In clinical trials, new once-daily Farxiga, in addition to diet and exercise, improved glycemic control by removing glucose from the body.

The robust Farxiga clinical development program included 24 clinical studies evaluating safety and efficacy. The studies included more than 11,000 adults with type 2 diabetes, including more than 6,000 patients treated with Farxiga.

Farxiga causes intravascular volume contraction. Symptomatic hypotension can occur after initiating Farxiga particularly in patients with impaired renal function (eGFR less than 60 mL/min/1.73 m²), elderly patients, or patients on loop diuretics. Before initiating Farxiga in patients with one or more of these characteristics, volume status should be assessed and corrected. Monitor for signs and symptoms of hypotension after initiating therapy. Farxiga increases serum creatinine and decreases eGFR. Elderly patients and patients with impaired renal function may be more susceptible to these changes. Adverse reactions related to renal function can occur after initiating Farxiga. Renal function should be evaluated prior to initiation of Farxiga and monitored periodically thereafter.

In a 24-week, add-on to metformin clinical trial, adult patients with type 2 diabetes treated with Farxiga 5 mg (n=137; baseline HbA1c 8.2%) or 10 mg (n=135; baseline A1c 7.9%) had significant reductions in HbA1c of -0.7% and -0.8%, respectively, compared with placebo plus metformin reductions of -0.3% (n=137; baseline HbA1c 8.1%). In the same study, the placebo-adjusted reduction in body weight was -2.2 kg with Farxiga 5 mg (baseline 84.7 kg) and -2.0 kg with 10 mg (baseline 86.3 kg). Also, mean changes from baseline in systolic blood pressure relative to placebo plus metformin were -4.5 mmHg and -5.3 mmHg with Farxiga 5 mg or 10 mg plus metformin, respectively. No major episodes of hypoglycemia were seen in any of the treatment arms. Minor episodes of hypoglycemia were reported in 1.5%, 0.7%, and 0% with Farxiga 5 mg, 10 mg, and placebo plus metformin, respectively.
DECLARE, a large, randomized, placebo-controlled study of more than 17,000 adult patients with type 2 diabetes designed to determine the effect of Farxiga, when added to the patients’ current anti-diabetes therapy, on the risk of CV events, such as CV death, myocardial infarction or ischemic stroke, compared with placebo. The study, which will also provide additional data on the long-term safety profile, initiated enrollment in April 2013 and has an anticipated completion date of 2019.

INDICATION AND LIMITATION OF USE FOR FARXIGA™ (dapagliflozin)

Farxiga is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Farxiga is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

IMPORTANT SAFETY INFORMATION FOR FARXIGA

Contraindications

• History of a serious hypersensitivity reaction to Farxiga

• Severe renal impairment, end stage renal disease, or patients on dialysis

Warnings and Precautions

• Hypotension: Farxiga causes intravascular volume contraction. Symptomatic hypotension can occur after initiating Farxiga, particularly in patients with impaired renal function (eGFR <60 ml/min/1.73 m²), elderly patients, or patients on loop diuretics. Before initiating Farxiga in patients with one or more of these characteristics, assess and correct volume status. After initiating therapy, monitor for signs and symptoms of hypotension.

• Impairment in Renal Function: Farxiga increases serum creatinine and decreases eGFR. Elderly patients and patients with impaired renal function may be more susceptible to these changes. Adverse reactions related to renal function can occur after initiating Farxiga. Before initiating Farxiga, evaluate renal function and monitor periodically thereafter. Discontinue Farxiga when eGFR is persistently <60 ml/min/1.73 m².

• Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues: Insulin and insulin secretagogues are known to cause hypoglycemia. Farxiga can increase the risk of hypoglycemia when combined with these agents. Consider a lower dose of insulin or the insulin secretagogue to reduce the risk of hypoglycemia when used in combination with Farxiga.

• Genital Mycotic Infections: Farxiga increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections were more likely to develop genital mycotic infections. Monitor and treat appropriately.

• Increases in Low-Density Lipoprotein Cholesterol (LDL-C): Increases in LDL-C occur with Farxiga. After initiating Farxiga, monitor LDL-C and treat per standard of care.

