Invokamet®
canagliflozin/metformin HCl
tablets

We invite you to join your colleagues and your Janssen Pharmaceuticals, Inc., Sales Representative for

INVOKAMET®: A Fixed-Dose Combination Option to Go Further in the Treatment of Type 2 Diabetes

OUR GUEST SPEAKER WILL BE

Carlos Campos, MD, MPH, CDE

President, Private Practice

New Braunfels, TX

Dr. Campos is a paid speaker for Janssen Pharmaceuticals, Inc.

Wednesday, October 12, 2016 at 6:30 PM

Adobe Verde

1724 Hunter Road, New Braunfels, TX

Phone: (830) 629-0777

Please RSVP to your Janssen Representative by Wednesday, October 05, 2016

CALEB SNYDER

Phone: or visit http://www.medforcereg.net/SOMP103523

In adherence with PhRMA guidelines, spouses or other guests are not permitted to attend company-sponsored programs.

For all attendees, please be advised that information such as your name and the value and purpose of any educational item, meal, or other items of value you receive may be publicly disclosed. If you are licensed in any state or other jurisdiction, or are an employee or contractor of any organization or governmental entity, that limits or prohibits meals from pharmaceutical companies, please identify yourself so that you (and we) are able to comply with such requirements.

Please note that the company prohibits the offering of gifts, gratuities, or meals to federal government employees/officials. Thank you for your cooperation.

This promotional educational activity is not accredited. The program content is developed by Janssen Pharmaceuticals, Inc. Speakers present on behalf of the company and are required to present information in compliance with FDA requirements for communications about its medicines.

The personal information you provide may be used to contact you about your request to attend the Janssen Pharmaceuticals, Inc., educational program using your preferred method of communication as indicated by you. This information may be shared with Janssen Pharmaceuticals, Inc., its affiliates, and a third party for the sole purpose of completing your registration for this program and as required by law.

INVOKAMET® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both canagliflozin and metformin is appropriate.

INVOKAMET® is not recommended in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

IMPORTANT SAFETY INFORMATION

WARNING: LACTIC ACIDOSIS

Postmarketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. The onset of metformin-associated lactic acidosis is often subtle, accompanied only by nonspecific symptoms such as malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Metformin-associated lactic acidosis was characterized by elevated blood lactate levels (>5 mmol/L); anion gap acidosis (without evidence of ketonuria or ketonemia); an increased lactate:pyruvate ratio; and metformin plasma levels generally >5 mcg/mL.

Risk factors for metformin-associated lactic acidosis include renal impairment, concomitant use of certain drugs (eg, cationic drugs such as topiramate), age 65 years old or greater, having a radiological study with contrast, surgery and other procedures, hypoxic states (eg, acute congestive heart failure), excessive alcohol intake, and hepatic impairment.

Steps to reduce the risk of and manage metformin-associated lactic acidosis in these high-risk groups are provided in the full prescribing information.

If metformin-associated lactic acidosis is suspected, immediately discontinue INVOKAMET® and institute general supportive measures in a hospital

Please see Important Safety Information, continued on next page.

Please see accompanying full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

Janssen Pharmaceuticals, Inc.

Janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

- Moderate to severe renal impairment (eGFR below 45 mL/min/1.73 m^2), end stage renal disease (ESRD), or patients on dialysis
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis
- History of a serious hypersensitivity reaction to canagliflozin or metformin, such as anaphylaxis or angioedema

WARNINGS and PRECAUTIONS

- **Lactic Acidosis:** Postmarketing cases of metformin-associated lactic acidosis, including fatal cases, were reported. These cases had a subtle onset and were accompanied by nonspecific symptoms such as malaise, myalgias, abdominal pain, respiratory distress, or increased somnolence; however, hypothermia, hypotension, and resistant bradyarrhythmias have occurred with severe acidosis. Metformin-associated lactic acidosis was characterized by elevated blood lactate concentrations (>5 mmol/L), anion gap acidosis (without evidence of ketonuria or ketonemia), an increased lactate:pyruvate ratio; and metformin plasma levels generally >5 mcg/mL. Metformin decreases liver uptake of lactate, increasing lactate blood levels which may increase the risk of lactic acidosis, especially in patients at risk.

