atherosclerotic Cardiovascular Disease (ASCVD)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>Stroke</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Heart Failure (HF)</td>
</tr>
<tr>
<td></td>
<td>Peripheral arterial disease</td>
</tr>
</tbody>
</table>
Reducing A1C Reduces Microvascular Risk

United Kingdom Prospective Diabetes Study

Reducing A1C Reduces Nephropathy Risk in Type 2 Diabetes

UKPDS

A1C reduction (%)*

Nephropathy risk reduction (%)*

*Intensive vs. standard glucose control


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# Use of Antihyperglycemic Agents in Kidney Disease

<table>
<thead>
<tr>
<th>Class: Medication(s)</th>
<th>Kidney Disease Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amylin analog:</strong> pramlintide</td>
<td>Not recommended for CKD stage ≥4</td>
</tr>
<tr>
<td><strong>Biguanide:</strong> metformin</td>
<td>GFR &lt;45 avoid initiation of drug, for existing users does reduce to maximum 500mg twice daily; GFR &lt;30 use contraindicated</td>
</tr>
<tr>
<td><strong>Bile acid sequestrant:</strong> colesevelam</td>
<td>No dosage adjustment</td>
</tr>
<tr>
<td><strong>Dopamine-2 agonist:</strong> bromocriptine</td>
<td>Use with caution</td>
</tr>
<tr>
<td><strong>DPP-4 inhibitors:</strong> alogliptin, linagliptin, saxagliptin, sitagliptin</td>
<td>Reduce dosage for alogliptin, saxagliptin and sitagliptin if CrCl &lt;50 mg/dL</td>
</tr>
<tr>
<td><strong>Glinides:</strong> nateglinide, repaglinide</td>
<td>Start at lowest effective dose if GFR &lt;30 mL/min/1.73 m²</td>
</tr>
<tr>
<td><strong>GLP-1 receptor agonists:</strong> albiglutide, dugalutide, exenatide, exenatide XR, liraglutide</td>
<td>Albiglutide has been removed from the market; Dugalutide not recommended for kidney adjustment; Exenatide not recommended with GFR &lt;30 mL/min/; Exenatide XR not recommended for GFR &lt;45</td>
</tr>
<tr>
<td><strong>α-Glucosidase inhibitors:</strong> acarbose, miglitol</td>
<td>Avoid if GFR &lt;25 (miglitol) or &lt;30 (acarbose) mL/min/1.73 m²</td>
</tr>
<tr>
<td><strong>Insulin:</strong> aspart, degludec, detemir, glargine, glulisine, lispro, NPH, regular</td>
<td>Adjust dose based on patient response</td>
</tr>
<tr>
<td><strong>SGLT inhibitors:</strong> canagliflozin, dapagliflozin, empagliflozin</td>
<td>Ineffective if GFR &lt;30 mL/min/1.73 m²</td>
</tr>
<tr>
<td><strong>Sulfonylureas:</strong> glimepiride, glipizide, glyburide</td>
<td>No dose adjustment for glipizide; start glimepiride conservatively; avoid glyburide and all other SUs</td>
</tr>
<tr>
<td><strong>Thiazolidinediones:</strong> pioglitazone, rosiglitazone</td>
<td>No dosage adjustment</td>
</tr>
</tbody>
</table>
Cardiovascular complications are the main cause of mortality in diabetes

Patients with microvascular complications due to T2D are more likely to have a major CV event^1^.
Hyperglycaemia has a causal effect on the risk of major CV events^2^.
Chronic hyperglycaemia is associated with low-grade inflammation and accelerated atherosclerosis^3^.

**Heart**
- 2/3 of deaths in T2D are attributable to CV disease^7^.
- 2–6x higher risk of mortality from CV events^8^.
- 2.5x higher risk of developing congestive heart failure^9^.

**Brain**
- 4x higher risk of coronary artery disease and stroke^4^.
- For every 1% increase in HbA1c, the risk of stroke is increased by up to 30%^5^.

