

# FDA Approves SGLT2 Inhibitor STEGLATRO™ (ertugliflozin) and Fixed-Dose Combination STEGLUJAN™ (ertugliflozin and sitagliptin) for Adults with Type 2 Diabetes

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Merck (NYSE:MRK), known as MSD outside the United States and Canada, and Pfizer Inc. (NYSE:PFE), today announced that the U.S. Food and Drug Administration (FDA) has approved STEGLATRO™ (ertugliflozin) tablets, an oral sodium-glucose cotransporter 2 (SGLT2) inhibitor, and the fixed-dose combination STEGLUJAN™ (ertugliflozin and sitagliptin) tablets.

STEGLATRO is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. STEGLUJAN is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both ertugliflozin and sitagliptin is appropriate. STEGLATRO and STEGLUJAN are not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. STEGLUJAN has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using STEGLUJAN. STEGLATRO and STEGLUJAN are contraindicated in patients with severe renal impairment, end-stage renal disease or on dialysis, or with a history of a serious hypersensitivity reaction to ertugliflozin. STEGLUJAN is also contraindicated in patients with a history of a serious hypersensitivity reaction to sitagliptin (such as anaphylaxis or angioedema). Additional safety information can be found below.

These FDA approvals are supported by seven Phase 3 studies of approximately 4,800 patients. STEGLATRO was studied as monotherapy and in combination with metformin and/or sitagliptin, as well as with insulin and a sulfonylurea, in adults with type 2 diabetes and moderate renal impairment. “In clinical trials, treatment with STEGLATRO resulted in significant A1C reductions when used alone or in combination with sitagliptin,” said Juan Pablo Frias, M.D., president and principal investigator, National Research Institute, Los Angeles. “This is important, as A1C-lowering is a key component of diabetes management, and many of my adult patients may need multiple medications to help manage their condition.”

“Merck welcomes the opportunity to provide adult patients with type 2 diabetes and their physicians these new medicines to help lower A1C, building on over a decade of experience with our diabetes portfolio and reflecting our continued commitment to diabetes research and patient care,” said Keith Kaufman, M.D., vice president, global clinical development and therapeutic area head for diabetes, endocrinology and women’s health, Merck Research Laboratories.

Diabetes is a chronic, progressive disease affecting approximately 30 million Americans (90 to 95 percent have type 2 diabetes). About one-third of adults with type 2 diabetes in the U.S. are not at their A1C goal.

“There remains a need to help adults with type 2 diabetes improve their glycemic control, and as the prevalence of the disease continues to rise, we are pleased to offer additional treatment options to these patients and the healthcare providers who treat them,” said James Rusnak, M.D., Ph.D., senior vice president and chief development officer, internal medicine, Pfizer Global Product Development.

One of the studies supporting the FDA approvals was VERTIS SITA2, a 26-week double-blind, placebo-controlled study. VERTIS SITA2 evaluated STEGLATRO (ertugliflozin) compared to placebo in 463 patients with type 2 diabetes inadequately controlled (baseline A1C of 7.0-10.5%) on background metformin (≥1,500 mg/day) and sitagliptin (100 mg/day). Patients were randomized to STEGLATRO 5 mg, STEGLATRO 15 mg or placebo administered once daily, in addition to continuation of background metformin and sitagliptin therapy. In the study, STEGLATRO provided significant additional A1C reductions on top of metformin plus sitagliptin of 0.7 percent and 0.8 percent, respectively, for the 5 and 15 mg doses, compared with 0.2 percent for placebo ( $p < 0.001$ , for both comparisons), which was the study’s primary endpoint.

