

SGLT2 inhibitors

Oral agents that block glucose reabsorption in the kidney's proximal tubule, producing therapeutic glucosuria alongside cardiovascular and renal benefits that now extend well past their original glucose-lowering indication - at the cost of a genuinely distinctive trap, euglycemic diabetic ketoacidosis, that can present without the high glucose level clinicians expect from DKA.

Online guide: <https://www.medguideglobal.com/pharmacology/endocrine-and-metabolic/sglt2-inhibitors>

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Quick revision

One Liner: SGLT2 inhibitors block glucose reabsorption in the kidney's proximal tubule to produce glucosuria, and have grown far beyond a glucose-lowering role into agents with independently proven heart-failure and chronic-kidney-disease benefit - while carrying a genuinely distinctive trap, euglycemic diabetic ketoacidosis, that can occur with a near-normal blood glucose.

1. SGLT2 inhibitors block the sodium-glucose cotransporter 2 in the proximal renal tubule, the transporter responsible for most filtered glucose reabsorption, producing glucosuria and a modest, insulin-independent glucose-lowering effect. [1][4]
2. Empagliflozin and dapagliflozin both carry FDA indications well beyond glycemic control: reducing cardiovascular death and heart failure hospitalisation, and slowing chronic kidney disease progression, in patients with or without type 2 diabetes. [1][2]
3. All three carry a warning for euglycemic diabetic ketoacidosis, in which blood glucose at presentation can be below the level typically expected for DKA (for example, under 250 mg/dL), which can delay recognition if clinicians rely on glucose alone. [1][2]
4. Empagliflozin, dapagliflozin and canagliflozin all warn of necrotizing fasciitis of the perineum (Fournier's gangrene), a rare but life-threatening infection identified through postmarketing surveillance across the class. [1][2][3]
5. Genital mycotic infection is the most common class-specific adverse effect, occurring at a materially higher rate than placebo in trial data, particularly in women and in patients with a prior history of such infections. [4][2]
6. Canagliflozin carried an FDA boxed warning for lower-limb amputation based on the CANVAS and CANVAS-R trials, which showed roughly double the amputation rate versus placebo; the FDA removed that boxed warning in 2020, though amputation risk is still described in the label's warnings and precautions. [4][3]
7. Volume depletion is a recognised risk across the class, particularly in the elderly and in patients on loop diuretics, and can cause symptomatic hypotension or acute kidney injury. [1][2]
8. SGLT2 inhibitors are typically withheld for at least 3 days before elective surgery or procedures involving prolonged fasting, reflecting the euglycemic-DKA risk in a fasting, physiologically stressed state. [1][2]

Overview

1. SGLT2 inhibitors work on an organ that most other glucose-lowering classes leave alone: the kidney. The sodium-glucose cotransporter 2 (SGLT2), expressed in the early proximal renal tubule, is responsible for the great majority of filtered glucose reabsorption back into the blood. Blocking it lets that glucose pass into the urine instead, an insulin-independent mechanism that also explains why the class does not itself cause hypoglycemia at typical glucose levels and pairs mechanistically cleanly with virtually any other diabetes drug, including insulin. [1][4]
2. What has reshaped this class's place in medicine since its original approval is evidence that its benefit extends well beyond glycemic control. Empagliflozin and dapagliflozin both now carry FDA indications for reducing cardiovascular death and heart failure hospitalisation, and for slowing chronic kidney disease progression, in patients with or without type 2 diabetes - indications earned through dedicated outcomes trials rather than glucose-lowering data alone. That is

a genuinely different evidentiary status from most of the other classes in this endocrine-and-metabolic hub, closer in spirit to how a cardiovascular drug earns a heart-failure indication than to how a typical antihyperglycemic label is built. [1][2]

