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Zegalogue® (dasiglucagon): A Sweet Medication to Treat Low Blood Sugar

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Diabetes mellitus is a condition resulting from sustained levels of high blood sugar due to pancreatic insulin deficiency and/or insulin resistance. In the United States, an estimated 37.3 million people have Type 1 or Type 2 diabetes.[1] Diabetes is the most expensive chronic condition in the United States, with an estimated $237 billion spent each year on direct medical costs, and an additional $90 billion lost due to reduced productivity.[2] In Type 1 diabetes, the pancreas does not make insulin, or it makes very little insulin.[3] In Type 2 diabetes, pancreatic β-cells progressively deteriorate, leading to impaired insulin secretion and hyperglycemia.[4] A rarer form of diabetes, gestational diabetes, occurs when a woman's body cannot make enough insulin while she is pregnant.[5] During a normal pregnancy, the placenta releases hormones which causes insulin resistance; if the body does not produce enough extra insulin to overcome this insulin resistance, gestational diabetes results. Regardless of pathophysiology, all types of diabetes carry the risk of hypoglycemia with medication therapy.

There are multiple risk factors associated with hypoglycemia. Diabetes medications that lower blood sugar rapidly, especially insulin and sulfonylureas, can increase the risk of hypoglycemia. Other risk factors include patients at an older age, long duration of diabetes, missing meals or having erratic timing of meals, low carbohydrate content of meals, chronic kidney disease, increased exercise, and alcohol consumption.[6] In addition, a past history of hypoglycemia also indicates a future risk of hypoglycemic episodes. Hypoglycemia can cause unpleasant symptoms and can be lethal if not treated. Common symptoms include tremor, palpitations, sweating, dizziness, weakness, and delirium.[7]

The American Diabetes Association defines hypoglycemia as all episodes of low plasma glucose concentrations with or without symptoms that expose the individual to harm.[8] Each person will vary in regard to what values represent too low of a glucose concentration for them. Generally, however, glucose levels of ≤ 70 mg/dL are considered hypoglycemic for most people.[9] Hypoglycemia is categorized into three levels: level 1 hypoglycemia is defined as a blood glucose concentration of ≥ 54 mg/dL to < 70 mg/dL, level 2 hypoglycemia is a blood glucose concentration of < 54 mg/dL, and level 3 hypoglycemia is a severe event with altered mental or physical status that requires another person assisting to treat the hypoglycemia.[9] Due to clinical concern for patient safety with medication use, several FDA-approved products have been introduced to market for treatment of hypoglycemia.

The first Food and Drug Administration (FDA) approved treatment for hypoglycemia was glucagon, which was approved in 1960.[10] Glucagon is a hormone made naturally by the α-cells in the pancreas and acts to increase blood glucose concentrations. Glucagon activates hepatic glucagon receptors, which stimulates the breakdown of glycogen, the storage form of glucose in the body.[11] Glycogen breaks down into glucose, which is released from the liver and circulates throughout the bloodstream, raising blood glucose concentrations. Initially, the only formulation available was a glucagon powder for injection that needed to be reconstituted with solution prior to administration. Reconstitution posed many problems for patients and caregivers alike, as patients are not always capable of reconstituting the medication when in a hypoglycemic state, caregivers may be uncomfortable or unfamiliar with the reconstitution process, caregivers may provide inaccurate dosing, and the speed of administration is reduced by this multi-step process.[12] As a response to these challenges, next-generation glucagon rescue treatments were created. The first new formulation to market was Baqsimi®, an intranasal glucagon that is easier to administer and is FDA-approved for the treatment of severe hypoglycemia.[13] The next FDA-approved treatment for severe hypoglycemia was Gvoke®, a ready-to-use injectable glucagon dosed by age and weight that requires no reconstitution.[14]

Finally, the latest treatment available is Zegalogue® (dasiglucagon), which was FDA-approved in March 2021 for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ≥ 6 years old.[15] Dasiglucagon is a glucagon receptor agonist, increasing the blood glucose concentration by activating hepatic glucagon receptors, just like glucagon.[15] Dasiglucagon is a great option available for patients in a severe hypoglycemic state unwilling or unable to consume glucose by mouth. Unlike the alternative ready-to-use injectable glucagon formulation, dasiglucagon dosing is the same for all patients, regardless of age or weight.[15]

This paper aims to discuss the pharmacology and important

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features of dasiglucagon, as well as detail the clinical trials that led to the FDA approval of this new medication.

