Invokana®
(canagliflozin) tablets

~1 in 3 patients with T2D also has DKD[1,2*]

The FIRST T2D therapy approved by the FDA to reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in adults with T2D and diabetic nephropathy with albuminuria >300 mg/day[3]

In adults who have T2D and diabetic nephropathy (ie, DKD) with albuminuria >300 mg/day, INVOKANA®: the FIRST SGLT2i indicated to slow the progression of DKD and reduce the risk of HHF[3-6]

See next page for a selection of ICD-10 codes and information about submitting prior authorizations ►

CV=cardiovascular; DKD=diabetic kidney disease; HHF=hospitalization for heart failure; SGLT2i=sodium-glucose co-transporter 2 inhibitor; T2D=type 2 diabetes.

* US population with T2D from the National Health and Nutrition Examination Survey 1999-2012. DKD based on either eGFR or albuminuria criteria defined by Kidney Disease: Improving Global Outcomes. The overall prevalence of DKD based on either eGFR (CKD-EPI) or albuminuria criteria was 43.5% (95% CI: 41.6, 45.4).

References: 1. Bailey RA, Wang Y, Shu V, Rupnow MF. Chronic kidney disease in US adults with type 2 diabetes: an updated national estimate of prevalence based on Kidney Disease: Improving Global Outcomes (KDIGO) staging. *BMC Res Notes*. 2014;7:415. **2.** What is diabetic kidney disease? National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/diabetic-kidney-disease. Accessed November 16, 2022. **3.** INVOKANA® [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals, Inc. **4.** Jardiance® [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc. **5.** Farxiga® [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP. **6.** Steglatro™ [prescribing information]. Whitehouse Station, NJ. Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.

INDICATIONS

INVOKANA® (canagliflozin) is indicated:

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD)
- To reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria greater than 300 mg/day

Limitations of Use

INVOKANA® is not recommended for use to improve glycemic control in patients with type 1 diabetes mellitus.

INVOKANA® is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 m^2. INVOKANA® is likely to be ineffective in this setting based upon its mechanism of action.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Serious hypersensitivity reaction to INVOKANA®, such as anaphylaxis or angioedema

Please read additional Important Safety Information on the following pages. Please read full Prescribing Information and Medication Guide for INVOKANA®.

ICD-10 codes[1]

Invokana® (canagliflozin) tablets

DIABETIC KIDNEY DISEASE (DKD)

E11.2: Type 2 diabetes mellitus with kidney complications
E11.21: Type 2 diabetes mellitus with diabetic nephropathy
E11.22: Type 2 diabetes mellitus with diabetic chronic kidney disease
E11: Type 2 diabetes mellitus + **N18:** Chronic kidney disease (CKD)

TYPE 2 DIABETES (T2D)

E11: Type 2 diabetes mellitus

CARDIOVASCULAR DISEASE (CVD)

E11.5: Type 2 diabetes mellitus with circulatory complications
E11.51: Type 2 diabetes mellitus with diabetic peripheral angiopathy without gangrene
E11: Type 2 diabetes mellitus + **one of the following codes:**

Myocardial infarction

I21.09: ST elevation (STEMI) myocardial infarction involving other coronary artery of anterior wall

Coronary artery disease

I24.8: Other forms of acute ischemic heart disease
I25.2: Old myocardial infarction
I25.5: Ischemic cardiomyopathy
I25.89: Other forms of chronic ischemic heart disease
I25.9: Chronic ischemic heart disease, unspecified
I25.10: Atherosclerotic heart disease of native coronary artery without angina pectoris

CARDIOVASCULAR DISEASE (CVD), continued

Stroke

I60.9: Nontraumatic subarachnoid hemorrhage, unspecified
I61.9: Nontraumatic intracerebral hemorrhage, unspecified
I63.22: Cerebral infarction due to unspecified occlusion or stenosis of basilar artery
I63.139: Cerebral infarction due to embolism of unspecified carotid artery
I63.239: Cerebral infarction due to unspecified occlusion or stenosis of unspecified carotid artery

Peripheral arterial disease

I70.209: Unspecified atherosclerosis of native arteries of extremities, unspecified extremity
I70.399: Other atherosclerosis of unspecified type of bypass graft(s) of the extremities, unspecific extremity
I73.9: Peripheral vascular disease, unspecified
I74.2: Embolism and thrombosis of arteries of the upper extremities
I74.3: Embolism and thrombosis of arteries of the lower extremities
I74.5: Embolism and thrombosis of iliac artery
I75: Atheroembolism

Heart failure

I50: Heart failure
I50.1: Left ventricular failure, unspecified
I50.20: Unspecified systolic (congestive) heart failure
I50.30: Unspecified diastolic (congestive) heart failure
I50.40: Unspecified combined systolic (congestive) and diastolic (congestive) heart failure

Collected on September 3, 2020, and subject to change.

