

Media Fact Sheet:

INVOKANA™ (canagliflozin)

FAST FACTS

- INVOKANA™ (canagliflozin) is the first in a new class of medications called SGLT2 inhibitors available in the United States for use, along with diet and exercise, to improve blood glucose control in adults with type 2 diabetes.
- INVOKANA™ reduces blood glucose in a novel way, by acting on the kidneys as a “glucuretic” to promote the loss of glucose in the urine.
- INVOKANA™ is the only oral, once-daily medication available in the United States offering improved blood glucose control while also showing reduced body weight and systolic blood pressure in clinical trials.
- The INVOKANA™ global Phase 3 clinical program enrolled 10,285 patients in nine studies and is one of the largest clinical programs in type 2 diabetes submitted to health authorities to date.

What Is INVOKANA™?

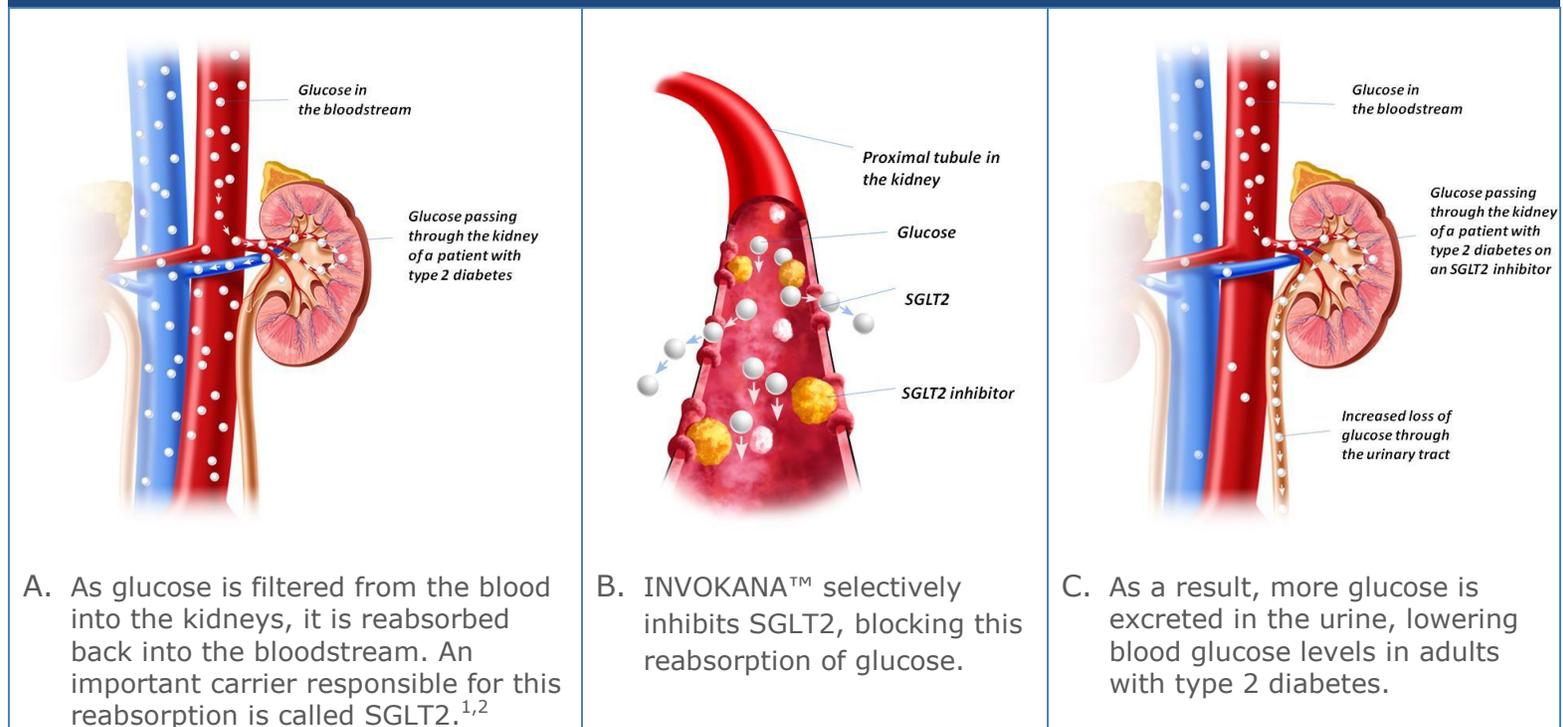
INVOKANA™ is the first in a new class of medications called SGLT2 inhibitors available in the United States for use, along with diet and exercise, to improve blood glucose control (glycemic control) in adults with type 2 diabetes. It is also the only oral, once-daily type 2 diabetes medication available in the United States showing reduced body weight and systolic blood pressure in clinical trials.