Pharmacology

Mechanism of Action

Dasiglucagon is a glucagon receptor agonist.[15] Like its parent compound glucagon, dasiglucagon activates hepatic glucagon receptors, stimulating the breakdown of glycogen.[11] Glycogen then breaks down into glucose, which is released from the liver into the bloodstream and raises blood glucose concentrations. Dasiglucagon has improved physical and chemical stability compared to glucagon due to seven amino acids changes.[15] **Figure 1** highlights the differences between dasiglucagon and glucagon, with the amino acid changes highlighted in red.[16,17] These molecular modifications increase electrostatic repulsions between molecules and prevent fibril formation, allowing the medication to be soluble in aqueous solution, and thereby avoiding the necessity of reconstitution.[18]

Pharmacokinetics

When administered subcutaneously, dasiglucagon achieves peak concentration of 5,110 pg/mL in 35 minutes in adults with a mean increase in glucose concentration at 90 minutes from baseline of 168 mg/dL. In contrast, peak concentration of 3,920 pg/mL occurs in 21 minutes for pediatrics with an increase in glucose concentration of 162 mg/dL after 60 minutes.[15] The volume of distribution is 47-57 L, and the half-life is 30 minutes.[15] Dasiglucagon is cleared like native glucagon through proteolytic degradation pathways in the plasma, liver, and kidneys.[15] As a protein, it is metabolized into smaller polypeptides and amino acids. Dasiglucagon does not significantly inhibit CYP enzymes 1A2, 2C9, 2C19, 2D6, or 3A4A.[19] A summary of these pharmacokinetic properties can be found in **Table 1.**

Clinical Trials

Dasiglucagon was approved by the FDA for severe hypoglycemia based on safety and efficacy data from three randomized controlled trials. This section will review these trials that led to dasiglucagon entering the market. In the first trial, *Pieber et al* sought to confirm safety and efficacy of dasiglucagon in adults with type 1 diabetes. This trial used a prefilled syringe for dasiglucagon dosages. Trial 2, conducted by *Bailey et al,* was completed afterwards to confirm safety and efficacy of dasiglucagon when using an autoinjector delivery device. Finally, the third trial by *Battelino et al* focused on the pediatric population, using very similar methods as the first trial but changing the study population to children 6-17 years of age. Summaries comparing the primary and secondary outcomes of each trial can be found in **Table 2** and **Table 3,** respectively.

Figure 1 | Glucagon and Dasiglucagon Chemical Structures[16,17]

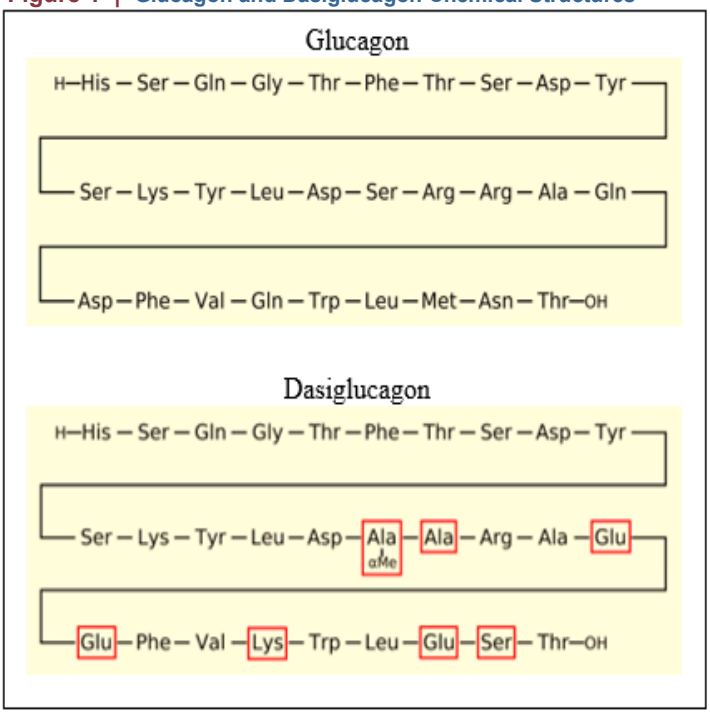

Table 1 | Select Dasiglucagon Pharmacokinetics[15,20]