In this study, STEGLATRO significantly reduced body weight by 6.6 pounds with the 5 mg dose and 6.2 pounds with the 15 mg dose, on top of metformin plus sitagliptin, compared with 2.2 pounds with placebo. Baseline body weight was 193.1 pounds, 190.9 pounds and 190.6 pounds for the 5 mg, 15 mg and placebo groups, respectively. The difference from placebo was -4.2 pounds for STEGLATRO 5 mg (95% CI: -5.7, -2.9) and -4.0 pounds for STEGLATRO 15 mg (95% CI: -5.3, -2.6). STEGLATRO 5 mg and 15 mg were also associated with significant reductions in fasting plasma glucose (25.7 mg/dL and 32.1 mg/dL, respectively, vs. 6.5 mg/dL for placebo;  $p < 0.001$ , for both comparisons). Baseline fasting plasma glucose levels were 167.7 mg/dL, 171.7 mg/dL and 169.6 mg/dL for the 5 mg, 15 mg and placebo groups, respectively. Significant reductions in systolic blood pressure were also observed for STEGLATRO (3.8 mmHg for 5 mg and 4.5 mmHg for 15 mg, vs. 0.2 mmHg for placebo). Baseline systolic blood pressure values were 132.1 mmHg, 131.6 mmHg and 130.2 mmHg for the 5 mg, 15 mg and placebo groups, respectively. For systolic blood pressure, the difference from placebo was -3.7 mmHg for STEGLATRO (ertugliflozin) 5 mg (95% CI: -6.1, -1.2) and -4.3 mmHg for STEGLATRO 15 mg (95% CI: -6.7, -1.9). STEGLATRO is not indicated for weight loss or hypertension.

STEGLATRO causes intravascular volume contraction. Symptomatic hypotension may occur after initiating STEGLATRO, particularly in patients with impaired renal function (estimated glomerular filtration rate [eGFR] less than 60 mL/min/1.73 m<sup>2</sup>), elderly patients (≥65 years), patients with low systolic blood pressure or patients on diuretics. Before initiating STEGLATRO, volume status should be assessed and corrected if indicated. Monitor for signs and symptoms after initiating therapy. Additional safety information can be found below.

In addition to STEGLATRO and STEGLUJAN (ertugliflozin and sitagliptin), the only fixed-dose combination of an SGLT2 inhibitor and the dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin, the FDA also approved the fixed-dose combination SEGLUROMET™ (ertugliflozin and metformin hydrochloride). SEGLUROMET is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin. SEGLUROMET is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. The labeling for SEGLUROMET contains a boxed warning for lactic acidosis. SEGLUROMET is contraindicated in patients with severe renal impairment, end-stage renal disease or on dialysis, acute or chronic metabolic acidosis, including diabetic ketoacidosis, or a history of a serious hypersensitivity reaction to SEGLUROMET, ertugliflozin or metformin hydrochloride. Additional safety information is found below.

STEGLATRO is available in 5 mg and 15 mg tablets. STEGLUJAN combines 5 mg or 15 mg of ertugliflozin with 100 mg of sitagliptin. SEGLUROMET combines 2.5 mg or 7.5 mg of ertugliflozin with 500 mg or 1,000 mg of metformin hydrochloride.

### **Merck-Pfizer Collaboration and Product Availability**

In 2013, Merck and Pfizer announced that they entered into a worldwide collaboration, except Japan, for the co-development and co-promotion of ertugliflozin. The Merck sales force will exclusively promote STEGLATRO and the two fixed-dose combination products in the United States. Merck and Pfizer will share potential revenues and certain costs on a 60/40 percent basis, respectively, and Pfizer may be entitled to additional milestone payments.

Merck has established a list price (Wholesale Acquisition Cost) of \$8.94 per day for STEGLATRO, \$17.45 per day for STEGLUJAN and \$8.94 per day for SEGLUROMET. Wholesale acquisition costs do not include discounts that may be paid on the products. STEGLATRO (ertugliflozin) and STEGLUJAN (ertugliflozin and sitagliptin) are expected to be available in pharmacies in January 2018. SEGLUROMET (ertugliflozin and metformin hydrochloride) is expected to be available in February 2018.