3. The safety trade-off for that mechanism is a trap worth taking seriously: euglycemic diabetic ketoacidosis. Because SGLT2 inhibition promotes glucose loss through the urine regardless of the ketogenic process happening in parallel, a patient can develop ketoacidosis with a blood glucose at presentation below the level clinicians are trained to expect for DKA - sometimes under 250 mg/dL. A clinician anchored on a high glucose reading as the entry criterion for considering DKA can miss the diagnosis in exactly this setting, which is why the labels specifically direct ketone assessment based on symptoms rather than glucose level alone. [1][2]

4. The rest of the class's safety profile follows fairly directly from its mechanism: more glucose sitting in the urine means a favourable environment for genital yeast and, rarely, a life-threatening perineal infection (Fournier's gangrene); more sodium and glucose delivered to the distal nephron contributes to a natriuretic, volume-losing effect that is part of both the cardiorenal benefit and the hypotension/volume-depletion risk; and canagliflozin's own trial programme surfaced a lower-limb amputation signal substantial enough to justify, and later remove, a boxed warning as more data accumulated. None of these are separate class members with different core mechanisms - they are one mechanism's benefits and costs, distributed slightly differently across the three drugs covered here. [4][3]

Classification and drug examples

Intro: All three agents covered here inhibit the same transporter, SGLT2, with broadly similar selectivity over SGLT1 (the intestinal glucose transporter). What differs between them is chiefly their breadth of FDA-approved non-glycemic indications and their individual outcomes-trial history, rather than a distinct subclass mechanism.

Name: SGLT2-selective inhibitors

Note: The three most widely used members; ertugliflozin is a fourth FDA-approved agent in the same class with a comparatively smaller non-glycemic indication footprint and is not detailed separately here.

1. Name: Empagliflozin

Jardiance

1. Route: Oral

1. Note: Indicated for glycemic control, cardiovascular death reduction in T2DM with established cardiovascular disease, heart failure (across the ejection fraction range), and chronic kidney disease. [1]

2. Name: Dapagliflozin

Farxiga

2. Route: Oral

2. Note: Indicated for glycemic control, heart failure (across the ejection fraction range), and chronic kidney disease at risk of progression, with or without type 2 diabetes. [2]

3. Name: Canagliflozin

Invokana

3. Route: Oral

3. Note: Indicated for glycemic control, major adverse cardiovascular event reduction, and reducing the risk of end-stage kidney disease and cardiovascular death in type 2 diabetes with diabetic nephropathy; the drug whose trial programme first surfaced the class's amputation signal. [3] [4]

Mechanism of action

Summary: In the healthy kidney, essentially all glucose that is filtered at the glomerulus is reabsorbed back into the blood rather than excreted, chiefly through SGLT2 in the early proximal tubule (with a smaller contribution from SGLT1 further along the nephron). SGLT2 inhibitors block this transporter, lowering the renal glucose threshold so that filtered glucose above a much lower level is excreted in the urine instead of reabsorbed. The resulting glucosuria lowers blood glucose without requiring any change in insulin secretion or action, and the accompanying natriuresis and osmotic

diuresis are what link the same mechanism to the class's blood-pressure, volume, and cardiorenal effects.

Target: Sodium-glucose cotransporter 2 (SGLT2) in the early proximal renal tubule

Cidal Static: Not applicable - an insulin-independent renal transport effect, not an action against a pathogen

Kill Kinetics: Glucosuric effect begins within the first dose and is present for as long as the drug occupies the transporter; the cardiorenal benefit accrues over a longer, trial-measured timescale

1. Step: 1

1. Title: Glucose is filtered at the glomerulus

1. Detail: The kidney filters plasma glucose freely at the glomerulus as part of normal renal blood filtration. [4]

2. Step: 2

2. Title: SGLT2 normally reabsorbs most of that filtered glucose

2. Detail: SGLT2, expressed in the early proximal tubule, is the transporter responsible for the great majority of filtered glucose reabsorption back into the circulation. [1][4]

3. Step: 3

3. Title: The SGLT2 inhibitor blocks this transporter

3. Detail: Binding and inhibiting SGLT2 reduces glucose reabsorption in the proximal tubule, lowering the renal threshold at which glucose begins to appear in the urine. [1]