Absorption	
T_{max}[a]	~35 min (adults) ~21 min (pediatric)
Onset of Action	10 min
Distribution	
V_{ss}[b]	47-57 L
Bioavailability	51%
Metabolism	
	Proteolytic degradation
Elimination	
$T_{1/2}$[c]	11 hours

[a]Time to maximum concentration; [b]Steady state volume of distribution; [c]Half-life

NCT03378635 Pieber, et al.[12]

A phase 3, global, multicenter, randomized, parallel-group, placebo-controlled, and double-blind clinical trial was conducted to evaluate the safety and efficacy of dasiglucagon for insulin-induced hypoglycemia in participants with type 1 diabetes.[12] The primary objective of this study was to demonstrate superiority of dasiglucagon over placebo.[12] Glucagon was included as a reference only. The trial was conducted in a clinical research inpatient setting, with centers in Germany, Austria, Canada, and the United States. The study included 168 adults aged 18-75 years with type 1 diabetes.[12] Inclusion criteria included having type 1 diabetes, receiving stable insulin therapy (either through a pump or injections), and having an HbA1c <10%.[12] Participants were excluded if they had received dasiglucagon in the past, had an allergy to any of the products in the trial, experienced hypoglycemia with seizure in the last year, had severe hypoglycemia in the last month, or received any of the following medications in the 28 days prior to being screened: β-blockers, indomethacin, warfarin, or anticholinergic medications.[12]

There were three treatment arms in this study, with baseline characteristics similar across all three arms. The participants were randomized using a 2:1:1 ratio to receive either 0.6 mg dasiglucagon subcutaneously via a prefilled syringe (n = 82), placebo (n = 43), or 1 mg reconstituted glucagon (n = 43).[12] The participants' insulin therapies were stopped prior to treatment. Intravenous insulin glulisine was administered at 150% of each participant's usual basal rate and then adjusted to reach a target plasma glucose level of 55 mg/dL. Once the participant's glucose concentration was between 45-60 mg/dL, the treatment or placebo was administered.[12]

The primary end point was time to plasma glucose recovery, which was defined as an increase of ≥ 20 mg/dL from baseline

Table 2 | Summary of Primary Outcomes[12,18,21]

Trial	Treatment Arms	Endpoint	Results (95% CI)	P-Value	True Time to Recovery (95% CI)	P-Value
NCT03378635[12]	Dasiglucagon 0.6 mg (n=82)	Time to plasma glucose recovery (increase of glucose ≥ 20 mg/dL from baseline), in minutes	10 (10—10)	<0.001	9 (8.4—9.7)	<0.001
	Placebo (n=43)		40 (30—40)		33.7 (26.1—36.1)	
	Glucagon 1mg (n=43)		12 (10—12)	—-	10 (9.0—10.6)	—-
NCT03688711[18]	Dasiglucagon 0.6mg (n=34)		10 (8—12)	<0.001	9.3 (7.8—10.4)	<0.001
	Placebo (n=10)		35 (20—NE*)		32.0 (19.2—NE*)	
NCT03667053[21]	Dasiglucagon 0.6mg (n=20)		10 (8—12)	<0.001	8.7 (6.9—10.6)	—-
	Placebo (n=11)		30 (20—NE*)		29.3 (18.5—NE*)	
	Glucagon 0.5mg or 1mg (n=10)		10 (8—12)	—-	9.8 (7.4—10.6)	—-

without rescue intravenous glucose given. Recovery needed to occur within 45 minutes. The median time to plasma glucose recovery was 10 minutes with dasiglucagon versus 40 minutes with placebo ($P < 0.001$), and 12 minutes with reconstituted glucagon.[12] An analysis using linear interpolation was also conducted to determine the true time to plasma glucose recovery, when an exact 20 mg/dL increase in plasma glucose occurred. The median true time to plasma glucose recovery was 9 minutes with dasiglucagon versus 33.7 minutes with placebo ($P < 0.001$), and 10 minutes with reconstituted glucagon.[12] Dasiglucagon provided a rapid reversal of hypoglycemia that was statistically significant.[12]