How Does INVOKANA™ Work?

INVOKANA™ reduces blood glucose in a novel way, by acting on the kidneys as a “glucuretic” to promote the loss of glucose in the urine.

The kidneys make an important contribution to balancing blood glucose. As glucose is filtered from the blood into the kidneys, it is reabsorbed back into the bloodstream. An important carrier responsible for this reabsorption is called sodium glucose co-transporter 2 (SGLT2).^{1,2} INVOKANA™ selectively inhibits SGLT2, and as a result promotes the loss of glucose in the urine, lowering blood glucose levels in adults with type 2 diabetes. (See Figure: How INVOKANA™ Works).

Figure: How INVOKANA™ Works



How Effective is INVOKANA™?

The INVOKANA™ global Phase 3 clinical program enrolled 10,285 patients in nine studies; it is one of the largest clinical programs in type 2 diabetes submitted to health authorities to date.

INVOKANA™ was evaluated at the starting doses of 100 milligrams (mg) and at the 300 mg doses in placebo- and active comparator-controlled studies, as well as two large studies in special populations: older patients and patients with moderate kidney impairment.

Results across the studies showed that both doses of INVOKANA™, when used as a single agent (monotherapy) or as combination therapy with other glucose-lowering medications, significantly improved glycemic control. For example, when used as monotherapy, INVOKANA™ 100 mg and 300 mg reduced A1C by 0.91 percent and 1.16 percent, respectively, compared to placebo (See Table). A1C, also called hemoglobin A1c, is the percent of red blood cell hemoglobin with glucose attached to it and an indicator of average blood glucose over the previous 2 to 3 months.³ Studies show that every percentage point drop in A1C can reduce the risk of diabetes complications by 40 percent.⁴

In addition to improved glycemic control, both doses of INVOKANA™ also produced significant reductions in the prespecified secondary endpoints of body weight and systolic blood pressure (See Table: Summary of Efficacy Data for INVOKANA™ Across Phase 3 Studies).

In two studies comparing INVOKANA™ to current standard treatments – one studying sitagliptin and the other studying glimepiride – INVOKANA™ dosed at 300 mg provided greater reductions in A1C levels and body weight than either comparator. In the two studies, the overall incidence of adverse events was similar with INVOKANA™ and the comparators.

The efficacy findings were generally consistent across different patient subgroups.

Table: Summary of Efficacy Data for INVOKANA™ Across Phase 3 Studies
All differences are statistically significant unless shown as NS (not significant).

Study INVOKANA™ Compared to:	INVOKANA™ dose, mg/d	A1C change (baseline 7.7 percent to 8.4 percent)	Body weight percent change* (baseline 83 to 97 kg)	Systolic BP mmHg change* (baseline 127 to 138 mmHg)
Placebo, monotherapy	100	- 0.91	-2.2	-3.7
	300	- 1.16	-3.3	-5.4
Placebo, add-on to other therapies (sulfonylurea, metformin, pioglitazone, or insulin)	100	- 0.62 to -0.74	- 1.4 to - 2.7	-2.6 to -5.4
	300	- 0.73 to -0.92	- 1.8 to - 3.7	-3.5 to -6.6
Glimepiride, add- on to metformin	100	- 0.01 (NS)	- 5.2	--
	300	- 0.12 (NS)	- 5.7	--
Sitagliptin, add-on to metformin and sulfonylurea	300 (the only dose studied)	-0.37 (NS)	- 2.8	- 5.9

*Change in body weight and systolic blood pressure were prespecified secondary endpoints in studies with results shown in this chart.