4. Step: 4

4. Title: Glucosuria and a modest osmotic diuresis follow

4. Detail: Unreabsorbed glucose is excreted in the urine, producing glucosuria and, through the associated osmotic and natriuretic effect, mild volume and blood-pressure reduction. [4]

5. Step: 5

5. Title: Blood glucose falls through an insulin-independent route

5. Detail: Because this whole pathway operates on renal glucose handling rather than pancreatic insulin secretion or peripheral insulin sensitivity, the mechanism does not itself cause hypoglycemia and functions even in patients with substantial insulin resistance or beta-cell decline. [4]

Major clinical uses

1. Drug: Empagliflozin

1. Organism: Not applicable

1. Indication: Glycemic control in adults and pediatric patients 10 years and older with type 2 diabetes; cardiovascular death reduction in adults with T2DM and established cardiovascular disease; heart failure (cardiovascular death and hospitalisation reduction); chronic kidney disease (reducing eGFR decline and end-stage kidney disease risk)

1. Line: increasingly used early for cardiorenal benefit independent of glycemic status

1. Note: One of the broadest non-glycemic indication sets in the class. [1]

2. Drug: Dapagliflozin

2. Organism: Not applicable

2. Indication: Glycemic control in adults and pediatric patients 10 years and older with type 2 diabetes; heart failure (cardiovascular death, hospitalisation and urgent visit reduction) across the ejection fraction range; chronic kidney disease at risk of progression, with or without diabetes

2. Line: used for heart failure and CKD indications even in patients without diabetes

2. Note: Renal and heart-failure indications are approved independent of a diabetes diagnosis. [2]

3. Drug: Canagliflozin

3. Organism: Not applicable

3. Indication: Glycemic control in adults with type 2 diabetes; reduction of major adverse cardiovascular events in T2DM with established cardiovascular disease; reduction of end-stage kidney disease, doubling of serum creatinine, cardiovascular death and heart failure hospitalisation in T2DM with diabetic nephropathy

3. Line: renal-outcomes indication specifically tied to diabetic nephropathy

3. Note: The drug with the longest-standing, most extensively characterised amputation-risk data in the class. [3]
4. Drug: All three as a class
4. Organism: Not applicable
4. Indication: Type 2 diabetes mellitus, generally added early given cardiovascular or renal risk rather than reserved until glycemic targets are missed
4. Line: positioned early alongside metformin, or ahead of a sulfonylurea, when cardiovascular, renal, or heart-failure risk is present
4. Note: The ADA Standards of Care direct this early-addition approach independent of current glycemic control. [5]

Pharmacokinetics

1. Drug: Empagliflozin
1. Route: Oral
1. Absorption: Well absorbed orally; peak plasma concentration reached within a few hours
1. Csf Penetration: Not clinically relevant to this drug's mechanism
1. Metabolism: Primarily via glucuronidation, with minor cytochrome P450 contribution
1. Elimination: Renal and faecal, roughly split, as parent drug and metabolites
1. Dose Adjust: Not recommended for glycemic-control initiation below an eGFR threshold specified in the current label; withheld before surgery or prolonged fasting [1]
2. Drug: Dapagliflozin
2. Route: Oral
2. Absorption: Rapidly absorbed orally
2. Csf Penetration: Not clinically relevant to this drug's mechanism
2. Metabolism: Primarily via glucuronidation to an inactive major metabolite
2. Elimination: Renal and faecal
2. Dose Adjust: Glycemic-control initiation is not recommended below eGFR 45 mL/min/1.73 m²; the heart-failure and CKD indications extend down to a lower eGFR threshold specified in the label [2]
3. Drug: Canagliflozin
3. Route: Oral
3. Absorption: Well absorbed orally
3. Csf Penetration: Not clinically relevant to this drug's mechanism
3. Metabolism: Primarily via glucuronidation
3. Elimination: Renal and faecal
3. Dose Adjust: Dose and eligibility are eGFR-dependent, with lower-limb monitoring recommended regardless of renal function given the amputation signal from its outcomes trials [3]
1. This page gives no dose regimens by design. Starting dose, titration and renal eligibility thresholds differ by indication and by agent, and belong in a current prescribing reference used by the treating clinician.
2. All three agents lose glucose-lowering efficacy as eGFR falls, because the mechanism depends on filtered glucose reaching a functioning tubule to be blocked from reabsorption - but the heart-failure and chronic-kidney-disease indications for empagliflozin and dapagliflozin are specifically retained at lower eGFR levels than the glycemic-control indication, since the cardiorenal benefit does not depend on the glucosuric effect alone. [1][2]
3. Each of the three is withheld for at least 3 days before elective surgery or a procedure involving prolonged fasting, reflecting the shared euglycemic-ketoacidosis risk in a fasting, physiologically stressed state rather than any single agent's unique pharmacokinetics. [1][2]