### **Selected Important Risk Information about STEGLATRO (continued)**

Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, has been reported in patients with type 1 and type 2 diabetes receiving SGLT2 inhibitors including STEGLATRO. Some cases were fatal. Assess patients with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If ketoacidosis is suspected, STEGLATRO should be discontinued, patient should be evaluated, and prompt treatment should be instituted. Before initiating STEGLATRO, consider risk factors for ketoacidosis, including pancreatic insulin deficiency from any cause, caloric restriction, and alcohol abuse. In patients treated with STEGLATRO, consider monitoring for ketoacidosis and temporarily discontinuing STEGLATRO in clinical situations known to predispose to ketoacidosis (e.g., prolonged fasting due to acute illness or surgery).

STEGLATRO causes intravascular volume contraction and can cause renal impairment. There have been postmarketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients receiving SGLT2 inhibitors. Before initiating STEGLATRO, consider factors that may predispose patients to acute kidney injury. Consider temporarily discontinuing STEGLATRO 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 STEGLATRO promptly and institute treatment.

STEGLATRO increases serum creatinine and decreases eGFR. Patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m<sup>2</sup>) may be more susceptible to these changes. Renal function abnormalities can occur after initiating STEGLATRO. Renal function should be evaluated prior to initiating STEGLATRO and periodically thereafter. Use of STEGLATRO is not recommended when eGFR is persistently between 30 and less than 60 mL/min/1.73 m<sup>2</sup> and is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m<sup>2</sup>.

There have been postmarketing reports of serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization in patients receiving SGLT2 inhibitors. Cases of pyelonephritis also have been reported in patients treated with STEGLATRO in clinical trials. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated.

An increased risk for lower limb amputation has been observed in clinical studies with another SGLT2 inhibitor. Across seven Phase 3 clinical trials with STEGLATRO, non-traumatic lower limb amputations were reported in

1 (0.1%) patient in the comparator group, 3 (0.2%) patients in the STEGLATRO 5 mg group, and 8 (0.5%) patients in the STEGLATRO 15 mg group. A causal association between STEGLATRO (ertugliflozin) and lower limb amputation has not been definitively established. Before initiating STEGLATRO, consider factors that may predispose patients to the need for amputations. Counsel patients about the importance of routine preventative foot care. Monitor patients and discontinue STEGLATRO if complications occur.

Insulin and insulin secretagogues (e.g., sulfonylurea) are known to cause hypoglycemia. STEGLATRO may increase the risk of hypoglycemia when used in combination with insulin and/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 STEGLATRO.

STEGLATRO increases the risk of genital mycotic infections. Patients who have a history of genital mycotic infections or who are uncircumcised are more likely to develop genital mycotic infections. Monitor and treat appropriately.

Dose-related increases in low-density lipoprotein cholesterol (LDL-C) can occur with STEGLATRO. Monitor and treat as appropriate.

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with STEGLATRO.

The most common adverse reactions associated with STEGLATRO (incidence ≥5%) were female genital mycotic infections.

### **Selected Important Risk Information about STEGLUJAN (ertugliflozin and sitagliptin) (continued)**

There have been postmarketing reports of acute pancreatitis, including fatal and nonfatal hemorrhagic or necrotizing pancreatitis, in patients taking sitagliptin. After initiating STEGLUJAN, patients should be observed carefully for signs and symptoms of pancreatitis. If pancreatitis is suspected, STEGLUJAN should promptly be discontinued and appropriate management should be initiated. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using STEGLUJAN.

Ertugliflozin causes intravascular volume contraction. Symptomatic hypotension may occur after initiating STEGLUJAN, particularly in patients with impaired renal function (eGFR less than 60 mL/min/1.73 m<sup>2</sup>), elderly patients (≥65 years), in patients with low systolic blood pressure, and in patients on diuretics. Before initiating STEGLUJAN, volume status should be assessed and corrected if indicated. Monitor for signs and symptoms after initiating therapy.

Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, has been reported in patients with type 1 and type 2 diabetes receiving SGLT2 inhibitors, including STEGLUJAN. Some cases were fatal. Assess patients with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If ketoacidosis is suspected, STEGLUJAN should be discontinued, patient should be evaluated, and prompt treatment should be instituted. Before initiating STEGLUJAN (ertugliflozin and sitagliptin), consider risk factors for ketoacidosis, including pancreatic insulin deficiency from any cause, caloric restriction, and alcohol abuse. In patients treated with STEGLUJAN, consider monitoring for ketoacidosis and temporarily discontinuing STEGLUJAN in clinical situations known to predispose to ketoacidosis (e.g., prolonged fasting due to acute illness or surgery).

