

**Question from the clinic: Is it true that you should avoid starting an SGLT2-inhibitor until the A1C is < 10%?**

**Answer:** Although “10%” isn’t listed in the package insert or in guidelines as the “limit”, it is a clinically acceptable limit to consider before starting one of these agents due to:

- Increased risk of Euglycemic Diabetic Ketoacidosis (DKA): This risk is magnified when the person already has other risk factors such as acute illness, infections, fasting or ketogenic diet, pancreatitis, alcohol abuse, dehydration/volume depletion, or current steroid therapy.
- Increased risk of infections at higher A1C levels: infections can be more severe and frequent at higher levels of A1C, which in turn can put the person at risk for DKA and other complications from infection.
- Insufficient glycemic control: SGLT2 inhibitors can reduce A1C ~ 0.5 – 1%. When A1C is > 10%, more efficacious drug therapies are warranted to get to goal levels.

**Supporting Data: DKA**

A nationwide cohort study in the US identified predictors of DKA in persons prescribed an SGLT2-Inhibitor.<sup>1</sup> The variables with the strongest association with DKA hospitalization were:

Variables:	Odds Ratio:	Confidence Interval
Prior intracranial hemorrhage	11.5	95% CI (1.46 - 91.1)
Use of dementia medications	7.76	95% CI (2.60 - 23.1)
Prior diagnosis of hypoglycemia	5.41	95% CI (1.92 - 15.3)
Baseline Bicarbonate < 18 mmol/L	5.09	95% CI (1.58 - 16.4)
Digoxin use	4.00	95% CI (1.21 - 13.2)
<b>Baseline A1C &gt; 10%</b>	<b>3.14</b>	95% CI (1.95 - 5.06)
Prior DKA	2.45	95% CI (0.33 - 18.0)

**Supporting Data: Infection**

The connection to yeast infection and higher A1C is well established. A retrospective cohort study looking specifically at genitourinary infection among patients on SGLT2 inhibitors showed the following<sup>2</sup>:

<b>A1C</b>	<b>Odds Ratio:</b>
≥7.0 to <8.0%	3.45 (p=0.001)
≥8.0 to <9.0%	8.56 (p<0.0001)
<b>≥9.0%</b>	<b>11.45 (p&lt;0.0001)</b>

**References:**

1. Fralick et al. Identifying Risk Factors for Diabetic Ketoacidosis Associated with SGLT2 Inhibitors: A Nationwide Cohort Study in the USA. Feb 2021. J Gen Intern Med. 36(9):2601-7
2. Katrina m, Cunanan E, Sjoberg K. Incidence and factors associated with genitourinary infections among Type 2 diabetes patients on SGLT2 Inhibitors: A single retrospective cohort study. Diabetes Epidemiology and Management 7 (2022). 100082.