Adverse effects

1. Effect: Genital mycotic infection
1. Detail: The most common class-specific adverse effect; in dapagliflozin trials, female genital infections occurred in

roughly 8.4% (5 mg) and 6.9% (10 mg) of patients versus about 1.5% on placebo. Risk is higher in women, in uncircumcised men, and in patients with a prior history of such infections. [2][4]

2. Effect: Urinary tract infection

2. Detail: Increased urinary glucose creates a favourable environment for urinary pathogens, raising UTI incidence across the class. [4]

3. Effect: Volume-depletion symptoms

3. Detail: Symptomatic hypotension, dizziness and postural symptoms occur more often than placebo, particularly in older patients and those on diuretics. [1][2]

1. Effect: Euglycemic diabetic ketoacidosis

1. Detail: Ketoacidosis can occur with a blood glucose at presentation below the level typically expected for DKA, for example under 250 mg/dL, through a combination of non-insulin-dependent glucose clearance, relative hyperglucagonemia and volume depletion. Risk is increased by insulin dose reduction, reduced caloric or fluid intake, surgery, acute illness, alcohol excess and a low-carbohydrate diet.

1. Action: Ketones are assessed based on symptoms - nausea, vomiting, abdominal pain, malaise, unusual fatigue, or difficulty breathing - regardless of the glucose reading, and the SGLT2 inhibitor is discontinued if ketoacidosis is confirmed or suspected until resolution. [1][2]

2. Effect: Necrotizing fasciitis of the perineum (Fournier's gangrene)

2. Detail: A rare, life-threatening necrotizing infection of the perineal and genital tissue, identified through postmarketing surveillance across empagliflozin, dapagliflozin and canagliflozin, requiring urgent surgical intervention.

2. Action: Patients presenting with pain, tenderness, erythema or swelling in the genital or perineal area together with fever or malaise require urgent evaluation; the SGLT2 inhibitor is discontinued and broad-spectrum antibiotics with surgical debridement are initiated promptly if confirmed. [1][2][3]

3. Effect: Lower-limb amputation

3. Detail: Canagliflozin's CANVAS and CANVAS-R trials showed higher amputation rates than placebo (5.9 versus 2.8 events per 1000 patient-years in CANVAS; 7.5 versus 4.2 in CANVAS-R), with toe and midfoot amputations most common; the FDA removed the boxed warning based on this finding in 2020 as further data accumulated, though the risk remains described in warnings and precautions.

3. Action: Patients are monitored for new pain, tenderness, ulcers or infection of the lower limb, and canagliflozin is discontinued if these develop; pre-existing amputation, peripheral vascular disease and neuropathy are the strongest risk factors considered before starting. [4][3]

4. Effect: Volume depletion and acute kidney injury

4. Detail: Intravascular volume contraction can cause symptomatic hypotension and a transient rise in serum creatinine, occasionally progressing to acute kidney injury, particularly in the elderly and in patients on loop diuretics or ACE inhibitors/ARBs.