**PAD**
- 1/3 of patients with T2D over 50 years of age have PAD. This increases the risk of heart attack and stroke^6^.
Macrovascular Risk Reduction in Type 2 Diabetes

- Hypertension control
- Dyslipidemia control
- Smoking cessation
- Glycemic control

- Aspirin therapy
- Lifestyle modification
- Weight loss
# Medications for T2D with CV Benefit

<table>
<thead>
<tr>
<th>SGLT2 Inhibitors</th>
<th>GLP-1 RAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxidative stress-induced endothelial cell dysfunction</td>
<td>Oxidative stress-induced endothelial cell dysfunction</td>
</tr>
<tr>
<td>Inflammation and atherogenesis</td>
<td>Inflammation and atherogenesis</td>
</tr>
<tr>
<td>Glucose lowering effect</td>
<td>Glucose lowering effect</td>
</tr>
<tr>
<td>Natriuretic / diuretic effect</td>
<td>Natriuretic / diuretic effect</td>
</tr>
<tr>
<td>RAAS effect</td>
<td>RAAS effect</td>
</tr>
<tr>
<td>Uriscosuric effect</td>
<td></td>
</tr>
<tr>
<td>Beta hydroxybutyrate increase</td>
<td></td>
</tr>
</tbody>
</table>
Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors

Currently available drugs:

• Canagliflozin (Invokana)
• Dapagliflozin (Farxiga)
• Empagliflozin (Jardiance)
• Ertugliflozin (Steglatro)
SGLT2 inhibitors

Physiological actions

- Selectively blocks the SGLT2 transporter responsible for > 90% of glucose reabsorption in the nephron.
- Reduced absorption of glucose and sodium, leads to glycosuria and natriuresis.
- Greatest rate of glycosuria occurs during periods of hyperglycemia.
- Minimal risk of hypoglycemia as the action is independent of insulin.

Figure 1. The sodium-glucose cotransporter 2 (SGLT2) mechanism in the proximal tubule. Modified from Bakris et al. with permission of the publisher. Copyright © 2009, Elsevier.
SGLT2 Inhibitors

Mechanisms for Cardioprotection
- Reduce preload and afterload segment
- Improved profile of anti-inflammatory vs. pro-inflammatory cytokine
- Reduced cardiac fibrosis
- Increased hematocrit and erythropoietin production
- Increased cardiac metabolic efficiency

Mechanisms for Renoprotection
- Glycosuria
- Natriuresis
- Decreased glomerular pressure
- Reduced albuminuria
## SGLT2 Inhibitors

### Summary of CV outcome trials

<table>
<thead>
<tr>
<th>Study</th>
<th>MACE HR (95%CI)</th>
<th>CV Death HR (95%CI)</th>
<th>HHF HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMPA-REG (empagliflozin)</td>
<td>0.86 (0.74-0.99)</td>
<td>0.62 (0.49-0.77)</td>
<td>0.65 (0.50-0.85)</td>
</tr>
<tr>
<td>CANVAS (canagliflozin)</td>
<td>0.86 (0.75-0.97)</td>
<td>0.87 (0.72-1.06)</td>
<td>0.67 (0.52-0.87)</td>
</tr>
<tr>
<td>DECLARE-TIMI (dapagliflozin)</td>
<td>0.93 (0.84-1.03)</td>
<td>0.98 (0.82-1.17)</td>
<td>0.73 (0.61-0.88)</td>
</tr>
<tr>
<td>VERTIS-CV (ertugliflozin)</td>
<td>0.97 (0.85-1.11)</td>
<td>0.92 (0.77-1.11)</td>
<td>0.70 (0.54-0.90)</td>
</tr>
</tbody>
</table>

MACE = composite of death from CV cause, nonfatal MI and nonfatal stroke  
CV death = cardiovascular death  
HHF = hospitalization for heart failure
Glucagon-Like Peptide 1 Receptor Agonists (GLP-1 RA)