STEGLUJAN causes intravascular volume contraction and can cause renal impairment. There have been postmarketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients receiving

SGLT2 inhibitors. Before initiating STEGLUJAN, consider factors that may predispose patients to acute kidney injury, including hypovolemia, chronic renal insufficiency, congestive heart failure, and concomitant medications. Consider temporarily discontinuing STEGLUJAN 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 STEGLUJAN promptly and institute treatment.

Ertugliflozin increases serum creatinine and decreases eGFR. Patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m<sup>2</sup>) may be more susceptible to these changes. Renal function abnormalities can occur. Renal function should be evaluated prior to initiating STEGLUJAN and periodically thereafter. Use of STEGLUJAN is not recommended when eGFR is persistently between 30 and less than 60 mL/min/1.73 m<sup>2</sup> and is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m<sup>2</sup>.

Serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization have been identified in patients receiving SGLT2 inhibitors. Cases of pyelonephritis also have been reported in ertugliflozin-treated patients in clinical trials. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly.

An increased risk for lower limb amputation has been observed in clinical studies with another SGLT2 inhibitor. Across seven Phase 3 clinical trials with ertugliflozin, non-traumatic lower limb amputations were reported in 1 (0.1%) patient in the comparator group, 3 (0.2%) patients in the ertugliflozin 5 mg group, and 8 (0.5%) patients in the ertugliflozin 15 mg group. A causal association between ertugliflozin and lower limb amputation has not been definitively established. Before initiating STEGLUJAN, consider factors that may predispose patients to the need for amputations. Counsel patients about the importance of routine preventative foot care. Monitor patients and discontinue STEGLUJAN if complications occur.

An association between DPP-4 inhibitor treatment and heart failure has been observed in cardiovascular outcomes trials for two other members of the DPP-4 inhibitor class. These trials evaluated patients with type 2 diabetes mellitus and atherosclerotic cardiovascular disease. Consider the risks and benefits of STEGLUJAN prior to initiating treatment in patients at risk for heart failure, such as those with a prior history of heart failure and a history of renal impairment, and observe these patients for signs and symptoms of heart failure during therapy. Advise patients to report any symptoms of heart failure. If heart failure develops, evaluate and manage appropriately, and consider discontinuation of STEGLUJAN (ertugliflozin and sitagliptin).

STEGLUJAN may increase the risk of hypoglycemia when combined with insulin and/or an insulin secretagogue. Consider lowering the dose of these agents when coadministered with STEGLUJAN.

Ertugliflozin increases the risk of genital mycotic infections, particularly in patients with a history of these infections or who are uncircumcised. Monitor and treat appropriately.

Serious hypersensitivity reactions (anaphylaxis, angioedema, and exfoliative skin conditions including Stevens-Johnson syndrome) have been reported in patients treated with sitagliptin. If a hypersensitivity reaction is suspected, discontinue STEGLUJAN, assess for other potential causes for the event, and institute alternative treatment for diabetes. Angioedema has also been reported with other DPP-4 inhibitors. Use caution in a patient with a history of angioedema with another DPP-4 inhibitor.

Dose-related increases in LDL-C can occur with STEGLUJAN.

Severe and disabling arthralgia has been reported in patients taking DPP-4 inhibitors. The time to onset of symptoms following initiation of drug therapy varied from 1 day to years. Patients experienced relief of symptoms upon discontinuation of medication. Consider DPP-4 inhibitors as a possible cause for severe joint

pain and discontinue drug if appropriate.

Bullous pemphigoid requiring hospitalization has been reported with DPP-4 inhibitor use. In reported cases, patients typically recovered with topical or systemic immunosuppressive treatment and discontinuation of the DPP-4 inhibitor. Tell patients to report any development of blisters or erosions. If bullous pemphigoid is suspected, discontinue STEGLUJAN and consider referral to a dermatologist.