4. Action: Volume status and renal function are assessed before starting and periodically during treatment, especially in higher-risk patients. [1][4]

1. Drug: Canagliflozin

1. Effect: The only member of this class with a dedicated, trial-derived lower-limb amputation signal substantial enough to have carried its own boxed warning until 2020. [4]

2. Drug: Dapagliflozin

2. Effect: Carries indications for heart failure and chronic kidney disease that extend to patients without type 2 diabetes at all, reflecting outcomes trials conducted in non-diabetic heart-failure and CKD populations. [2]

3. Drug: Empagliflozin

3. Effect: Approved across the full heart-failure ejection-fraction range and down to a pediatric glycemic-control indication from age 10, the broadest paediatric footprint discussed here. [1]

Contraindications, precautions and interactions

1. Known hypersensitivity to the specific SGLT2 inhibitor or its excipients, including reported cases of angioedema. [1]
2. Dialysis-dependent patients and those with severe renal impairment below the eGFR threshold specified in each label; dapagliflozin's non-glycemic indications are not recommended for initiation below eGFR 25 mL/min/1.73 m². [2]
1. A history of diabetic ketoacidosis, reduced caloric or fluid intake, acute illness, surgery, or a low-carbohydrate/ketogenic diet raises euglycemic-DKA risk and prompts temporary discontinuation. [1][2]
2. A history of genital mycotic infection, uncircumcised status in men, or recurrent urinary tract infection raises the risk of the class's most common adverse effect. [4]
3. Concurrent loop diuretic use, advanced age, or renal impairment raises volume-depletion and acute-kidney-injury risk with any SGLT2 inhibitor. [1]
4. A history of lower-limb amputation, peripheral vascular disease, neuropathy, or active foot ulcer is specifically weighed before starting canagliflozin. [3][4]
5. Held for at least 3 days before elective surgery or a procedure associated with prolonged fasting. [1][2]
1. With: Insulin or an insulin secretagogue
 1. Effect: Combined use increases hypoglycemia risk; a lower dose of the concomitant agent is often considered when adding an SGLT2 inhibitor. [4]
2. With: Loop diuretics
 2. Effect: Additive volume depletion and hypotension risk, particularly in the elderly. [1]
3. With: UGT enzyme inducers (for canagliflozin specifically)
 3. Effect: Can reduce canagliflozin exposure and glycemic effect through increased glucuronidation clearance. [3]

Comparison tables

Title: One mechanism, three different non-glycemic footprints

Caption: All three block the same renal transporter; what differs is the breadth of dedicated outcomes-trial indications and the specific safety signal each has become best known for.

1. Key: drug
 1. Label: Drug
 1. Is Row Header: true
 2. Key: signature_indication
 2. Label: Distinguishing non-glycemic indication
 3. Key: signature_risk
 3. Label: Best-characterised distinguishing risk
 4. Key: non_diabetic_use
 4. Label: Approved without diabetes?
1. Drug: Empagliflozin
 1. Signature Indication: Heart failure across the full ejection-fraction range plus chronic kidney disease
 1. Signature Risk: Class-wide euglycemic DKA and Fournier's gangrene warnings, no unique additional signal beyond the class
 1. Non Diabetic Use: Yes, for heart failure and CKD indications [1]
2. Drug: Dapagliflozin
 2. Signature Indication: Heart failure and CKD indications extending to patients entirely without diabetes
 2. Signature Risk: Highest reported genital mycotic infection incidence figures among the three in its own trial data
 2. Non Diabetic Use: Yes, for heart failure and CKD indications [2]
3. Drug: Canagliflozin
 3. Signature Indication: Renal-outcomes indication tied specifically to diabetic nephropathy
 3. Signature Risk: The class's dedicated lower-limb amputation signal, formerly its own boxed warning