The secondary end points studied were achieving plasma glucose recovery within 30, 20, 15, and 10 minutes. The proportion of participants who achieved plasma glucose recovery were as follows: in 30 minutes, 100% in the dasiglucagon group (compared to 47% in placebo group and 100% in the glucagon group); in 20 minutes, 99% in the dasiglucagon group (compared to 14% in placebo group and 98% in the glucagon group); in 15 minutes, 99% in the dasiglucagon group (compared to 2% in placebo group and 95% in the glucagon group); and in 10 minutes, 65% in the dasiglucagon group (compared to 0% in placebo group and 49% in the glucagon group).[12] For each of the four time points, statistical significance was met ($P < 0.001$). After 30 minutes, the mean plasma glucose increase was 90.0 mg/dL for dasiglucagon, compared to 19.1 mg/dL in the placebo group and 88.5 mg/dL in the reconstituted glucagon group.[12] The safety and tolerability of dasiglucagon were similar to the safety and tolerability of reconstituted glucagon.

NCT03688711 Bailey et al.[18]

This phase 3, multicenter, randomized, double-blind, parallel-group, placebo-controlled study aimed to evaluate the clinical efficacy and safety of dasiglucagon for rescue treatment of hypoglycemia in participants with type 1 diabetes compared to placebo.[18] The primary endpoint of this study was time to plasma glucose recovery, which was defined as an increase of ≥ 20 mg/dL from baseline without rescue intravenous glucose. The trial was conducted in three centers in the United States. The study included 44 adults aged 18-75 years with type 1 diabetes.[18] Inclusion criteria included having type 1 diabetes for at least one year and receiving stable insulin therapy before the trial screening.[18] Participants were excluded if they had received dasiglucagon in the past, had an allergy to any of the products in the trial, or had a history of severe systemic allergy or anaphylaxis.[18]

There were two treatment arms in this study. The participants were randomized using a 3:1 ratio to receive either 0.6 mg dasiglucagon subcutaneously via an autoinjector delivery device (n = 34) or placebo (n = 10).[18] The participants' insulin therapies were stopped prior to treatment, and participants fasted starting at 10 pm the night before dosing, except for up to 20 g of carbohydrates allowed to prevent hypoglycemia.[18] Intravenous insulin glulisine was administered at 150% of each participant's basal rate and then adjusted to reach a target plasma glucose level of 45-60 mg/dL. Once the participant's glucose concentration was < 60 mg/dL, the treatment or placebo was administered.[18]

The primary end point was time to plasma glucose recovery, which was defined as an increase of ≥ 20 mg/dL from baseline without rescue intravenous glucose given. Participants were con-

Table 3 | Summary of Secondary Outcomes[12,18,21]

Trial	Treatment Arms	Plasma Glucose Recovery within 30 mins		Plasma Glucose Recovery within 20 mins		Plasma Glucose Recovery within 15 mins		Plasma Glucose Recovery within 10 mins	
		Result (%)	P-value	Result (%)	P-value	Result (%)	P-value	Result (%)	P-value
NCT03378635[12]	Dasiglucagon 0.6 mg (n=82)	100	<0.001	99	<0.001	99	<0.001	65	<0.001
	Placebo (n=43)	47		14		2		0	
	Glucagon 1mg (n=43)	100	—-	98	—-	95	—-	49	—-
NCT03688711[18]	Dasiglucagon 0.6 mg (n=34)	97	<0.01	94	<0.01	88	<0.01	62	<0.01
	Placebo (n=10)	50		10		0		0	
NCT03667053[21]	Dasiglucagon 0.6 mg (n=20)	100	0.007	100	<0.001	95	<0.001	65	<0.001
	Placebo (n=11)	55		18		0		0	
	Glucagon 0.5mg or 1mg (n=10)	100	—-	100	—-	100	—-	60	—-