  If metformin-associated lactic acidosis is suspected, general supportive measures should be instituted promptly in a hospital setting, along with immediate discontinuation. In INVOKAMET®-treated patients with a diagnosis or strong suspicion of lactic acidosis, prompt hemodialysis is recommended to correct the acidosis and remove accumulated metformin. Hemodialysis has often resulted in reversal of symptoms and recovery.

  Educate patients and their families about the symptoms of lactic acidosis and if symptoms occur instruct them to discontinue INVOKAMET® and report these symptoms to their healthcare provider.

  For each of the known and possible risk factors for metformin-associated lactic acidosis, recommendations to reduce the risk of and manage metformin-associated lactic acidosis are provided below:

  Renal Impairment: Postmarketing metformin-associated lactic acidosis cases primarily occurred in patients with significant renal impairment. The risk of metformin accumulation and metformin-associated lactic acidosis increases with the severity of renal impairment because metformin is substantially excreted by the kidney. Obtain an eGFR before initiation and at least annually thereafter, and more frequently in patients at increased risk of renal impairment.

  Drug Interactions: The concomitant use of INVOKAMET® with specific drugs may increase the risk of metformin-associated lactic acidosis: those that impair renal function, result in significant hemodynamic change, interfere with acid-base balance, or increase metformin accumulation (eg, cationic drugs). Consider more frequent monitoring of patients.

  Age 65 or Greater: The risk of metformin-associated lactic acidosis increases with the patient's age due to a greater likelihood of hepatic, renal, or cardiac impairment. Assess renal function more frequently in elderly patients.

  Radiological Studies with Contrast: Administration of intravascular iodinated contrast agents in metformin-treated patients has led to an acute decrease in renal function and the occurrence of lactic acidosis. Stop INVOKAMET® at the time of, or prior to, an iodinated contrast imaging procedure in patients with an eGFR of 45 to 60 mL/min/1.73 m^2; in patients with a history of hepatic impairment, alcoholism, or heart failure; or in patients who will be administered intra-arterial iodinated contrast. Re-evaluate eGFR 48 hours after the imaging procedure, and restart INVOKAMET® if renal function is stable.

  Surgery and Other Procedures: Withholding of food and fluids during surgical or other procedures may increase the risk for volume depletion, hypotension, and renal impairment.

  INVOKAMET® should be temporarily discontinued while patients have restricted food and fluid intake.

  Hypoxic States: Many postmarketing cases of metformin-associated lactic acidosis occurred in the setting of acute congestive heart failure. Cardiovascular collapse (shock), acute myocardial infarction, sepsis, and other conditions associated with hypoxemia have been associated with lactic acidosis and may also cause pre-renal azotemia. When such events occur, discontinue INVOKAMET®.

  Excessive Alcohol Intake: Alcohol potentiates the effect of metformin on lactate metabolism and this may increase the risk of metformin-associated lactic acidosis. Warn patients against excessive alcohol intake while receiving INVOKAMET®.

  Hepatic Impairment: Patients with hepatic impairment have developed metformin-associated lactic acidosis. This may be due to impaired lactate clearance resulting in higher lactate blood levels. Avoid use of INVOKAMET® in patients with clinical or laboratory evidence of hepatic disease.