3. Non Diabetic Use: No, indications remain tied to type 2 diabetes [3][4]

High-yield exam pearls

1. Pearl: SGLT2 inhibitors cause glucosuria by blocking reabsorption, not by increasing insulin.
 1. Why: It is the mechanistic reason the class does not itself cause hypoglycemia and is the single fact every other mechanism question in this class builds on. [1]
2. Pearl: Euglycemic DKA can present with a glucose under 250 mg/dL - do not rule out DKA on a near-normal glucose alone in a patient on this class.
 2. Why: This is the single highest-yield safety trap associated with SGLT2 inhibitors and the one most likely to delay diagnosis in practice. [1][2]
3. Pearl: The heart-failure and CKD indications for empagliflozin and dapagliflozin apply even without a diabetes diagnosis.
 3. Why: It is a genuinely different indication logic from most of this hub's other drug classes, which exist specifically to treat diabetes. [1][2]
4. Pearl: Canagliflozin's amputation boxed warning was removed by the FDA in 2020, but the underlying trial signal (CANVAS/CANVAS-R) and the warnings-and-precautions language have not disappeared.
 4. Why: It is a nuanced, frequently mis-stated fact - students often assume either that the warning was never real or that it is still a boxed warning today; neither is accurate. [4]
5. Pearl: SGLT2 inhibitors are held for at least 3 days before elective surgery.
 5. Why: It is a concrete, testable perioperative rule tied directly to the euglycemic-DKA risk in a fasting, physiologically stressed state. [1][2]

Common exam traps

1. Trap: Ruling out diabetic ketoacidosis in a patient on an SGLT2 inhibitor because their glucose is only mildly elevated or normal.
 1. Correction: Euglycemic DKA is specifically defined by a lower-than-expected glucose at presentation; ketone assessment should be symptom-driven, not glucose-gated, in any patient on this class with a compatible clinical picture. [1][2]
2. Trap: Assuming canagliflozin's amputation warning means the whole class carries an equally well-characterised amputation signal.
 2. Correction: The amputation signal comes specifically from canagliflozin's own CANVAS/CANVAS-R trial programme; it is not a demonstrated class-wide finding for empagliflozin or dapagliflozin in the material reviewed here. [4]
3. Trap: Treating SGLT2 inhibitors as glucose-lowering drugs first and cardiorenal drugs second.
 3. Correction: For empagliflozin and dapagliflozin, the heart-failure and CKD indications are approved independent of diabetes status, reflecting outcomes-trial evidence as robust as, or in some contexts more central to modern prescribing than, the original glycemic-control indication. [1][2]
4. Trap: Believing SGLT2 inhibitors are safe to continue right up to the day of major surgery.
 4. Correction: Labelling directs withholding the drug for at least 3 days before elective surgery or prolonged fasting because of the euglycemic-DKA risk in that setting. [1][2]

Self-test questions

1. Question: What transporter do SGLT2 inhibitors block, and where?
 1. GLUT4 in skeletal muscle
 2. SGLT2 in the early proximal renal tubule
 3. SGLT1 in the small intestine
 4. GLUT2 in the pancreatic beta cell

1. Explanation: SGLT2, expressed in the early proximal renal tubule, is responsible for most filtered glucose reabsorption; blocking it produces glucosuria. [1]
2. Question: What makes euglycemic diabetic ketoacidosis with SGLT2 inhibitors diagnostically tricky?
 1. It only occurs in type 1 diabetes
 2. Blood glucose at presentation can be below the level typically expected for DKA, sometimes under 250 mg/dL
 3. It never involves ketones
 4. It always presents with severe hyperglycemia first
2. Explanation: Euglycemic DKA can present with a near-normal or only mildly elevated glucose, which can delay recognition if ketone assessment is gated on a high glucose reading. [1][2]
3. Question: Which SGLT2 inhibitor's amputation signal led to a boxed warning that was later removed by the FDA?
 1. Empagliflozin
 2. Dapagliflozin
 3. Canagliflozin
 4. All three carried this boxed warning
3. Explanation: Canagliflozin's CANVAS and CANVAS-R trials showed an increased lower-limb amputation rate, prompting a boxed warning that the FDA removed in 2020 as further data accumulated. [4]
4. Question: Which indications for empagliflozin and dapagliflozin apply even in patients without type 2 diabetes?
 1. Genital mycotic infection prophylaxis
 2. Heart failure and chronic kidney disease
 3. Hypoglycemia prevention
 4. Weight-loss maintenance
4. Explanation: Both drugs carry heart-failure and CKD indications approved on the strength of outcomes trials conducted in populations including patients entirely without diabetes. [1][2]
5. Question: How long before elective surgery should an SGLT2 inhibitor typically be withheld?
 1. No need to withhold
 2. At least 24 hours
 3. At least 3 days
 4. At least 3 weeks
5. Explanation: The labels direct withholding the drug for at least 3 days before elective surgery or a procedure involving prolonged fasting, reflecting euglycemic-DKA risk in that setting. [1][2]
6. Question: What is the most common class-specific adverse effect of SGLT2 inhibitors?
 1. Lactic acidosis
 2. Genital mycotic infection
 3. Severe hypoglycemia
 4. Agranulocytosis
6. Explanation: Genital mycotic infection is the most frequently reported class-specific adverse effect, reflecting the glucosuria the mechanism itself produces. [4][2]

