Name: XXXX
ASHP Membership Number: XXXX

Dapagliflozin propanediol (Farxiga – Bristol-Myers Squibb; AstraZeneca) Antidiabetic Agent

New Drug Comparison Rating (NDCR) = 3
Indication: Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
Comparable drug(s): Canagliflozin (Invokana)

Disease State/Drug Class Summary: Sodium-glucose cotransporter 2 (SGLT2) is expressed in the proximal renal tubules and is responsible for the reabsorption of the majority of glucose filtered by the kidney and these agents reduce the reabsorption of filtered glucose, thereby increasing urinary glucose secretion and lowering blood glucose and glycosylated hemoglobin (hemoglobin A1c [HbA1c]) concentrations. The use of dapagliflozin resulted in reductions in HbA1c and fasting plasma glucose (FPG) concentrations and, in many patients, weight reduction.

Efficacy: In a placebo-controlled study, the percentage of patients achieving a HbA1c of less than 7% was 44% and 51% in patients receiving daily doses of 5 mg and 10 mg of dapagliflozin, respectively, compared with 32% of those receiving placebo. The use of dapagliflozin in combination with other antidiabetic agents
resulted in greater reductions in HbA1c and FPG concentrations. Patients treated with regimens that included dapagliflozin typically lost an average of 1 to 3 kg of body weight over a 24-week period, whereas those who were treated with other antidiabetic agents usually either lost less weight or experienced weight gain.

Most important risks/adverse events: Renal function impairment (contraindicated in patients with severe renal impairment; renal function should be monitored during therapy); hypersensitivity reactions (contraindicated in patients with a history of a serious hypersensitivity reaction); hypotension (risk is increased in patients with impaired renal function or low systolic blood pressure, the elderly, and in patients treated with a diuretic); hypoglycemia (when used concomitantly with insulin or an insulin secretagogue [e.g., a sulfonylurea]); bladder cancer (reported infrequently in clinical studies but at a higher rate that in patients treated with comparator antidiabetic agents or placebo; should not be used in patients with active bladder cancer)

Most common adverse events (and the incidence in patients treated with a dosage of 10 mg daily): Female genital mycotic infections (7%; e.g., vulvovaginal candidiasis), nasopharyngitis (6%), urinary tract infections (4%), increased urination (4%), back pain (4%), male genital mycotic infections (3%; e.g., balanitis), nausea (3%), dyslipidemia (3%; e.g., increased LDL-C).

Advantages: May be less likely to cause hypersensitivity reactions and hyperkalemia. May be less likely to interact with other medications. May be used in patients with severe hepatic impairment, whereas canagliflozin has not been studied in patients with severe hepatic impairment and use is not recommended.

Disadvantages:Bladder cancer has been infrequently reported in clinical studies and should not be used in patients with active bladder cancer. Recommendations for use in patients with impaired renal function are more restrictive (e.g., treatment should not be initiated in patients with an estimated glomerular filtration rate [eGFR] less than 60 mL/min/1.73 m2, whereas treatment with canagliflozin should not be initiated in patients with an eGFR less than 45 mL/min/1.73 m2).

Usual dosage: Initially, 5 mg once a day in the morning; in patients who tolerate treatment and require additional glycemic control, dosage may be increased to 10 mg once a day in the morning; treatment should not be initiated in patients with an eGFR less than 60 mL/min/1.73 m2, and treatment should be discontinued if the eGFR is persistently below this value.

Available Products: Film-coated tablets – 5 mg, 10 mg