- **Hypotension:** Canagliflozin causes intravascular volume contraction. Symptomatic hypotension can occur after initiating INVOKAMET®, particularly in patients with an eGFR <60 mL/min/1.73 m^2, elderly patients, patients on either diuretics or medications that interfere with the renin-angiotensin-aldosterone system, or patients with low systolic blood pressure. Before initiating INVOKAMET® in patients with ≥1 of these characteristics who were not already on canagliflozin, volume status should be assessed and corrected. Monitor for signs and symptoms after initiating therapy.
- **Ketoacidosis:** Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, have been identified in patients with type 1 and 2 diabetes mellitus receiving SGLT2 inhibitors, including canagliflozin. Before initiating INVOKAMET®, consider factors in patient history that may predispose to ketoacidosis, including pancreatic insulin deficiency, caloric restriction disorders, and alcohol abuse. In patients treated with INVOKAMET®, consider monitoring for ketoacidosis and temporarily discontinuing in clinical situations known to predispose to ketoacidosis (eg, prolonged fasting due to acute illness or surgery).
- **Acute Kidney Injury and Impairment in Renal Function:** Canagliflozin causes intravascular volume contraction and can cause renal impairment. Postmarketing reports of acute kidney injury, some requiring hospitalization and dialysis, were reported; some reports involved patients younger than 65 years of age. Before initiation, consider factors that may predispose patients to acute kidney injury including hypovolemia, chronic renal insufficiency, congestive heart failure, and concomitant medications. Consider temporarily discontinuing INVOKAMET® in any setting of reduced oral intake or fluid losses; monitor patients for signs and symptoms of acute kidney injury. If acute kidney injury occurs, discontinue promptly and institute treatment.

  Canagliflozin increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Renal function abnormalities can occur after initiation. Renal function should be evaluated prior to initiation and periodically thereafter. Dose adjustment and more frequent renal function monitoring are recommended in patients with an eGFR <60 mL/min/1.73 m^2.
- **Hyperkalemia:** Canagliflozin can lead to hyperkalemia. Patients with moderate renal impairment who are taking medications that interfere with potassium excretion, such as potassium-sparing diuretics, or medications that interfere with the renin-angiotensin-aldosterone system are at an increased risk of developing hyperkalemia.

  Monitor serum potassium levels periodically after initiating INVOKAMET® in patients with impaired renal function and in patients predisposed to hyperkalemia due to medications or other medical conditions.
- **Urosepsis and Pyelonephritis:** There have been reports of serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization in patients receiving SGLT2 inhibitors, including canagliflozin. Treatment with SGLT2 inhibitors increases this risk. Evaluate patients for signs and symptoms and treat promptly.
- **Impaired Hepatic Function:** Metformin use in patients with impaired hepatic function has been associated with some cases of lactic acidosis. Therefore, INVOKAMET® is not recommended in patients with clinical or laboratory evidence of hepatic impairment.
- **Use With Medications Known to Cause Hypoglycemia**

  Canagliflozin

  Canagliflozin can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKAMET®.

  Metformin

  Hypoglycemia does not occur in patients receiving metformin alone under usual circumstances of use, but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, or when used concomitantly with other glucose-lowering agents (such as sulfonylureas or insulin) or ethanol. Elderly, debilitated, or malnourished patients, and those with adrenal or pituitary insufficiency or alcohol intoxication, are particularly susceptible to hypoglycemic effects. Hypoglycemia may be difficult to recognize in the elderly and in people who are taking beta-adrenergic blocking drugs. Monitor for a need to lower the dose of INVOKAMET® to minimize the risk of hypoglycemia in these patients.
- **Genital Mycotic Infections:** Canagliflozin increases risk of genital mycotic infections. Patients with a history of these infections and uncircumcised males were more likely to develop these infections. Monitor and treat appropriately.
- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema and anaphylaxis, were reported with canagliflozin; these reactions generally occurred within hours to days after initiation. If reactions occur, discontinue INVOKAMET®; treat and monitor until signs and symptoms resolve.