Frequently asked questions

1. Question: How can diabetic ketoacidosis happen with a nearly normal blood glucose?
 1. Answer: SGLT2 inhibition promotes glucose loss through urine regardless of what is happening with fat metabolism and ketone production. Under stress - reduced food or fluid intake, illness, surgery, alcohol excess, or a very low-carbohydrate diet - ketogenesis can proceed even while the drug keeps blood glucose from rising as high as typical DKA. That is why clinicians are advised to assess ketones based on symptoms (nausea, vomiting, abdominal pain, unusual fatigue, difficulty breathing) rather than waiting for a high glucose reading. [1][2]
 2. Question: Is canagliflozin still considered to increase amputation risk?
 2. Answer: The FDA removed canagliflozin's dedicated boxed warning on amputation risk in 2020 as further data

accumulated, but the underlying trial finding from CANVAS and CANVAS-R (roughly double the amputation rate versus placebo) has not been retracted, and the risk is still described in the label's warnings and precautions. Patients with prior amputation, peripheral vascular disease or neuropathy are the group in whom this risk is weighed most carefully. [4][3]

3. Question: Why are SGLT2 inhibitors used in heart failure patients who don't have diabetes?

3. Answer: Empagliflozin and dapagliflozin both earned dedicated heart-failure indications through outcomes trials that included patients without diabetes, on the strength of the same natriuretic, volume- and metabolism-modifying effects that come from blocking SGLT2 in the kidney. The benefit does not depend on the patient having elevated blood glucose to begin with. [1][2]

4. Question: Who is most at risk of genital mycotic infection on this class?

4. Answer: Women, uncircumcised men, and anyone with a prior history of genital yeast infection are at highest risk, because the mechanism itself increases urinary glucose, creating a more favourable environment for yeast overgrowth. It is usually manageable with standard antifungal treatment and does not typically require stopping the drug unless infections are recurrent or severe. [4][2]

References

[1] JARDIANCE (empagliflozin) - prescribing information. DailyMed, U.S. National Library of Medicine . <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=faf3dd6a-9cd0-39c2-0d2e-232cb3f67565>

[2] FARXIGA (dapagliflozin) - prescribing information. DailyMed, U.S. National Library of Medicine . <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=01f90c94-71cb-4a1f-81ff-8004b850529b>

[3] INVOKANA (canagliflozin) - prescribing information. DailyMed, U.S. National Library of Medicine . <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=9679460c-55f7-4826-b55c-fe116f020358>

[4] Sodium-Glucose Transport 2 (SGLT2) Inhibitors. StatPearls Publishing / NCBI Bookshelf 2024. <https://www.ncbi.nlm.nih.gov/books/NBK576405/>

[5] 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2026. American Diabetes Association, Diabetes Care 2026. https://diabetesjournals.org/care/article/49/Supplement_1/S183/163934/9-Pharmacologic-Approaches-to-Glycemic-Treatment

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