sidered not recovered if they needed IV glucose or recovery did not occur within 45 minutes.[18] The median time to plasma glucose recovery was statistically shorter for dasiglucagon (10 minutes) compared with placebo (35 minutes) ($P < 0.001$).[18] An analysis using linear interpolation was also conducted to determine the true time to plasma glucose recovery. The median true time to plasma glucose recovery was 9.3 minutes with dasiglucagon versus 32.0 minutes with placebo ($P < 0.001$).[18]

The secondary end points were achieving plasma glucose recovery within 30, 20, 15, and 10 minutes.[18] The proportion of participants who achieved plasma glucose recovery were as follows: in 30 minutes, 97% in the dasiglucagon group (compared to 50% in placebo group); in 20 minutes, 94% in the dasiglucagon group (compared to 10% in placebo group); in 15 minutes, 88% in the dasiglucagon group (compared to 0% in placebo group); and in 10 minutes, 62% in the dasiglucagon group (compared to 0% in placebo group).[18] For each of the four time points, statistical significance was met ($P < 0.01$).[18]

The authors concluded that a single 0.6 mg dose of dasiglucagon in an autoinjector device provided quick and effective hypoglycemia reversal in adults with type 1 diabetes. The safety and tolerability were similar to the safety and tolerability of reconstituted glucagon.

NCT036667053 Battelino et al.[21]

A phase 3, multicenter, randomized, double-blind, parallel-group, placebo-controlled trial focused on assessing the safety and efficacy of dasiglucagon in children and adolescents with type 1 diabetes mellitus who use insulin.[21] The primary objective was time to plasma glucose recovery compared to placebo. Recovery was defined as an increase of ≥ 20 mg/dL from baseline without rescue intravenous glucose given.[21] The trial was conducted in an inpatient setting at five sites in Germany, Slovenia, and the United States. A total of 41 participants were included in the study. Inclusion criteria included age of 6 to 17 years old, diagnosis of type 1 diabetes for at least one year, using daily insulin, and weight of ≥ 20 kg.[21] Participants were excluded if they had a presence or history of pheochromocytoma or insulinoma, past hypoglycemic events with seizures, hypoglycemia unawareness in the last year, severe hypoglycemia in the last month, or use of any of the following medications in the 28 days prior to screening: beta blockers, indomethacin, warfarin, anticholinergic medications, or medications that cause QT prolongation.[21]

Participants were randomized into one of three treatment arms using a 2:1:1 ratio to receive either 0.6 mg dasiglucagon subcutaneously (n = 20), placebo (n = 11), or GlucaGen®, a reconstituted glucagon (n = 10) dosed by body weight (1 mg if ≥ 25 kg; 0.5 mg if < 25 kg).[21] Glucagon was included only as a reference. The participants' insulin therapies were stopped prior to treatment, and participants fasted starting at 10 pm the night before dosing. Intravenous insulin glulisine was administered using an unspecified dose and infusion rate chosen by the investigators to achieve a controlled decline in plasma glucose. The insulin infusion was stopped once a target plasma glucose level of < 80 mg/dL was reached. After five minutes, if the participant's glucose concentration was ≥ 54 mg/dL and < 80 mg/dL, the treatment or placebo was administered.[21]

The primary end point was time to plasma glucose recovery, which was defined as an increase of ≥ 20 mg/dL from baseline without IV glucose rescue needed.[21] Recovery needed to occur within 45 minutes. The median time to plasma glucose recovery was 10 minutes with dasiglucagon versus 30 minutes with placebo ($P < 0.001$), and 10 minutes with reconstituted glucagon.[21] An analysis using linear interpolation was also conducted to determine the true time to plasma glucose recovery, when an exact 20 mg/dL increase in plasma glucose occurred. The median true time to plasma glucose recovery was 8.7 minutes with dasiglucagon versus 29.3 minutes with placebo, and 9.8 minutes with reconstituted glucagon.[21] No p value was included for true time to plasma glucose recovery, so it is unknown if this was statistically significant. The median time to plasma glucose recovery was statistically significantly shorter for dasiglucagon versus placebo, with recovery time in children closely matching recovery time seen in adults in other studies.[12,18,21]