Please see additional Important Safety Information on the following page.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

- Moderate to severe renal impairment (eGFR below 45 mL/min/1.73 m^2), end stage renal disease (ESRD), or patients on dialysis
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis
- History of a serious hypersensitivity reaction to canagliflozin or metformin, such as anaphylaxis or angioedema

WARNINGS and PRECAUTIONS

- **Lactic Acidosis:** Postmarketing cases of metformin-associated lactic acidosis, including fatal cases, were reported. These cases had a subtle onset and were accompanied by nonspecific symptoms such as malaise, myalgias, abdominal pain, respiratory distress, or increased somnolence; however, hypothermia, hypotension, and resistant bradyarrhythmias have occurred with severe acidosis. Metformin-associated lactic acidosis was characterized by elevated blood lactate concentrations (>5 mmol/L), anion gap acidosis (without evidence of ketonuria or ketonemia), an increased lactate:pyruvate ratio; and metformin plasma levels generally >5 mcg/mL. Metformin decreases liver uptake of lactate, increasing lactate blood levels which may increase the risk of lactic acidosis, especially in patients at risk.

  If metformin-associated lactic acidosis is suspected, general supportive measures should be instituted promptly in a hospital setting, along with immediate discontinuation. In INVOKAMET®-treated patients with a diagnosis or strong suspicion of lactic acidosis, prompt hemodialysis is recommended to correct the acidosis and remove accumulated metformin. Hemodialysis has often resulted in reversal of symptoms and recovery.

  Educate patients and their families about the symptoms of lactic acidosis and if symptoms occur instruct them to discontinue INVOKAMET® and report these symptoms to their healthcare provider.

  For each of the known and possible risk factors for metformin-associated lactic acidosis, recommendations to reduce the risk of and manage metformin-associated lactic acidosis are provided below:

  Renal Impairment: Postmarketing metformin-associated lactic acidosis cases primarily occurred in patients with significant renal impairment. The risk of metformin accumulation and metformin-associated lactic acidosis increases with the severity of renal impairment because metformin is substantially excreted by the kidney. Obtain an eGFR before initiation and at least annually thereafter, and more frequently in patients at increased risk of renal impairment.

  Drug Interactions: The concomitant use of INVOKAMET® with specific drugs may increase the risk of metformin-associated lactic acidosis: those that impair renal function, result in significant hemodynamic change, interfere with acid-base balance, or increase metformin accumulation (eg, cationic drugs). Consider more frequent monitoring of patients.

  Age 65 or Greater: The risk of metformin-associated lactic acidosis increases with the patient's age due to a greater likelihood of hepatic, renal, or cardiac impairment. Assess renal function more frequently in elderly patients.

  Radiological Studies with Contrast: Administration of intravascular iodinated contrast agents in metformin-treated patients has led to an acute decrease in renal function and the occurrence of lactic acidosis. Stop INVOKAMET® at the time of, or prior to, an iodinated contrast imaging procedure in patients with an eGFR of 45 to 60 mL/min/1.73 m^2; in patients with a history of hepatic impairment, alcoholism, or heart failure; or in patients who will be administered intra-arterial iodinated contrast. Re-evaluate eGFR 48 hours after the imaging procedure, and restart INVOKAMET® if renal function is stable.

  Surgery and Other Procedures: Withholding of food and fluids during surgical or other procedures may increase the risk for volume depletion, hypotension, and renal impairment.

  INVOKAMET® should be temporarily discontinued while patients have restricted food and fluid intake.

  Hypoxic States: Many postmarketing cases of metformin-associated lactic acidosis occurred in the setting of acute congestive heart failure. Cardiovascular collapse (shock), acute myocardial infarction, sepsis, and other conditions associated with hypoxemia have been associated with lactic acidosis and may also cause pre-renal azotemia. When such events occur, discontinue INVOKAMET®.

  Excessive Alcohol Intake: Alcohol potentiates the effect of metformin on lactate metabolism and this may increase the risk of metformin-associated lactic acidosis. Warn patients against excessive alcohol intake while receiving INVOKAMET®.

  Hepatic Impairment: Patients with hepatic impairment have developed metformin-associated lactic acidosis. This may be due to impaired lactate clearance resulting in higher lactate blood levels. Avoid use of INVOKAMET® in patients with clinical or laboratory evidence of hepatic disease.