This document is presented for informational purposes only and is not intended to provide reimbursement or legal advice, nor does it promise or guarantee coverage, levels of reimbursement, payment, or charge. Similarly, all HCPCS codes are supplied for informational purposes only and represent no statement, promise, or guarantee by Janssen Pharmaceuticals, Inc., that these codes will be appropriate or that reimbursement will be made. It is not intended to increase or maximize reimbursement by any payer. Laws, regulations, and policies concerning reimbursement are complex and are updated frequently. While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. We strongly recommend you consult the payer organization for its reimbursement policies.

Reference: 1. Centers for Medicare & Medicaid Services. 2020 ICD-10-CM: 2020 code descriptions in tabular order. https://www.cms.gov/Medicare/Coding/ICD10/2020-ICD-10-CM. Accessed November 16, 2022.

IMPORTANT SAFETY INFORMATION for INVOKANA®, continued

WARNINGS AND PRECAUTIONS

- **Diabetic Ketoacidosis in Patients with Type 1 Diabetes Mellitus and Other Ketoacidosis:** In patients with type 1 diabetes mellitus, INVOKANA® significantly increases the risk of diabetic ketoacidosis, a life-threatening event, beyond the background rate. In placebo-controlled trials of patients with type 1 diabetes mellitus, the risk of ketoacidosis was markedly increased in patients who received SGLT2 inhibitors compared to placebo; this risk may be greater with higher doses of INVOKANA®. INVOKANA® is not indicated for glycemic control in patients with type 1 diabetes mellitus.

  Type 2 diabetes mellitus and pancreatic disorders are also risk factors for ketoacidosis. There have been postmarketing reports of fatal events of ketoacidosis in patients with type 2 diabetes mellitus using SGLT2 inhibitors, including INVOKANA®.

  Precipitating conditions for diabetic ketoacidosis or other ketoacidosis include acute febrile illness, reduced caloric intake, ketogenic diet, surgery, insulin dose reduction, volume depletion, and alcohol abuse.

Please read full Prescribing Information and Medication Guide for INVOKANA®.

Sample prior authorization form

Invokana® (canagliflozin) tablets

The form below is an example of a prior authorization form. Requests for prior authorization to prescribe INVOKANA® should be completed based on independent clinical judgment. Be sure to provide documentation from the patient's medical history to support your request.

1 MEDICATION

INVOKANA® (for appropriate patients). Please see Indications in #4 below.

2 STRENGTH

INVOKANA® is available in two dose strengths (100 mg and 300 mg).[1] Choose the dose that is appropriate for your patient.

3 FREQUENCY

The recommended starting dose of **INVOKANA®** is 100 mg once daily, taken before the first meal of the day.[1] Dose can be increased to 300 mg once daily in patients tolerating **INVOKANA®** 100 mg once daily who have an eGFR of 60 mL/min/1.73 m^2 or greater and require additional glycemic control.[1]

4 DIAGNOSIS

Insert your patient's diagnosis here.

INDICATIONS

INVOKANA® (canagliflozin) is indicated:

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD)
- To reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria greater than 300 mg/day

INVOKANA® is not recommended for the treatment of type 1 diabetes or to improve glycemic control in patients with type 2 diabetes and an eGFR less than 30 mL/min/1.73 m^2.

Formulary Exception/Prior Authorization Request Form

Patient Information		Prescriber Information		
Patient Name:		Prescriber Name:		
Patient ID#:				
Address:		Address:		
City:	State:	City:		State:
Home Phone:	ZIP:	Office Phone #:	Office Fax #:	ZIP:
Gender: M or F	DOB:	Contact Person at Doctor's Office:		

Diagnosis and Medical Information

1 Medication: 2 Strength: 3 Directions for use (Frequency):

Expected Length of Therapy: | Qty: | Day Supply: | If this is a continuation of therapy, how long has the patient been on the medication?

4 Diagnosis: 5 Diagnosis (ICD) Code(s):

FORM CANNOT BE EVALUATED WITHOUT REQUIRED CLINICAL INFORMATION

☐ **Expedited/Urgent Review Requested:** By checking this box and signing below, I certify that applying the standard review time frame may seriously jeopardize the life or health of the patient or the patient's ability to regain maximum function.

What condition is the drug being prescribed for? _____

6 Please list all medications the patient has tried specific to the diagnosis and specify below:

Medication name, reason for failure, including trial year: _____

Drug(s) contraindicated: _____

Adverse event (e.g., toxicity, allergy) for each drug: _____

5 ICD-10 CODE(S)

Insert the appropriate ICD-10 code(s) for your patient on page 2. The ICD-10 codes provided here are for T2D, CVD, and DKD. Select any appropriate disease-specific code(s) based on your patient's diagnosis. There may be additional codes that are utilized for T2D, CVD, and DKD. For additional codes please refer to a coding resource or **www.cms.gov**.