What Are the Side Effects of INVOKANA™?

Phase 3 trials also showed INVOKANA™ was generally well tolerated. The most common adverse events with INVOKANA™ are genital mycotic (fungal) infections, urinary tract infections and increased urination. These specific adverse events were generally mild to moderate in intensity in Phase 3 studies. Discontinuations due to adverse events were higher than those seen in control groups, but were generally low. Overall, the rate of discontinuation due to adverse events was 4.3 percent for INVOKANA™ 100 mg, 3.6 percent for INVOKANA™ 300 mg and 3.1 percent versus competitors.

In studies of INVOKANA™ as monotherapy or in combination with agents not associated with hypoglycemia (metformin or metformin and pioglitazone), the incidence of hypoglycemic episodes was less than 5 percent across the groups (INVOKANA™ 100 mg, 3.8 percent; INVOKANA™ 300 mg, 4.3 percent; and placebo, 2.2 percent). The incidence of hypoglycemia was lower with INVOKANA™ than with glimepiride (INVOKANA™ 100 mg, 5.6 percent; INVOKANA™ 300 mg, 4.9 percent; glimepiride, 34.2 percent) and similar to that of sitagliptin.

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with INVOKANA™ or any other antidiabetic medication. Additional data are being collected to further characterize the cardiovascular profile of INVOKANA™.

Important Safety Information follows.

INDICATION STATEMENT

WHAT IS INVOKANA™?

- INVOKANA™ is a prescription medicine used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.
- INVOKANA™ is not for people with type 1 diabetes.
- INVOKANA™ is not for people with diabetic ketoacidosis (increased ketones in blood or urine).
- It is not known if INVOKANA™ is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT INVOKANA™?

INVOKANA™ can cause important side effects, including:

- **Dehydration. INVOKANA™ can cause some people to have dehydration (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, lightheaded, or weak, especially when you stand up (orthostatic hypotension).**

You may be at higher risk of dehydration if you:

- have low blood pressure
- take medicines to lower your blood pressure, including diuretics (water pill)
- are on low sodium (salt) diet
- have kidney problems
- are 65 years of age or older
- **Vaginal yeast infection.** Women who take INVOKANA™ may get vaginal yeast infections. Symptoms of a vaginal yeast infection include:
 - vaginal odor
 - white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese)
 - vaginal itching
- **Yeast infection of the penis (balanitis or balanoposthitis).** Men who take INVOKANA™ may get a yeast infection of the skin around the penis. Certain men who are not circumcised may have swelling of the penis that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of yeast infection of the penis include:
 - redness, itching, or swelling of the penis
 - rash of the penis
 - foul smelling discharge from the penis
 - pain in the skin around penis

Talk to your doctor about what to do if you get symptoms of a yeast infection of the vagina or penis. Your doctor may suggest you use an over-the-counter antifungal medicine. Talk to your doctor right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

WHO SHOULD NOT TAKE INVOKANA™?

Do not take INVOKANA™ if you:

- are allergic to canagliflozin or any of the ingredients in INVOKANA™. See the end of the Medication Guide for a list of ingredients in INVOKANA™. Symptoms of allergic reaction to INVOKANA™ may include:
 - rash
 - raised red patches on your skin (hives)
 - swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing
- have severe kidney problems or are on dialysis

Important Safety Information Continued on Next Page

WHAT SHOULD I TELL MY DOCTOR BEFORE TAKING INVOKANA™?

Before you take INVOKANA™, tell your doctor if you:

- have kidney problems
- have liver problems
- are on a low sodium (salt) diet. Your doctor may change your diet or your dose of INVOKANA™.
- have ever had an allergic reaction to INVOKANA™
- have other medical conditions
- are pregnant or plan to become pregnant. It is not known if INVOKANA™ will harm your unborn baby. If you are pregnant, talk with your doctor about the best way to control your blood sugar while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if INVOKANA™ passes into your breast milk. Talk with your doctor about the best way to feed your baby if you are taking INVOKANA™.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

INVOKANA™ may affect the way other medicines work, and other medicines may affect how INVOKANA™ works. Especially tell your doctor if you take:

- diuretics (water pills)
- rifampin (used to treat or prevent tuberculosis)
- phenytoin or phenobarbital (used to control seizures)
- ritonavir (Norvir®, Kaletra®, Lopinavir®)* (used to treat HIV infection)
- digoxin (Lanoxin®)* (used to treat heart problems)

Ask your doctor or pharmacist for a list of these medicines if you are not sure if your medicine is listed above.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

HOW SHOULD I TAKE INVOKANA™?