Currently available drugs:

- Exenatide (Byetta, Bydureon)
- Liraglutide (Victoza)
- Lixisenatide (Adlyxin, component of Soliqua)
  (Available in US as a fixed ratio combination drug)
- Semaglutide (Ozempic, Rybelsus)
- Dulaglutide (Trulicity)
Glucagon-Like Peptide 1 (GLP-1) Receptor Agonists

Mechanisms for Cardioprotection
• GLP-1 receptor is also expressed in cardiomyocytes and coronary endothelial cells

Mechanisms for Renoprotection
• Increased natriuresis
• Increased diuresis
• Blood glucose lowering
• Blood pressure lowering effects
• Decreased insulin levels
• Weight loss
## GLP-1 RA: Summary of CV Outcome Trials

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lixisenatide</th>
<th>Liraglutide</th>
<th>Semaglutide</th>
<th>Exenatide</th>
<th>Albiglutide</th>
<th>Dulaglutide</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE, HR (95% CI)</td>
<td>1.02 (0.89-1.17)</td>
<td>0.87 (0.78-0.97)</td>
<td>0.74 (0.58-0.95)</td>
<td>0.91 (0.83-1.00)</td>
<td>0.78 (0.68-0.90)</td>
<td>0.88 (0.79-0.99)</td>
</tr>
<tr>
<td>CV death, HR (95% CI)</td>
<td>0.98 (0.78-1.22)</td>
<td>0.78 (0.66-0.93)</td>
<td>0.98 (0.65-1.48)</td>
<td>0.88 (0.76-1.02)</td>
<td>0.93 (0.73-1.19)</td>
<td>0.91 (0.78-1.06)</td>
</tr>
<tr>
<td>Fatal or nonfatal MI, HR (95% CI)</td>
<td>1.03 (0.87-1.22)</td>
<td>0.86 (0.73-1.00)</td>
<td>0.74 (0.51-1.08)</td>
<td>0.97 (0.85-1.10)</td>
<td><strong>0.75 (0.61-0.90)</strong></td>
<td>0.96 (0.79-1.15)</td>
</tr>
<tr>
<td>Fatal or nonfatal stroke, HR (95% CI)</td>
<td>1.12 (0.79-1.58)</td>
<td>0.86 (0.71-1.06)</td>
<td><strong>0.61 (0.38-0.99)</strong></td>
<td>0.85 (0.70-1.03)</td>
<td>0.86 (0.66-1.14)</td>
<td><strong>0.76 (0.62-0.94)</strong></td>
</tr>
<tr>
<td>All-cause mortality, HR (95% CI)</td>
<td>0.94 (0.78-1.13)</td>
<td><strong>0.85 (0.74-0.97)</strong></td>
<td>1.05 (0.74-1.50)</td>
<td><strong>0.86 (0.77-0.97)</strong></td>
<td>0.95 (0.79-1.16)</td>
<td>0.90 (0.80-1.01)</td>
</tr>
<tr>
<td>HF hospitalization, HR (95% CI)</td>
<td>0.96 (0.75-1.23)</td>
<td>0.87 (0.73-1.05)</td>
<td>1.11 (0.77-1.61)</td>
<td>0.94 (0.78-1.13)</td>
<td>0.93 (0.77-1.12)</td>
<td></td>
</tr>
</tbody>
</table>
## Improved Renal Outcomes in GLP-1 RA and SGLT2 Inhibitor Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEADER(^{1,a})</td>
<td>Liraglutide</td>
<td>0.78 (0.67, 0.92)</td>
<td>0.003</td>
</tr>
<tr>
<td>SUSTAIN 6(^{2,b})</td>
<td>Semaglutide</td>
<td>0.64 (0.46, 0.88)</td>
<td>0.005</td>
</tr>
<tr>
<td>EMPA-REG OUTCOME(^{3,c})</td>
<td>Empagliflozin</td>
<td>0.61 (0.53, 0.70)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CANVAS(^{4,d})</td>
<td>Canagliflozin</td>
<td>0.60 (0.47, 0.77)</td>
<td></td>
</tr>
<tr>
<td>DAPA-CKD(^{5,e})</td>
<td>Dapagliflozin</td>
<td>0.56 (0.45, 0.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CREDENCE(^{6,f})</td>
<td>Canagliflozin</td>
<td>0.70 (0.59, 0.82)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Composite Renal Outcomes:*
- \(^{a}\)Macroalbuminuria, doubling of serum creatinine, and eGFR ≤45 mL/min/1.73 m², ESRD, or renal death; 
- \(^{b}\)Macroalbuminuria, doubling of serum creatinine, and eGFR ≤45 mL/min/1.73 m² or need for continuous renal replacement therapy; 
- \(^{c}\)Macroalbuminuria, doubling of serum creatinine level, eGFR ≤45 mL/min/1.73 m², initiation of renal-replacement therapy or renal death; 
- \(^{d}\)40% reduction in eGFR, ESRD, or renal death; 
- \(^{e}\)sustained decline in eGFR ≥ 50%, ESRD, or death from renal causes; 
- \(^{f}\)doubling of serum creatinine, ESRD (GFR <15 mL/min/1.73 m², dialysis or transplant), renal death or CV death.
GLP-1 RAs Added to 1-2 Oral Agents: Weight Effects