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with STEGLUJAN.

The most common adverse reactions associated with ertugliflozin (incidence ≥5%) were female genital mycotic infections. The most common adverse reactions with sitagliptin (incidence ≥5%) were upper respiratory tract infection, nasopharyngitis, and headache. In the add-on to sulfonylurea and add-on to insulin studies, hypoglycemia was more commonly reported in patients treated with sitagliptin.

### **Selected Important Risk Information about SEGLUROMET (ertugliflozin and metformin hydrochloride)**

**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/Liter), 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 (e.g., carbonic anhydrase inhibitors such as topiramate), age 65 years old or greater, having a radiological study with contrast, surgery and other procedures, hypoxic states (e.g., acute congestive heart failure), excessive alcohol intake, and hepatic impairment.**

**If metformin-associated lactic acidosis is suspected, immediately discontinue SEGLUROMET (ertugliflozin and metformin hydrochloride) and institute general supportive measures in a hospital setting. Prompt hemodialysis is recommended.**

Educate patients and their families about the symptoms of lactic acidosis and, if these symptoms occur, instruct them to discontinue SEGLUROMET and promptly notify their health care provider.

Recommendations to reduce the risk include:

- **Renal Impairment:** Obtain an estimated eGFR prior to initiating therapy and annually or more frequently in patients at increased risk of developing renal impairment.
- **Drug Interactions:** More frequent monitoring is recommended when administered with drugs that impair renal function, result in hemodynamic change, interfere with acid-base balance, or increase metformin accumulation.
- **Age 65 or Greater:** Assess renal function more frequently.
- **Radiological Studies with Contrast:** Stop SEGLUROMET at the time of, or prior to, an iodinated contrast imaging procedure in patients with an eGFR of less than 60 mL/min/1.73 m<sup>2</sup>; patients with a history of hepatic impairment, alcoholism, or heart failure; or patients who will be administered intra-arterial iodinated contrast. Re-evaluate eGFR 48 hours after the procedure and restart SEGLUROMET if renal function is stable.
- **Surgery and Other Procedures:** Discontinue while patients have restricted food and fluid intake.

- Hypoxic States: Discontinue in conditions associated with hypoxemia.
- Excessive Alcohol Intake: Warn patients against excessive alcohol intake.
- Hepatic Impairment: Avoid use in patients with evidence of hepatic disease.

Ertugliflozin causes intravascular volume contraction and symptomatic hypotension may occur after initiating SEGLUROMET, particularly in patients with impaired renal function (eGFR less than 60 mL/min/1.73 m<sup>2</sup>), elderly patients (≥65 years), or patients on diuretics. Before initiating SEGLUROMET (ertugliflozin and metformin hydrochloride), assess and correct volume status. Monitor for hypotension.

Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, has been reported in patients with type 1 and type 2 diabetes receiving SGLT2 inhibitors, including ertugliflozin. Some cases were fatal. Assess patients with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If ketoacidosis is suspected, SEGLUROMET should be discontinued, patient should be evaluated, and prompt treatment should be instituted. Before initiating SEGLUROMET, consider risk factors for ketoacidosis, including pancreatic insulin deficiency from any cause, caloric restriction, and alcohol abuse. In patients treated with SEGLUROMET, consider monitoring for ketoacidosis and temporarily discontinuing SEGLUROMET in clinical situations known to predispose to ketoacidosis (e.g., prolonged fasting due to acute illness or surgery).

SEGLUROMET causes intravascular volume contraction and can cause renal impairment. There have been reports of acute kidney injury, some requiring hospitalization and dialysis, in patients receiving SGLT2 inhibitors. Before initiating SEGLUROMET, consider factors that may predispose patients to acute kidney injury. Consider temporarily discontinuing SEGLUROMET 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 SEGLUROMET promptly and institute treatment.

