# Indian Health Service
# National Pharmacy and Therapeutics Committee
# SGLT-2 Inhibitors in the Treatment of Diabetes
# NPTC Updates
# February 2014

**Background:**
The IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed recent clinical data concerning the use of an emerging new drug class Sodium Glucose Cotransport-2 (SGLT-2) inhibitors in the treatment of Type 2 Diabetes at their February 2014 meeting. Evaluation criteria included published evidence on the pharmacology, pharmacodynamics, pharmacokinetics, safety, and efficacy of the SGLT-2 inhibitors canagliflozin and dapagliflozin[1-3]. Based on the information presented, the committee **made no changes** to the IHS National Core Formulary (NCF).

**Discussion:**
The Indian Health Service has made significant improvements in key diabetes risk factors through the SDPI Diabetes Prevention Programs[4,5]. Despite this improvement, the prevalence rate of diabetes in AI/AN adults is still almost twice the rate for the total U.S. adult population. Pharmacologic therapy for hyperglycemia in Type 2 diabetes remains an important therapeutic modality when combined with lifestyle interventions. SGLT-2 Inhibitors became available in the United States in March of 2013. This new drug class works by reducing reabsorption of filtered glucose from the proximal tubular lumen in the kidney, lowering the renal threshold for glucose resulting in glucosuria[6-12].

Clinical trials for this drug class demonstrated HbA1C lowering from 0.77% to 1.03%. There was also a decrease in fasting and 2-hour post prandial serum glucose levels. Weight reductions ranging from 2.2% to 4.4% were also observed. In the CANTATA-D2 trial comparing canagliflozin vs. sitagliptin at 52 weeks, canagliflozin reduced systolic blood pressure by 5.1 mm HG vs. a 0.9 mm HG increase ($P<0.001$) in the DPP-4 group. It is recommended to assess volume status and blood pressure before initiating SGLT-2 inhibitors[14, 15].

SGLT-2 inhibitors are associated with transient decreases in renal function and currently available products are contraindicated in patients with severe renal impairment, ESRD, or on dialysis. Additionally, dapagliflozin is not recommended in patients with a history of bladder cancer. This is due to safety concerns because of a higher rate of bladder cancer observed during clinical trials. Also of concern is the increase in bladder infections (5%) and female mycotic infections (11%) [6-14].

A recent meta-analysis assessing the efficacy and safety of SGLT-2 inhibitors conducted by Vasilakou, et al., concluded that most of the trials reviewed had a high risk of bias because of missing data and last-observation-carried-forward methods used. They also concluded that while the SGLT-2 drug class may improve short-term outcomes, the long-term outcomes and safety are still unclear[13, 16].

**Findings:**
SGLT-2 inhibition is a novel treatment for diabetes. In clinical trials, SGLT-2 inhibition has shown reductions in glucose, blood pressure and body weight when compared with placebo and DPP-4 inhibitors. The development of novel antidiabetic agents currently should not only focus on the potent glucose-lowering properties but also on long-term safety aspects and potential cardiovascular benefits. Due to the lack of long-term safety and cardiovascular endpoint data available at this time, the NPTC took no action to regarding the SGLT-2 class.

If you have any questions regarding this document, please contact the NPTC at nptc1@ihs.gov.

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