BAQSIMI™ (glucagon) Nasal Powder 3 mg, the First and Only Nasally Administered Glucagon to Treat Severe Hypoglycemia in Adults and Children with Diabetes Ages Four Years and Older, Approved by FDA

July 25, 2019

BAQSIMI is expected to be available in U.S. pharmacies within one month

INDIANAPOLIS, July 24, 2019 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has approved BAQSIMI™ (glucagon) nasal powder 3 mg for the treatment of severe hypoglycemia in people with diabetes ages four years and above, Eli Lilly and Company (NYSE: LLY) announced today. BAQSIMI is the first and only nasally administered glucagon, and it was designed with severe hypoglycemia rescue in mind. It is compact, portable and ready to use (no reconstitution required) in a single, fixed, 3 mg dose.

BAQSIMI is contraindicated in patients with pheochromocytoma, insulinoma, and known hypersensitivity to glucagon or to any of the excipients in BAQSIMI. Allergic reactions have been reported with glucagon and include anaphylactic shock with breathing difficulties and hypotension.

People can sign up for direct updates on BAQSIMI availability, patient and caregiver resources, and affordability options at BAQSIMI.com. BAQSIMI is expected to be stocked in retail pharmacies within one month.

Severe hypoglycemia (very low blood sugar) is a serious medical condition that constitutes an emergency for people with type 1 and type 2 diabetes.[1] It is characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.[2] If untreated, severe hypoglycemia can lead to serious consequences, such as loss of consciousness, seizure, coma and death.[2,3]

"Severe hypoglycemia is an unpredictable event for people with diabetes that can happen anytime, anywhere. It's an experience that can be very stressful and difficult for those helping a person in a low blood sugar emergency," said Dr. Sherry Martin, Vice President of Lilly Medical Affairs. "The FDA's approval of BAQSIMI may help people prepare for these moments with an innovative product that has the simplicity of nasal administration."

Acquired by Lilly from Locemia Solutions in 2015, BAQSIMI is a new formulation of rescue glucagon that builds upon Lilly's diabetes heritage. Dr. Claude Piche, CEO and co-founder of Locemia Solutions, credits co-founder Robert Oringer as the original inspiration behind BAQSIMI.

"With two sons diagnosed with type 1 diabetes, he understood the importance of having a rescue treatment that could be used by a broad network of people...one that would be different from other low blood sugar emergency treatments, because it is delivered as a puff in the nose, instead of as an injection," said Dr. Piche.

Lilly is in discussions with insurance providers to make BAQSIMI available to as many people as possible. Eligible commercially insured people with diabetes can pay as little as $25 for up to two BAQSIMI devices (1 two-pack or 2 one-packs) if they use the savings card.* This prescription is generally filled on an annual basis. Lilly may also be able to help people who don't have commercial insurance coverage with options found through the Lilly Diabetes Solutions Center when BAQSIMI is available in U.S. pharmacies. The U.S. list price for a BAQSIMI one-pack is $280.80 and for a two-pack is $561.60.

"We understand the financial impact that managing diabetes has on families. Lilly is committed to helping make BAQSIMI affordable and accessible to as many people living with diabetes as possible by securing access with payers as well as through our affordability offerings," said Tony Ezell, Vice President, U.S. Connected Care and Insulins, Lilly.

Patients and healthcare professionals with questions about BAQSIMI can visit www.BAQSIMI.com or call The Lilly Answers Center at 1-800-LillyRx (1-800-545-5979).

Clinical Overview
In adult patients, BAQSIMI had comparable efficacy to injectable glucagon. One hundred percent of pediatric patients (age 4 and above) given BAQSIMI met treatment success and 100% of pediatric patients (age 4 and above) given glucagon for injection met treatment success.[4,5,6] Common cold with nasal congestion did not impair absorption of BAQSIMI.[4,7] Most common (≥10%) adverse reactions associated with BAQSIMI are nausea, vomiting, headache, upper respiratory tract irritation (i.e., rhinorrhea, nasal discomfort, nasal congestion, cough, and epistaxis), watery eyes, redness of eyes, itchy nose, throat and eyes.[4]

Clinical Studies in Adult Patients
Two randomized, multicenter, open-label, 2-period crossover trials compared a 3 mg dose of nasally administered BAQSIMI to a 1 mg dose of glucagon for injection for treatment of insulin-induced hypoglycemia. Study 1 included 70 adult patients with type 1 diabetes. Study 2 included 83 adult patients with type 1 or type 2 diabetes; 80 patients were included in the efficacy analysis of Study 2. Primary efficacy measure was the proportion of patients achieving treatment success.

BAQSIMI demonstrated noninferiority to glucagon for injection in both studies in raising blood glucose after insulin-induced hypoglycemia, with 100% of patients treated with BAQSIMI and 100% of glucagon for injection-treated patients achieving treatment success in Study 1, and 98.8% and 100%,

respectively, in Study 2. Treatment success was defined as an increase in plasma glucose levels to ≥ 70 mg/dL or a ≥20 mg/dL rise in plasma glucose from nadir within 30 minutes of receiving the study glucagon.