Mean change in weight from baseline after $24 \pm 4$ weeks, kg (range)

-7.0 -6.0 -5.0 -4.0 -3.0 -2.0 -1.0 0.0 1.0 2.0

GLAR
PBO
SITA 100 mg QD
DULA 0.75 mg QW
EXN 2 mg QW
EXN 5 $\mu$g BID
LIRA 1.2 mg QD
LIXI 10-20 $\mu$g QD
DULA 1.5 mg QW
LIRA 1.8 mg QD
EXN 10 $\mu$g BID
SEMA 0.5 mg QW
SEMA 1.0 mg QW

*a Systematic review of 41 randomized controlled clinical trials*
Meta-analyses of effects of SLGT2 inhibitors vs Control on HbA1C levels.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5850151/pdf/JAH3-7-e007165.pdf
Meta-analyses of effects of SLGT2 inhibitors vs Control on HbA1C levels.

- **Empagliflozin**
  - Ridderstrale, et al (2014)\(^{29}\)
  - EMPA-REG OUTCOME (2015)\(^{11}\)
  - Subtotal \((I^2 = 0.0\%, \, P = 0.934)\)
    - WMD (95% CI): \(-0.11 (\text{-0.19, -0.02})\)
    - Weight: 8.18

- **Canagliflozin**
  - Leiter, et al (Canagliflozin 100mg) (2015)\(^{27}\)
  - Leiter, et al (Canagliflozin 300mg) (2015)\(^{27}\)
  - Bode, et al (Canagliflozin 100mg) (2015)\(^{28}\)
  - Bode, et al (Canagliflozin 300mg) (2015)\(^{29}\)
  - CANVAS Program (2017)\(^{12}\)
  - Subtotal \((I^2 = 90.5\%, \, P = 0.000)\)
    - WMD (95% CI): \(-0.20 (\text{-0.34, -0.06})\)
    - Weight: 7.72

- **Dapagliflozin**
  - Wilding, et al (Dapagliflozin 2.5mg) (2014)\(^{30}\)
  - Wilding, et al (Dapagliflozin 5mg) (2014)\(^{30}\)
  - Wilding, et al (Dapagliflozin 10mg) (2014)\(^{30}\)
  - Bailey, et al (Dapagliflozin 2.5mg) (2014)\(^{28}\)
  - Bailey, et al (Dapagliflozin 5mg) (2014)\(^{28}\)
  - Bailey, et al (Dapagliflozin 10mg) (2014)\(^{28}\)
  - Prato, et al (2015)\(^{26}\)
  - Subtotal \((I^2 = 59.2\%, \, P = 0.023)\)
    - WMD (95% CI): \(-0.21 (\text{-0.41, -0.01})\)
    - Weight: 7.07