6 PRIOR MEDICATIONS

Provide a brief account of your patient's prior medication history, including medication name, reason for failure, and trial year.

CVD=cardiovascular disease; DKD=diabetic kidney disease; T2D=type 2 diabetes.

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Reference: 1. INVOKANA® [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals, Inc.

IMPORTANT SAFETY INFORMATION for INVOKANA®, continued

WARNINGS AND PRECAUTIONS, continued

- **Diabetic Ketoacidosis in Patients with Type 1 Diabetes Mellitus and Other Ketoacidosis (continued):** Signs and symptoms are consistent with dehydration and severe metabolic acidosis and include nausea, vomiting, abdominal pain, generalized malaise, and shortness of breath. Blood glucose levels at presentation may be below those typically expected for diabetic ketoacidosis (eg, less than 250 mg/dL). Ketoacidosis and glucosuria may persist longer than typically expected. Urinary glucose excretion persists for 3 days after discontinuing INVOKANA®; however, there have been postmarketing reports of ketoacidosis and glucosuria lasting greater than 6 days and some up to 2 weeks after discontinuation of SGLT2 inhibitors.

Please read full Prescribing Information and Medication Guide for INVOKANA®.

IMPORTANT SAFETY INFORMATION for INVOKANA®, continued

WARNINGS AND PRECAUTIONS, continued

- **Diabetic Ketoacidosis in Patients with Type 1 Diabetes Mellitus and Other Ketoacidosis (continued):** Consider ketone monitoring in patients at risk for ketoacidosis if indicated by the clinical situation. Assess for ketoacidosis regardless of presenting blood glucose levels in patients who present with signs and symptoms consistent with severe metabolic acidosis. If ketoacidosis is suspected, discontinue INVOKANA®, promptly evaluate, and treat ketoacidosis, if confirmed. Monitor patients for resolution of ketoacidosis before restarting INVOKANA®.

  Withhold INVOKANA®, if possible, in temporary clinical situations that could predispose patients to ketoacidosis. Resume INVOKANA® when the patient is clinically stable and has resumed oral intake. "
- **Lower-Limb Amputation:** An increased risk of lower-limb amputations associated with INVOKANA® use versus placebo was observed in CANVAS (5.9 vs 2.8 events per 1000 patient-years) and CANVAS-R (7.5 vs 4.2 events per 1000 patient-years), two randomized, placebo-controlled trials evaluating patients with type 2 diabetes who had either established cardiovascular disease or were at risk for cardiovascular disease. The risk of lower-limb amputations was observed at both the 100-mg and 300-mg once-daily dosage regimens.

  Amputations of the toe and midfoot (99 out of 140 patients with amputations receiving INVOKANA® in the two trials) were the most frequent; however, amputations involving the leg, below and above the knee, were also observed (41 out of 140 patients with amputations receiving INVOKANA® in the two trials). Some patients had multiple amputations, some involving both lower limbs.

  Lower-limb infections, gangrene, and diabetic foot ulcers were the most common precipitating medical events leading to the need for an amputation. The risk of amputation was highest in patients with a baseline history of prior amputation, peripheral vascular disease, and neuropathy.

  Before initiating INVOKANA®, consider factors in the patient history that may predispose to the need for amputations, such as a history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers. Counsel patients about the importance of routine preventative foot care. Monitor patients for signs and symptoms of infection (including osteomyelitis), new pain or tenderness, sores, or ulcers involving the lower limbs, and discontinue if these complications occur.
- **Volume Depletion:** INVOKANA® can cause intravascular volume contraction, which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. There have been postmarketing reports of acute kidney injury which are likely related to volume depletion, some requiring hospitalizations and dialysis, in patients with type 2 diabetes mellitus receiving SGLT2 inhibitors, including INVOKANA®. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m^2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating INVOKANA® in patients with one or more of these characteristics, assess and correct volume status. Monitor for signs and symptoms of volume depletion after initiating therapy.
- **Urosepsis and Pyelonephritis:** Serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization have been reported in patients receiving INVOKANA®. Treatment with INVOKANA® increases this risk. Evaluate for signs and symptoms and treat promptly.
- **Hypoglycemia With Concomitant Use With Insulin and Insulin Secretagogues:** Insulin and insulin secretagogues are known to cause hypoglycemia. INVOKANA® may increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKANA®.
- **Necrotizing Fasciitis of the Perineum (Fournier's Gangrene):** Necrotizing fasciitis of the perineum, a rare but serious and life-threatening necrotizing infection requiring urgent surgical intervention, has been identified in postmarketing surveillance in female and male patients with diabetes mellitus receiving SGLT2 inhibitors, including INVOKANA®. Serious outcomes have included hospitalization, multiple surgeries, and death. If suspected, start treatment immediately with broad-spectrum antibiotics and, if necessary, surgical debridement. Discontinue INVOKANA®.
- **Genital Mycotic Infections:** INVOKANA® increases risk of genital mycotic infections, especially in uncircumcised males or patients with prior infections. Monitor and treat appropriately.
- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema and anaphylaxis, were reported with INVOKANA®; these reactions generally occurred within hours to days after initiation. If reactions occur, discontinue INVOKANA®, treat, and monitor until signs and symptoms resolve.