In Study 1, the mean nadir blood glucose was 54.5 mg/dL for BAQSIMI and 55.8 mg/dL for glucagon for injection. In Study 2, the mean nadir blood glucose was 44.1 mg/dL for BAQSIMI and 47.1 mg/dL for glucagon for injection.[4,5]

Spontaneous adverse reactions in adult patients (pooled results for Study 1 and Study 2) for BAQSIMI 3 mg (n=153) compared to glucagon for injection 1 mg (n=151) were nausea (26.1% vs. 33.8%), headache (18.3% vs. 9.3%), vomiting (15.0% vs. 13.9%) and upper respiratory tract irritation (rhinorrhea, nasal discomfort, nasal congestion, cough, and epistaxis) (12.4% vs. 1.3%).

A patient-solicited questionnaire identified (treatment-emergent) nasal and ocular symptoms for BAQSIMI 3 mg compared to glucagon for injection 1 mg, including watery eyes (58.8% vs. 2.0%), nasal congestion (42.5% vs. 6.0%), runny nose (34.6% vs. 0%), nasal itching (39.2% vs. 4.6%), itchy eyes (21.6% vs. 1.3%), redness of eyes (24.8% vs. 2.6%), sneezing (19.6% vs. 0.7%), itching of throat (12.4% vs. 1.3%) and itching of ears (3.3% vs. 0.7%). Subjects were asked to report whether they had the symptom after glucagon administration. The frequency was based on severity increase over baseline.[4,8,9]

Clinical Study in Pediatric Patients
A randomized, multicenter study evaluated the pharmacokinetics/pharmacodynamics (PK/PD), safety, and efficacy of BAQSIMI compared with glucagon for injection in children and adolescents aged 4 to <17 years with type 1 diabetes (N=48) divided into 3 cohorts. Young children (ages 4 to <8 years, n=18) and children (ages 8 to <12 years, n=18) were randomized 2:1 to receive either BAQSIMI 2 mg or 3 mg at visit 1 and the alternative BAQSIMI dose at visit 2; or weight-based glucagon for injection at a single study visit. Adolescents (ages 12 to <17, n=12) were randomized 1:1 to receive BAQSIMI 3 mg or glucagon for injection 1 mg with crossover to alternate glucagon at dosing visit 2. Insulin was used to reduce blood glucose levels, and glucagon was administered after glucose reached <80 mg/dL.

Following insulin-induced glucose reduction, 100% of patients achieved treatment success with nasally administered BAQSIMI compared to 100% of patients treated with glucagon for injection. Treatment success was defined as the proportion of participants achieving an increase in plasma glucose of ≥20 mg/dL from the nadir glucose concentration within 30 minutes of glucagon dosing.

The mean nadir blood glucose across different age cohorts was 67-73 mg/dL for BAQSIMI and 69-72 mg/dL for glucagon for injection.[4,6]

Spontaneous adverse reactions in pediatric patients for BAQSIMI 3 mg (n=36) compared to weight-based glucagon for injection (n=24) were vomiting (30.6% vs. 37.5%), headache (25.0% vs. 12.5%), nausea (16.7% vs. 33.3%) and upper respiratory tract irritation (nasal discomfort, nasal congestion, and sneezing) (16.7% vs. 0%).

A patient-solicited questionnaire identified (treatment-emergent) nasal and ocular symptoms for BAQSIMI 3 mg vs. weight-based glucagon for injection, including watery eyes (47.2% vs. 0%), nasal congestion (41.7% vs. 0%), nasal itching (27.8% vs. 4.2%), runny nose (25.0% vs. 0%), sneezing (19.4% vs. 4.2%), itchy eyes (16.7% vs. 12.5%), redness of eyes (13.9% vs. 0%), itching of throat (2.8% vs. 4.2%) and itching of ears (2.8% vs. 0%). Subjects were asked to report whether they had the symptom after glucagon administration. The frequency was based on severity increase over baseline.[4,10,11]

Clinical Study in Nasal Congestion
A randomized, single center, open-label, repeated-measures, parallel-design, phase 1 study examined the safety and PK/PD of BAQSIMI in otherwise healthy adult participants with nasal congestion resulting from common cold.

Adult patients in cohort 1 (n=18) received 2 doses of BAQSIMI 3 mg: one while experiencing nasal congestion and another after recovery from cold symptoms. Adult patients in cohort 2 (n=18), who also had colds with nasal congestion, received a single dose of BAQSIMI 3 mg 2 hours after treatment with the decongestant oxymetazoline. Blood glucagon and glucose concentrations were measured before and at 5-, 10-, and 30-minute intervals until 180 minutes after BAQSIMI administration.