Overall \((I^2 = 92.6\%, \, P = 0.000)\)
- WMD (95% CI): \(-0.39 (\text{-0.52, -0.26})\)
- Weight: 100.00

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5850151/pdf/JAH3-7-e007165.pdf
## GLP-1 RAs and Cognitive Impairment

<table>
<thead>
<tr>
<th></th>
<th>Dulaglutide (REWIND Trial)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Liraglutide&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Cognitive Outcome</strong></td>
<td>&gt; 1.5 SDs on MoCA or DSST below the baseline mean score</td>
<td>Change in neuropsychological assessment (attention, memory, and executive control) after achievement of target weight loss</td>
</tr>
<tr>
<td><strong>Trial Findings</strong></td>
<td>Baseline MoCA score: 25</td>
<td>Mean Di8git Span Z score: -0.06 to 0.80, P = .024</td>
</tr>
<tr>
<td></td>
<td>Baseline DSST score: 37</td>
<td>Mean memory composite z-score: -0.67 to 0.032, P = .0065</td>
</tr>
<tr>
<td></td>
<td>HI 0.86 (95% CI 0.79, 0.95; P = .0018)&lt;sup&gt;*&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><strong>Conclusions</strong></td>
<td>Patients on dulaglutide had a 14% reduction in substantive cognitive impairment</td>
<td>Liraglutide might slow down memory function decline in diabetes patients early, and possibly preclinical stages of the disease</td>
</tr>
</tbody>
</table>

*After post hoc adjustment for individual standardized baseline scores.


Drug selection: SGLT2 inhibitor vs. GLP1-RA

AACE/ADA/EASD/ACC

• Can begin with metformin monotherapy for DM2, but consider adding GLP-1 RA or SGLT2 inhibitor independent of HbA1c target.

• Can consider beginning therapy with GLP-1 RA or SGLT2 inhibitor prior to metformin in patients with higher cardiovascular risk.

• If atherosclerotic CVD or stroke predominates:
  Choose GLP-1 RA with proven benefit

• If heart failure or CKD predominates:
  Choose SGLT2 inhibitor with proven benefit
ESC/EASD Guidelines: Novel Glucose-Lowering Drugs

A. T2DM -- Drug-naive patients

- ASCVD, or high/very high CV risk (target organ damage or multiple risk factors)
  - SGLT2 inhibitor or GLP-1 RA*
  - Metformin
  - Add SGLT2 inhibitor or GLP-1 RA*

B. T2DM -- On metformin

- ASCVD, or high/very high CV risk (target organ damage or multiple risk factors)
  - Continue metformin

---

<table>
<thead>
<tr>
<th>Very high CV risk</th>
<th>High CV risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with DM and established CVD</td>
<td></td>
</tr>
<tr>
<td>• or other target organ damage†</td>
<td></td>
</tr>
<tr>
<td>• or three or more major risk factors‡</td>
<td></td>
</tr>
<tr>
<td>• or early onset T1DM of long duration (&gt; 20 years)</td>
<td></td>
</tr>
<tr>
<td>Patients with DM duration ≥ 10 years without target organ damage plus any other additional risk factor</td>
<td></td>
</tr>
</tbody>
</table>

*Use drugs with proven CVD benefit.
†Proteinuria, renal impairment defined as eGFR < 30 mL/min/1.73 m², LVH, or retinopathy.
‡Age, hypertension, dyslipidemia, smoking, obesity.
AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm

Glycemic Control Algorithm

Individualize Goals

A1C ≤6.5%

For patients without concurrent serious illness and at low hypoglycemic risk

A1C >6.5%

For patients with concurrent serious illness and at risk for hypoglycemia

Lifestyle Therapy and Ongoing Glucose Monitoring (CGM preferred)