• Bladder cancer: Across 22 clinical studies, newly diagnosed cases of bladder cancer were reported in 0.17% of Farxiga-treated patients and 0.03% of placebo/comparator-treated patients. After excluding patients in whom exposure to study drug was <1 year at the time of diagnosis of bladder cancer, there were 4 cases with Farxiga and no cases with placebo/comparator. Bladder cancer risk factors and hematuria (a potential indicator of pre-existing tumors) were balanced between treatment arms at baseline. There were too few cases to determine whether the emergence of these events is related to Farxiga.

There are insufficient data to determine whether Farxiga has an effect on pre-existing bladder tumors. Farxiga should not be used in patients with active bladder cancer. Use with caution in patients with a prior history of bladder cancer.

Macrovascular Outcomes: There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Farxiga or any other anti-diabetic drug.

Adverse Reactions

• In a pool of 12 placebo-controlled studies, the most common adverse reactions (≥5%) treated with Farxiga 5 mg, 10 mg, and placebo respectively were female genital mycotic infections (8.4% vs 6.9% vs 1.5%), nasopharyngitis (6.6% vs 6.3% vs 6.2%), and urinary tract infections (5.7% vs 4.3% vs 3.7%).

Use in Specific Populations

• Pregnant Women: There are no adequate and well-controlled studies of Farxiga in pregnant women. Consider appropriate alternative therapies, especially during the second and third trimesters.

• Nursing Mothers: It is not known whether Farxiga is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Farxiga, discontinue nursing or discontinue Farxiga.

• Geriatric Use: A higher proportion of patients ≥65 years treated with Farxiga had adverse reactions related to volume depletion and renal impairment or failure compared to patients treated with placebo. No Farxiga dose change is recommended based on age.

Please click here for US Full Prescribing Information and Medication Guide for Farxiga.

About Type 2 Diabetes

Diabetes is estimated to affect 25.8 million people in the U.S. and more than 382 million people worldwide. The prevalence of diabetes is projected to reach more than 592 million people worldwide by 2035. Type 2 diabetes accounts for approximately
90-95 percent of all cases of diagnosed diabetes. Type 2 diabetes is a chronic disease characterized by pathophysiologic defects leading to elevated glucose levels. Over time, this sustained hyperglycemia contributes to further progression of the disease. Significant unmet needs still exist, as many patients remain inadequately controlled on their current glucose-lowering regimen.

**About SGLT2 Inhibition**

The kidney plays a contributing role in maintaining normal glucose balance, in part by filtering and subsequently reabsorbing glucose back into circulation. SGLT2, a sodium-glucose cotransporter found predominantly in the kidney, is responsible for the majority of glucose reabsorption. Selective inhibition of SGLT2 reduces the reabsorption of glucose and enables its removal via the urine, which is associated with reductions in HbA1c, weight and systolic blood pressure.

**About the AstraZeneca/Bristol-Myers Squibb Diabetes Alliance**

Dedicated to addressing the global burden of diabetes by advancing individualized patient care, AstraZeneca and Bristol-Myers Squibb are working in collaboration to develop and commercialize a versatile portfolio of innovative treatment options for diabetes and related metabolic disorders that aim to provide treatment effects beyond glucose control. Find out more about the Alliance and our commitment to meeting the needs of health care professionals and people with diabetes at [www.astrazeneca.com](http://www.astrazeneca.com) or [www.bms.com](http://www.bms.com).

On December 19, 2013 AstraZeneca and Bristol-Myers Squibb announced an agreement under which AstraZeneca will acquire the entirety of Bristol-Myers Squibb’s interests in the companies’ diabetes alliance to consolidate worldwide ownership of the diabetes business within AstraZeneca. The closing of the transactions contemplated by the agreement is subject to customary terms and conditions, and is expected to occur during the first quarter of 2014.

**About AstraZeneca**

AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialization of prescription medicines, primarily for the treatment of cardiovascular, metabolic, respiratory, inflammation, autoimmune, oncology, infection and neuroscience diseases. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: [www.astrazeneca.com](http://www.astrazeneca.com).

**About Bristol-Myers Squibb**

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit [www.bms.com](http://www.bms.com) or follow us on Twitter at [http://twitter.com/bmsnews](http://twitter.com/bmsnews).

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**Ticker Slug:**

*Ticker: AZN<br>Exchange: NYSE*