Common cold with nasal congestion tested with or without use of decongestant did not impair absorption of BAQSIMI.[4,7]

About Severe Hypoglycemia (Very Low Blood Sugar) and Rescue Treatment
People with diabetes on insulin are at risk of severe hypoglycemia.[1] In the U.S., there are approximately 6.3 million people on insulin.[12] Very low blood sugar is often underreported.[13] Severe hypoglycemia can happen anywhere; in an analysis of emergency medical services responses, approximately 31% of severe hypoglycemic events happened outside the home.[14]

The American Diabetes Association identifies three levels of hypoglycemia and recommends all persons at risk of clinically significant hypoglycemia (glucose <54 mg/dL) have a glucagon prescription, so it is available should it be needed to treat a severe hypoglycemic event.[2]

ABOUT BAQSIMI
BAQSIMI is a portable, dry nasal spray form of glucagon, ready to use with no reconstitution or priming required in a single, fixed 3 mg dose. It is absorbed in the nose, so does not require inhalation. BAQSIMI does not need to be refrigerated and can be stored at temperatures up to 86°F/30°C in the shrink-wrapped tube provided. BAQSIMI was studied in patients as young as age four years.

The device and protective container used for BAQSIMI are supplied by Aptar Pharma, part of AptarGroup, Inc. (Crystal Lake, Illinois).

Indications and Usage
BAQSIMI is indicated for the treatment of severe hypoglycemia in patients with diabetes ages 4 years and above.

Important Safety Information

Contraindications
BAQSIMI is contraindicated in patients with pheochromocytoma, insulinoma, and known hypersensitivity to glucagon or to any of the excipients in BAQSIMI. Allergic reactions have been reported with glucagon and include anaphylactic shock with breathing difficulties and hypotension.

Warnings and Precautions
BAQSIMI is contraindicated in patients with pheochromocytoma because glucagon may stimulate release of catecholamines from the tumor. If the patient develops a dramatic increase in blood pressure and a previously undiagnosed pheochromocytoma is suspected, 5 to 10 mg of phentolamine mesylate, administered intravenously, has been shown to be effective in lowering blood pressure.

In patients with insulinoma, administration of glucagon may produce an initial increase in blood glucose; however, BAQSIMI administration may directly or indirectly (through an initial rise in blood glucose) stimulate exaggerated insulin release from an insulinoma and cause hypoglycemia. BAQSIMI is contraindicated in patients with insulinoma. If a patient develops symptoms of hypoglycemia after a dose of BAQSIMI, give glucose orally or intravenously.

Allergic reactions have been reported with glucagon, these include generalized rash, and in some cases anaphylactic shock with breathing difficulties and hypotension. BAQSIMI is contraindicated in patients with a prior hypersensitivity reaction.

BAQSIMI is effective in treating hypoglycemia only if sufficient hepatic glycogen is present. Patients in states of starvation, with adrenal insufficiency or chronic hypoglycemia may not have adequate levels of hepatic glycogen for BAQSIMI administration to be effective. Patients with these conditions should be treated with glucose.

Adverse Reactions
Most common (≥10%) adverse reactions associated with BAQSIMI are nausea, vomiting, headache, upper respiratory tract irritation (i.e., rhinorrhea, nasal discomfort, nasal congestion, cough, and epistaxis), watery eyes, redness of eyes, and itchy nose, throat and eyes.

Drug Interactions
Patients taking beta-blockers may have a transient increase in pulse and blood pressure when given BAQSIMI. In patients taking indomethacin, BAQSIMI may lose its ability to raise blood glucose or may even produce hypoglycemia. BAQSIMI may increase the anticoagulant effect of warfarin.

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Please see Full Prescribing Information including Patient Information Provided. Please see Instructions for Use included with your BAQSIMI device.

Savings card information
This offer expires on 12/31/2020. Patient must have commercial drug insurance coverage to pay as little as $25 for up two BAQSIMI devices (1 two pack or 2 one packs). All subsequent fills and refills could be as low as $25 for eligible, commercially insured patients up to a maximum of 12 fills per year. This offer is subject to a cap of wholesale acquisition cost plus usual and customary pharmacy charges. Patient is responsible for any applicable taxes, fees, or amounts exceeding monthly or annual caps. **This offer is invalid for patients without commercial drug insurance or those whose prescription claims are eligible to be reimbursed, in whole or in part, by any governmental program, including, without limitation, Medicaid, Medicare, Medicare Part D, Medigap, DOD, VA, TRICARE/CHAMPUS, or any state patient or pharmaceutical assistance program.** Offer void where prohibited by law and subject to change or discontinue without notice. Card activation is required. Subject to additional terms and conditions, which can be found at www.baqsimi.com.

About Lilly Diabetes
Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Thirty years later, Lilly scientists crystalized the first glucagon and we introduced the first commercial injectable glucagon in 1960. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research, collaboration and quality manufacturing we strive to make life better for people affected by diabetes. We offer a wide range of therapies and a continued determination to provide real solutions—from medicines and technologies to support programs and more. For the latest updates, visit http://www.lillydiabetes.com/ or follow us on Twitter: @LillyDiabetes and Facebook: LillyDiabetesUS.

About Eli Lilly and Company
Lilly is a global health care leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at lilly.com and lilly.com/newsroom. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about BAQSIMI™ (glucagon) nasal powder 3 mg as treatment of severe hypoglycemia in patients with diabetes ages 4 years and above and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that BAQSIMI will receive additional regulatory approvals or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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