Independent of Glycemic Control, if Established or High ASCVD Risk and/or CKD, Recommend SGLT2i and/or LA GLP1-RA

DUAL THERAPY

GLP1-RA

SGLT2i

TZD

SU/GLIN

TRIPLE THERAPY

GLP1-RA

SGLT2i

SU/GLIN

Basal Insulin

Coalescivan

Bremisorcs OR

AG

Progression of Disease

ADD OR INTENSIFY INSULIN

Refer to Insulin Algorithm

SYMPTOMS

NO

DUAL Therapy

OR

TRIPLE Therapy

INSULIN & Other Agents

YES

MET (another agent)
# AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm

## Profiles of Antihyperglycemic Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>MET</th>
<th>GLP1-RA</th>
<th>SGLT2i</th>
<th>DPP4i</th>
<th>AGl</th>
<th>TZD (moderate dose)</th>
<th>SU</th>
<th>GLN</th>
<th>COLSVL</th>
<th>BCR-QR</th>
<th>INSULIN</th>
<th>PRAML</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypo</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>Slight Loss</td>
<td>Loss</td>
<td>Loss</td>
<td>Neutral</td>
<td>Gain</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Loss</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Renal/GU**
- Contraindicated if eGFR < 30 ml/min/1.73 m²
- Not indicated for eGFR < 45 ml/min/1.73 m²
- Dose Adjustment: Necessary (Except Tinzaparinin)
- Effective in Reducing Albuminuria

**GI Sx**
- Moderate
- Moderate
- Neutral
- Moderate
- Neutral
- Neutral
- Mild
- Moderate
- Neutral

**CHF**
- Neutral
- Prevent HF Hospitalization: Manage HTN: See #2
- Neutral
- Moderate
- Neutral
- Neutral
- Neutral

**ASCVD**
- Neutral
- Potential Benefits of LA GLP1-RA: See #3
- Neutral
- May Reduce Stroke Risk
- Possible ASCVD Risk
- Lowers LDL-C
- Safe
- Neutral

**Bone**
- Neutral
- Neutral
- Neutral
- Moderate Fracture Risk
- Neutral
- Neutral
- Neutral

**Ketotic Acidosis**
- Neutral
- DKA Can Occur in Various Stress Settings
- Neutral
- Neutral
- Neutral
- Neutral
- Neutral
- Neutral

### Notes
1. Canagliflozin indicated for eGFR ≥ 30 ml/min/1.73 m² in patients with CKD 3a albuminuria.
2. Dapagliflozin—potential primary prevention of HF hospitalization & demonstrated efficacy in HFpEF.
3. Epedagliptin—Dx approved to reduce CVD mortality. Canagliflozin—Dx approved to reduce NACD events.
4. Potential increased hospitalizations for heart failure with albiglutide and saxagliptin.

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Medication Access/Medication Cost

• Despite promising data described above, many patients are unable to utilize these classes of medications due to high cost involved and economic hardship.

• Uninsured patients, and even some insured patients, with high copays or deductibles may be limited in their ability to obtain diabetes medications with the best profiles for organ protection.

• Often a particular insurance company will only cover one agent within a particular class so ability to select a specific drug may be limited.

• Be aware of limitations when prescribing and consider options for cost-reduction or alternative medications if cost remains prohibitive.
Conclusions

- Diabetes is a multifactorial disease
- Many people with T2DM have ASCVD, kidney disease, and/or HF
- Role for PCPs, cardiologists, nephrologists, and diabetologists in risk management for T2DM and CVD, or CKD, or risk factors
- We can prevent progression of diabetes complications
- Latest guidelines recommend SGLT2 inhibitors and GLP-1 RAs for organ protection in individualized diabetes care
- Novel glucose-lowering drugs have a role beyond T2DM: in HF, ASCVD, and kidney disease
References


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