The secondary end points were achieving plasma glucose recovery within 30, 20, 15, and 10 minutes.[21] The proportion of participants who achieved plasma glucose recovery were as follows: in 30 minutes, 100% in the dasiglucagon group (compared to 55% in placebo group and 100% in the glucagon group); in 20 minutes, 100% in the dasiglucagon group (compared to 18% in placebo group and 100% in the glucagon group); in 15 minutes, 95% in the dasiglucagon group (compared to 0% in placebo group and 100% in the glucagon group); and in 10 minutes, 65% in the dasiglucagon group (compared to 0% in placebo group and 60% in the glucagon group).[21] For each of the four time points, statistical significance was met for dasiglucagon versus placebo ($P < 0.01$).[21] After 30 minutes, the mean plasma glucose increased by 98.2 mg/dL for dasiglucagon, compared to 17.3 mg/dL in the placebo group and 84.4 mg/dL in the reconstituted glucagon group.[21] No p value or statistical significance was tested for comparing dasiglucagon versus glucagon as glucagon was only included as a reference.[21] The side effects for dasiglucagon treatment were similar to glucagon treatment, with the dasiglucagon group experiencing more events.

Table 4 | Common Adverse Effects with Dasiglucagon[12,18,21]

Adverse Effect	Incidence Rate
Nausea	55-65%
Vomiting	23-50%
Hypoglycemia	10-18%
Headache	10-12%
Injection site reaction	0-1%

Adverse Effects

Adverse effects observed in trial participants were similar among all three studies. The most common adverse effects seen with dasiglucagon include nausea, vomiting, headache, injection site erythema or pain, diarrhea, and hypoglycemia.[12,18,21] These adverse events are summarized in **Table 4**. No serious adverse events occurred in any of the three trials.

Safety & Contraindications

Dasiglucagon is contraindicated in patients with a pheochromocytoma (adrenal gland tumor), as this type of tumor may stimulate the release of catecholamines from the liver and cause large increases in blood pressure.[15] This medication is also contraindicated in patients with an insulinoma (pancreatic tumor) because of the risk of hypoglycemia.[15] A randomized, double-blind, placebo-controlled study found that dasiglucagon does not cause clinically relevant QTc prolongation in drug plasma concentrations up to five times higher than plasma concentrations seen using the approved 0.6 mg dose.[20]

A few important drug-drug interactions exist with dasiglucagon. Dasiglucagon may interact with beta-blockers, causing transient increases in pulse or blood pressure.[15] Dasiglucagon may lose its ability to raise blood glucose, or may cause hypoglycemia when given concomitantly with indomethacin.[15] The anticoagulant effect of warfarin can be potentiated by concomitant dasiglucagon, which may increase the risk of bleeding.[15] It is recommended to use caution with concomitant use of dasiglucagon and these medications, but patients do not need to avoid dasiglucagon; the dasiglucagon dose is for single use only and is used only during rare severe hypoglycemic events, limiting the effect of potential interactions.[19]

Dosage, Administration, & Cost

Dasiglucagon in only available as a brand name medication, Zegalogue®, as either a 0.6 mg/0.6 mL single-dose autoinjector or as a 0.6 mg/0.6 mL single-dose prefilled syringe.[15] The subcutaneous solution is approximately $335 for a supply of 0.6 mL.22 Zealand currently offers a Zegalogue Injection Co-Pay Savings Card, and eligible commercially-insured patients may pay as low as $25 for two doses.[23] All patients receive the same 0.6 mg dose, with no adjustments being needed for age, renal or hepatic impairment, or other characteristics. The maximum dose of dasiglucagon is 1.2 mg, as a second 0.6 mg dose may be given 15 minutes after the first dose provided that the first dose produced no response.[15]