SEGLUROMET increases serum creatinine and decreases eGFR. Patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m<sup>2</sup>) may be more susceptible to these changes. Renal function abnormalities can occur after initiating SEGLUROMET. Renal function should be evaluated prior to initiating SEGLUROMET and periodically thereafter. Use of SEGLUROMET is not recommended when eGFR is persistently between 30 and less than 60 mL/min/1.73 m<sup>2</sup> and is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m<sup>2</sup>.

There have been postmarketing reports of serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization in patients receiving SGLT2 inhibitors. Cases of pyelonephritis also have been reported in ertugliflozin-treated patients in clinical trials. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate for urinary tract infections and treat promptly.

An increased risk for lower limb amputation has been observed in clinical studies with another SGLT2 inhibitor. Across seven Phase 3 clinical trials with ertugliflozin, non-traumatic lower limb amputations were reported in 1 (0.1%) patient in the comparator group, 3 (0.2%) patients in the ertugliflozin 5 mg group, and 8 (0.5%) patients in the ertugliflozin 15 mg group. A causal association between ertugliflozin and lower limb amputation has not been definitively established. Before initiating SEGLUROMET, consider factors that may predispose patients to the need for amputations. Counsel patients about the importance of routine preventative foot care. Monitor patients and discontinue SEGLUROMET (ertugliflozin and metformin hydrochloride) if complications occur.

Ertugliflozin may increase the risk of hypoglycemia when combined with insulin and/or an insulin secretagogue. Consider lowering the dose of these agents when coadministered with SEGLUROMET. Hypoglycemia could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation or during concomitant use of other glucose-lowering agents or with the use of ethanol.

Ertugliflozin increases the risk of genital mycotic infections, particularly in patients with a history of these infections or who are uncircumcised. Monitor and treat appropriately.

Dose-related increases in LDL-C can occur with SEGLUROMET. Monitor and treat as appropriate.

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with SEGLUROMET.

The most common adverse reactions associated with ertugliflozin (incidence ≥5%) were female genital mycotic infections. The most common adverse reactions associated with metformin (incidence ≥5%) were diarrhea, nausea, vomiting, flatulence, abdominal discomfort, indigestion, asthenia and headache.

## **About Merck**

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on Twitter, Facebook, Instagram, YouTube and LinkedIn.

## **About Pfizer Inc.: Working together for a healthier world®**

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at [www.pfizer.com](http://www.pfizer.com). In addition, to learn more, please visit us on [www.pfizer.com](http://www.pfizer.com) and follow us on Twitter at @Pfizer and @Pfizer\_News, LinkedIn, YouTube and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

## **Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA**

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.



Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2016 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).

### **Pfizer Disclosure Notice**

The information contained in this release is current as of December 22, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about STEGLATRO (ertugliflozin), STEGLUJAN (ertugliflozin and sitagliptin) and SEGLUROMET (ertugliflozin and metformin hydrochloride), including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of STEGLATRO, STEGLUJAN and SEGLUROMET; the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether and when applications for STEGLATRO, STEGLUJAN, and SEGLUROMET may be filed in any other jurisdictions; whether and when any such other applications for STEGLATRO, STEGLUJAN and SEGLUROMET that may be pending or filed may be approved by regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of STEGLATRO, STEGLUJAN, and SEGLUROMET; and competitive developments. The competitive landscape for type 2 diabetes therapies, including SGLT2 inhibitors, continues to evolve. The success of our ertugliflozin program is dependent on developments in that space.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

### **Please see Prescribing Information for STEGLATRO at**

[http://www.merck.com/product/usa/pi\\_circulars/s/steglatro/steglatro\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/s/steglatro/steglatro_pi.pdf) and Patient Information for STEGLATRO at [http://www.merck.com/product/usa/pi\\_circulars/s/steglatro/steglatro\\_mg.pdf](http://www.merck.com/product/usa/pi_circulars/s/steglatro/steglatro_mg.pdf)

**Please see Prescribing Information for STEGLUJAN at**

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**Please see Prescribing Information for SEGLUROMET (ertugliflozin and metformin hydrochloride) at**

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