- **Hypotension:** Canagliflozin causes intravascular volume contraction. Symptomatic hypotension can occur after initiating INVOKAMET®, particularly in patients with an eGFR <60 mL/min/1.73 m^2, elderly patients, patients on either diuretics or medications that interfere with the renin-angiotensin-aldosterone system, or patients with low systolic blood pressure. Before initiating INVOKAMET® in patients with ≥1 of these characteristics who were not already on canagliflozin, volume status should be assessed and corrected. Monitor for signs and symptoms after initiating therapy.
- **Ketoacidosis:** Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, have been identified in patients with type 1 and 2 diabetes mellitus receiving SGLT2 inhibitors, including canagliflozin. Before initiating INVOKAMET®, consider factors in patient history that may predispose to ketoacidosis, including pancreatic insulin deficiency, caloric restriction disorders, and alcohol abuse. In patients treated with INVOKAMET®, consider monitoring for ketoacidosis and temporarily discontinuing in clinical situations known to predispose to ketoacidosis (eg, prolonged fasting due to acute illness or surgery).
- **Acute Kidney Injury and Impairment in Renal Function:** Canagliflozin causes intravascular volume contraction and can cause renal impairment. Postmarketing reports of acute kidney injury, some requiring hospitalization and dialysis, were reported; some reports involved patients younger than 65 years of age. Before initiation, consider factors that may predispose patients to acute kidney injury including hypovolemia, chronic renal insufficiency, congestive heart failure, and concomitant medications. Consider temporarily discontinuing INVOKAMET® in any setting of reduced oral intake or fluid losses; monitor patients for signs and symptoms of acute kidney injury. If acute kidney injury occurs, discontinue promptly and institute treatment.

  Canagliflozin increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Renal function abnormalities can occur after initiation. Renal function should be evaluated prior to initiation and periodically thereafter. Dose adjustment and more frequent renal function monitoring are recommended in patients with an eGFR <60 mL/min/1.73 m^2.
- **Hyperkalemia:** Canagliflozin can lead to hyperkalemia. Patients with moderate renal impairment who are taking medications that interfere with potassium excretion, such as potassium-sparing diuretics, or medications that interfere with the renin-angiotensin-aldosterone system are at an increased risk of developing hyperkalemia.

  Monitor serum potassium levels periodically after initiating INVOKAMET® in patients with impaired renal function and in patients predisposed to hyperkalemia due to medications or other medical conditions.
- **Urosepsis and Pyelonephritis:** There have been reports of serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization in patients receiving SGLT2 inhibitors, including canagliflozin. Treatment with SGLT2 inhibitors increases this risk. Evaluate patients for signs and symptoms and treat promptly.
- **Impaired Hepatic Function:** Metformin use in patients with impaired hepatic function has been associated with some cases of lactic acidosis. Therefore, INVOKAMET® is not recommended in patients with clinical or laboratory evidence of hepatic impairment.
- **Use With Medications Known to Cause Hypoglycemia**

  Canagliflozin

  Canagliflozin can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKAMET®.

  Metformin

  Hypoglycemia does not occur in patients receiving metformin alone under usual circumstances of use, but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, or when used concomitantly with other glucose-lowering agents (such as sulfonylureas or insulin) or ethanol. Elderly, debilitated, or malnourished patients, and those with adrenal or pituitary insufficiency or alcohol intoxication, are particularly susceptible to hypoglycemic effects. Hypoglycemia may be difficult to recognize in the elderly and in people who are taking beta-adrenergic blocking drugs. Monitor for a need to lower the dose of INVOKAMET® to minimize the risk of hypoglycemia in these patients.
- **Genital Mycotic Infections:** Canagliflozin increases risk of genital mycotic infections. Patients with a history of these infections and uncircumcised males were more likely to develop these infections. Monitor and treat appropriately.
- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema and anaphylaxis, were reported with canagliflozin; these reactions generally occurred within hours to days after initiation. If reactions occur, discontinue INVOKAMET®; treat and monitor until signs and symptoms resolve.

Please see additional Important Safety Information on the following page.