- Take INVOKANA™ by mouth 1 time each day exactly as your doctor tells you to take it.
- Your doctor will tell you how much INVOKANA™ to take and when to take it. Your doctor may change your dose if needed.
- It is best to take INVOKANA™ before the first meal of the day.
- Your doctor may tell you to take INVOKANA™ along with other diabetes medicines. Low blood sugar can happen more often when INVOKANA™ is taken with certain other diabetes medicines. See "**What are the possible side effects of INVOKANA™?**"
- If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at the next regularly scheduled time. Do not take two doses of INVOKANA™ at the same time. Talk to your doctor if you have questions about a missed dose.
- If you take too much INVOKANA™, call your doctor or go to the nearest hospital emergency room right away. When your body is under some types of stress, such as fever, trauma (such as a car accident), infection, or surgery, the amount of diabetes medicine you need may change. Tell your doctor right away if you have any of these conditions and follow your doctor's instructions.
- Stay on your prescribed diet and exercise program while taking INVOKANA™.
- Check your blood sugar as your doctor tells you to.
- INVOKANA™ will cause your urine to test positive for glucose.
- Your doctor may do certain blood tests before you start INVOKANA™ and during treatment as needed. Your doctor may change your dose of INVOKANA™ based on the results of your blood tests.
- Your doctor will check your diabetes with regular blood tests, including your blood sugar levels and your hemoglobin A1C.

Important Safety Information Continued on Next Page

WHAT ARE THE POSSIBLE SIDE EFFECTS OF INVOKANA™?

INVOKANA™ may cause serious side effects, including:

See “**What is the most important information I should know about INVOKANA™?**”

- **kidney problems**
- **a high amount of potassium in your blood (hyperkalemia)**
- **low blood sugar (hypoglycemia).** If you take INVOKANA™ with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take INVOKANA™.

Signs and symptoms of low blood sugar may include:

- headache
 - drowsiness
 - weakness
 - dizziness
 - confusion
 - irritability
 - hunger
 - fast heartbeat
 - sweating
 - shaking or feeling jittery
- **serious allergic reaction.** If you have any symptoms of a serious allergic reaction, stop taking INVOKANA™ and call your doctor right away or go to the nearest hospital emergency room. See “**Who should not take INVOKANA™?**”. Your doctor may give you a medicine for your allergic reaction and prescribe a different medicine for your diabetes.

The most common side effects of INVOKANA™ include:

- vaginal yeast infections and yeast infections of the penis (See “**What is the most important information I should know about INVOKANA™?**”)
- urinary tract infection
- changes in urination, including urgent need to urinate more often, in larger amounts, or at night

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of INVOKANA™. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

You may also report side effects to Janssen Scientific Affairs, LLC at 1-800-526-7736.

Please see the full [Prescribing Information](#) and [Medication Guide](#).

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About Janssen Pharmaceuticals, Inc.

As a member of the Janssen Pharmaceutical Companies of Johnson & Johnson, Janssen Pharmaceuticals, Inc. is dedicated to addressing and resolving the major unmet medical needs of our time. Driven by our commitment to patients, healthcare professionals, and caregivers, we strive to develop sustainable and integrated healthcare solutions by working in partnership with all stakeholders on the basis of trust and transparency. Our daily work is guided by meeting goals of excellence in quality, innovation, safety, and efficacy in order to advance patient care.

For more information on Janssen Pharmaceuticals, Inc., visit us at www.janssenpharmaceuticalsinc.com or follow us on Twitter at www.twitter.com/JanssenUS and on YouTube at www.Youtube.com/JanssenUS.

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