New Initiative Roll-Out: Optimization of SGLT-2 inhibitors in Patients with Heart Failure and Type 2 Diabetes

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As a network, we are focusing on reducing hospitalizations across all patient populations. We have started an initiative to help decrease hospitalizations related to heart failure (HF) by reviewing patients with heart failure and type 2 diabetes (T2DM) and the utilization of sodium-glucose cotransporter 2 inhibitors (SGLT2i). SGLT2is have been proven to not only help with blood glucose management, but also have cardiovascular benefits.[1,2] In the most recent HF guidelines, SGLT2is are now one of four classes of medications in guideline-directed medical therapy (GDMT) for treatment of heart failure with reduced ejection fraction (HFrEF) (COR 1A recommendation). SGLT2is are also recommended to be used for heart failure with mildly reduced ejection fraction (HFmrEF) (COR 2a) and heart failure with preserved EF (HFpEF) (COR 2a).[2] This is supported by data demonstrating that SGLT2i use results in reduced mortality and heart failure hospitalizations, regardless of if the patient also has type 2 diabetes.[2] SGLT2is have been shown to reduce heart failure hospitalizations by 30 percent.[2,3] The cardiovascular benefits align SGLT2i use well with the current initiative.

As stated above, we are starting to review patients who have claims data for both HF and T2DM in a rolling six-month period. Once the patients have been identified, a deeper dive into their medication claims is occurring to see if patients have claims for SGLT2is or Dipeptidyl peptidase 4 (DPP-4) inhibitors. DPP-4 inhibitors are medications utilized for type 2 diabetes, but have not demonstrated the cardiovascular benefits seen with SGLT2is.[1] Additionally, both saxagliptin and alogliptin may increase the risk of HF exacerbation with recommendations from the FDA to discontinue use in patients with HF.[1,2,4] By switching patients from a DPP-4 inhibitor to an SGLT2i, we can see a benefit in diabetes management (greater A1c lowering potential) and reduction in mortality and heart failure hospitalizations.[1-3] If attributed patients are identified as meeting the above criteria, a report will be distributed to the practice. Practices may review these patients and determine if an SGLT2i is appropriate for their HF and T2DM management.

It is recognized that not every patient is appropriate for an SGLT2i, despite guideline recommendations. Common concerns from providers are for patients with soft blood pressure or chronic kidney disease (CKD) and the potential for diabetic ketoacidosis (DKA). SGLT2is are often used in CKD to slow progression of the disease[1]. Patient-specific factors such as volume status, renal function and blood pressure should all be assessed prior to initiation and then ongoing during treatment.[5-9] On average, one can expect reduction in systolic blood pressure of 3-5mmHg for patients on an SGLT2i.[5] Regarding CKD, each SGLT2i has different dosing recommendations to follow (see table 1). Patients should be aware of factors that could

contribute to developing DKA and associated signs and symptoms. As a precaution, guidelines recommend holding the medication during illness, before a scheduled surgery, or during a prolonged fast.[1] Concomitant medications for blood pressure and blood glucose management should be assessed prior to and after initiation.[1,5]

Table 1. SGLT2i dosing information

Dosing Recommendations for SGLT-2 inhibitors				
Medication	Invokana® (canagliflozin)[6]	Farxiga® (dapagliflozin)[7]	Jardiance® (empagliflozin)[8]	Steglatro® (ertugliflozin)[9*]
Dosing	100mg po daily and can increase to 300mg po daily if needed for additional glycemic control	For glucose control: 5mg po daily and can be increased to 10mg po daily for additional glycemic control All other indications: 10mg po daily	10mg po daily and can be increased to 25mg po daily for additional glycemic control	5mg po daily and can be increased to 15mg po daily for additional glycemic control
Renal Dosing Adjustments	eGFR > 60 mL/min/1.73 m^2- no adjustment needed eGFR 30 to <60 mL/min/1.73 m^2- 100mg daily eGFR <30 mL/min/1.73 m^2- Initiation is not recommended, however, established patients with urinary albumin > 300mg/day can continue 100mg daily to reduce the risks of ESKD, doubling of serum creatinine, CV death, and hospitalizations for HF	eGFR > 45 mL/min/1.73 m^2- No adjustment needed eGFR: 25- <45 mL/min/1.73 m^2- 10mg orally once daily Not recommended for use for glycemic control based on mechanism of action eGFR <25 mL/min/1.73 m^2- Initiation is not recommended, however, patients may continue 10mg daily to reduce the risk of eGFR decline, ESKD, CV death and HF	eGFR > 30 mL/min/1.73 m^2- No dosage adjustment necessary eGFR < 30 mL/min/1.73 m^2- Not recommended if only using for glycemic control benefits Renal and cardiac benefits have been shown in patients with an eGFR ≥20 mL/min/1.73 m^2	eGFR ≥45 mL/min/1.73 m^2- no adjustment needed eGFR < 45 mL/min/1.73 m^2- Not recommended for use
*Based on a meta-analysis, ertugliflozin is the least potent SGLT2i, when compared to empagliflozin, canagliflozin, or dapagliflozin, to prevent cardiorenal events and all-cause mortality in patients with T2DM at high cardiovascular risk.[3]				

Overall, utilizing SGLT2is in patients with T2DM and HF can reduce HF hospitalizations and mortality. Consider reviewing your patient panels to determine if an SGLT2i is appropriate for them.

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