Please read full Prescribing Information and Medication Guide for INVOKANA®.

IMPORTANT SAFETY INFORMATION for INVOKANA®, continued

WARNINGS AND PRECAUTIONS, continued

- **Bone Fracture:** Increased risk of bone fracture, occurring as early as 12 weeks after treatment initiation, was observed in patients using INVOKANA®. Prior to initiation, consider factors that contribute to fracture risk.

DRUG INTERACTIONS

- **UGT Enzyme Inducers:** UGT enzyme inducers (eg, rifampin, phenytoin, phenobarbital, ritonavir) decrease canagliflozin exposure which may reduce the effectiveness of INVOKANA®. For patients with eGFR ≥60 mL/min/1.73 m^2, if an inducer of UGTs is administered with INVOKANA®, increase the dosage to 200 mg daily (taken as two 100-mg tablets) in patients currently tolerating INVOKANA® 100 mg daily. The total daily dosage may be increased to 300 mg daily in patients currently tolerating INVOKANA® 200 mg daily who require additional glycemic control.

  For patients with eGFR <60 mL/min/1.73 m^2, if an inducer of UGTs is administered with INVOKANA®, increase the dose to 200 mg daily (taken as two 100-mg tablets) in patients currently tolerating INVOKANA® 100 mg daily. Consider adding another antihyperglycemic agent in patients who require additional glycemic control.
- **Insulin or Insulin Secretagogues:** The risk of hypoglycemia is increased when INVOKANA® is used concomitantly with insulin secretagogues (eg, sulfonylurea) or insulin. Concomitant use may require a lower dosage of the insulin secretagogue of insulin to reduce the risk of hypoglycemia
- **Digoxin:** Canagliflozin increases digoxin exposure. Monitor patients taking INVOKANA® with concomitant digoxin for a need to adjust the dosage of digoxin
- **Lithium:** Concomitant use of an SGLT2 inhibitor with lithium may decrease serum lithium concentrations. Monitor serum lithium concentration more frequently during INVOKANA® initiation and dosage changes.

Drug/Laboratory Test Interference

- **Positive Urine Glucose Test:** SGLT2 inhibitors increase urinary glucose excretion which will lead to positive urine glucose tests. Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.
- **Interference With 1,5-Anhydroglucitol (1,5-AG) Assay:** Measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors. Monitoring glycemic control with 1,5-AG assay is not recommended in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** INVOKANA® is not recommended in pregnant women, especially during the second and third trimesters.
- **Lactation:** INVOKANA® is not recommended while breastfeeding.
- **Pediatric Use:** Safety and effectiveness in patients <18 years of age have not been established.
- **Geriatric Use:** Patients ≥65 years had a higher incidence of adverse reactions related to reduced intravascular volume, particularly with the 300-mg dose; more prominent increase in the incidence was seen in patients who were ≥75 years. Smaller reductions in HbA1c relative to placebo were seen in patients ≥65 years.
- **Renal Impairment:** The efficacy and safety of INVOKANA® for glycemic control were evaluated in a trial that included patients with moderate renal impairment (eGFR 30 to <50 mL/min/1.73 m^2). These patients had less overall glycemic efficacy, and patients treated with 300 mg per day had increases in serum potassium, which were transient and similar by the end of the study. Patients with renal impairment using INVOKANA® for glycemic control may be more likely to experience hypotension and may be at a higher risk for acute kidney injury.
  Efficacy and safety studies with INVOKANA® did not enroll patients with ESKD on dialysis or patients with an eGFR less than 30 mL/min/1.73 m2.
- **Hepatic Impairment:** INVOKANA® has not been studied in patients with severe hepatic impairment and is not recommended in this population.

OVERDOSAGE

- In the event of an overdose, contact the Poison Control Center and employ the usual supportive measures.

ADVERSE REACTIONS

- The most common adverse reactions (5% or greater incidence) were female genital mycotic infections, urinary tract infections, and increased urination.

Please read full Prescribing Information and Medication Guide for INVOKANA®.

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