

MTF Formulary Management for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors

Defense Health Agency Pharmacy Operations Division

Bottom Line

- **Step therapy exists in this class. Patients must first try metformin and at least one drug from two additional different oral non-insulin diabetes classes before using an SGLT2 inhibitor.**
- **Empagliflozin is on the Uniform Formulary and is the preferred SGLT2 inhibitor (step-preferred). Canagliflozin and dapagliflozin are nonformulary and non step-preferred.**
- **Step therapy applies to all new and current users of an SGLT2 inhibitor (no grandfathering). Patients must first try empagliflozin before using canagliflozin or dapagliflozin.**
- **An SGLT2 inhibitor was not selected for BCF status. Metformin remains the designated BCF selection. All patients with Type 2 diabetes mellitus (T2DM) should try metformin first unless, contraindications exist.**

Uniform Formulary Decision: The Director, DHA, approved the recommendations from the August 2015 DoD P&T Committee meeting on October 30, 2015. Implementation will occur by February 3, 2016.

Uniform Formulary (UF) Agents		Nonformulary Agents
BCF drugs – MTFs <u>must</u> have on formulary	MTFs <u>may</u> have on formulary	MTFs <u>must not</u> have on formulary
None	<u>Step-Preferred</u> <ul style="list-style-type: none"> • Empagliflozin (Jardiance) • Empagliflozin/Linagliptin (Glyxambi) 	<u>Non Step-Preferred</u> <ul style="list-style-type: none"> • Canagliflozin (Invokana) • Canagliflozin/metformin (Invokamet) • Dapagliflozin (Farxiga) • Dapagliflozin/metformin XR (Xigduo XR)
Step Therapy applies to ALL (new and current) users of the SGLT2 inhibitors; no grandfathering applies for any user. See below for detailed criteria.		

SGLT2 Inhibitors: Clinical Summary

- Canagliflozin, dapagliflozin, and empagliflozin are three parent SGLT2 inhibitors currently available in the United States.
- The SGLT2 inhibitors are effective in lowering A1c by 0.4% to 1% when used as monotherapy, by 0.5% to 2% as part of dual therapy, and by 0.3% to 1.3% as part of triple therapy.
- There are no head-to-head trials between any of the SGLT2 inhibitors, although there do not appear to be clinically relevant differences in their effects on lowering A1c when used as monotherapy or added on to other diabetes drugs.
- In general, the SGLT2 inhibitors decrease triglycerides and modestly increase both LDL and HDL cholesterol.
- The SGLT2 inhibitors slightly decrease systolic blood pressure (by 4 to 6 mm Hg) and body weight (reduction on average of 1.8 kg).
- The most common adverse drug reactions for the SGLT2 inhibitors are female genital mycotic infections and urinary tract infections.
- The SGLT2 inhibitors should be avoided in renal impairment. Empagliflozin and canagliflozin can be used in patients with estimated GFRs as low as 45 mL/min. There is a recent FDA safety alert for the class for ketoacidosis. Patients with a history of bladder cancer should avoid dapagliflozin.
- The cardiovascular (CV) safety profile of the SGLT2 inhibitors as a class remains unclear. To date, only one CV trial has been completed and published. The EMPA-REG OUTCOME Trial with empagliflozin showed a 2.2% absolute risk reduction in death from CV causes; however, limitations to the trial exist and results should not be extrapolated to the entire class.
- The SGLT2 inhibitors have a limited role in treating T2DM, due to a lack of clinically compelling advantages over current alternatives in lowering A1c, an incomplete CV safety profile, and undesirable side effects (genital mycotic infections, urinary tract infections).
- Other than the potential for weight loss, the SGLT2 inhibitors offer no additional clinical advantages over other non-insulin diabetes drugs on the UF.

Prior Authorization (PA) Criteria for the Non Step-Preferred SGLT2 Inhibitors

- All new users of an SGLT2 inhibitor are required to try metformin and at least one drug from 2 additional different oral non-insulin diabetes drug classes before receiving an SGLT2 inhibitor. Patients currently taking an SGLT2 inhibitor must have had a trial of metformin or a sulfonylurea (SU) and a DPP-4 inhibitor first.

Manual PA criteria—An SGLT2 inhibitor is approved (e.g., a trial of metformin and at least one drug from two additional different oral non-insulin diabetes drug classes are NOT required) if:

- The patient has had an inadequate response to metformin and at least one drug from two additional different oral non-insulin diabetes drug classes; or
 - The patient has experienced a significant adverse effect from metformin and at least one drug from two additional different oral non-insulin diabetes drug classes; or
 - The patient has a contraindication to metformin and at least one drug from two additional different oral non-insulin diabetes drug classes.
- Additionally, empagliflozin-containing products (Jardiance, Glyxambi) are the preferred agents for the SGLT2 inhibitors. New and current users of a canagliflozin- or dapagliflozin-containing product must try an empagliflozin product first.

Manual PA Criteria: In addition to the above criteria regarding metformin and at least one drug from two additional different oral non-insulin diabetes drug classes, the following PA criteria would apply specifically to all new and current users of canagliflozin (Invokana), canagliflozin/metformin (Invokamet), dapagliflozin (Farxiga), and dapagliflozin/ metformin ER (Xigduo XR):

- The patient has experienced significant adverse events from an empagliflozin-containing product (Jardiance or Glyxambi) that are not expected to occur with Invokana, Invokamet, Farxiga, or Xigduo XR.

References

- DoD P&T Committee minutes: <http://www.health.mil/PandT>
- Current/future drug classes under review by the DoD P&T Committee: <http://www.health.mil/PandT> (scroll down to DoD P&T Committee Meeting Schedule)
- TRICARE Formulary Search Tool: <http://www.health.mil/formulary>
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents (including this one) available at: <http://www.health.mil/DoDPTResources>
- Point of contact for additional information: dha.ibsa.pharmacy.list.poduf@mail.mil

Price Comparison at MTF	
Drug	MTF Cost (August 2015)
Basic Core Formulary	
None	
Uniform Formulary	
Empagliflozin (Jardiance) Empagliflozin/Linagliptin (Glyxambi)	\$ = Most Cost-Effective
Non-Formulary	
Canagliflozin (Invokana) Canagliflozin/Metformin (Invokamet)	\$\$\$\$ = Least Cost-Effective
Dapagliflozin (Farxiga) Dapagliflozin/Metformin XR (Xigduo XR)	\$\$\$\$ = Least Cost-Effective
Legend: \$ = "Most Cost-Effective" represents Rx's with the <u>lowest cost</u> and/or best clinical efficacy \$\$ = "Less Cost-Effective" represents <u>higher cost</u> Rx's with similar clinical efficacy \$\$\$ = "Less Cost-Effective" represents <u>next higher cost</u> Rx's with similar clinical efficacy \$\$\$\$ = "Least Cost-Effective" represents Rx's with the <u>highest cost</u> with similar clinical efficacy	