Caregivers, family, and friends should be trained along with patients on how to use dasiglucagon. This medication can be injected in the outer upper arms, lower abdomen 2 inches away from the belly button, front or back of thighs, or buttocks. It must be injected onto bare skin and not through clothes. To administer the autoinjector, remove the cap, push and hold down the autoinjector for 10 seconds, and check that the medicine window turned red to indicate the full dose was given.[15] The device can now be removed from the injection site, and emergency medical help should be called. The patient should be rolled onto their side and monitored closely after dasiglucagon administration. Zegalogue® has a 3-year expiration from the date of manufacture and may be stored in a refrigerator.[15] Once removed from refrigeration, it may be stored at room temperature for 12 months unless it expires prior to that time.[15]

Special Populations

Pregnancy & Breastfeeding

There is no human data on the effect of dasiglucagon in pregnancy or breastfeeding.[15] However, dasiglucagon is a large protein molecule, and the amount of medication in breastmilk is likely very low and unlikely to cause harm to an infant.[24] There is currently no data in infants or children less than 6 years old.[15] In animal studies, no fetal developmental effects were observed at doses corresponding to seven times the human dose.[15]

Renal & Hepatic Impairment

No dose adjustments are needed in either renal or hepatic impairment.[15] However, dasiglucagon works to treat hypoglycemia by using hepatic glycogen stores. In patients with decreased hepatic glycogen, dasiglucagon will not be as effective.[15] Low glycogen stores may occur in patients in a state of starvation, with adrenal insufficiency or chronic hypoglycemia; these patients should be treated with glucose instead.[15]

Clinical Implications

The American Diabetes Association recommends that glucagon should be prescribed for patients at risk of level 2 or level 3 hypoglycemia.[9] In practice, all diabetes mellitus patients are at risk for hypoglycemia, and should have glucagon available if needed.[9] In one study, 94% of trained caregivers were able to administer a dasiglucagon autoinjector successfully within 15 minutes, compared with only 56% of caregivers for the glucagon emergency kit.[25] The speed of medication administration is critical for a quick recovery from a severe hypoglycemic event. This discrepancy in successful administration may show that dasiglucagon will have an important place in therapy in the treatment of hypoglycemia.

In a health economic model study, dasiglucagon was predicted to decrease total direct medical costs compared to injectable glucagon and nasal glucagon. In a model covering 1 million patients, estimated annual treatment costs for dasiglucagon were $13.4 million, while the cost for injectable native glucagon was $16.7 million, nasal glucagon was $20.7 million, and reconstituted glucagon was $35.3 million.[26] Both treatment costs and healthcare utilization costs were decreased with dasiglucagon compared to glucagon preparations.[26]

Some limitations of the studies used for FDA approval of dasiglucagon include focusing on type 1 diabetes. No participants were included with type 2 diabetes or gestational diabetes so clinical applicability is decreased. For safety purposes, low blood glucose targets in the studies were higher than what a patient's low blood glucose level may actually reach. While dasiglucagon is efficacious, its real-world effectiveness may be different. Plasma glucose recovery time between dasiglucagon and glucagon were very similar in the trials, but this does not include reconstitution time for glucagon. Dasiglucagon may achieve plasma glucose recovery even more quickly than glucagon, and more studies will be needed to see how the medication performs now that it is approved for use. Lastly, the FDA approval is based on treating blood glucose levels and not symptoms, whereas in practice, patients often realize they are experiencing a hypoglycemic event due to symptoms. This factor may impact effectiveness in real-world hypoglycemic events.

Conclusion

Dasiglucagon is a glucagon receptor agonist that has been shown to be both safe and effective in treating severe hypoglycemia. As a first-in-class aqueous glucagon analog, dasiglucagon improves administration time and storage constraints seen with other medication formulations. Doctors should review the various options available for patients and decide with each patient what option would work best, considering the patient's comfort with different formulations, side effects, and caregiver capabilities to administer medications.

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Drug Update:
New Indications and Dosage Forms
October 2022

Imjudo® (tremelimumab) Intravenous Injection
New Molecular Entity: cytotoxic T-lymphocyte-associated antigen (CTLA-4) blocking antibody indicated for treatment of adults with hepatocellular carcinoma

Tecvayli® (teclistamab-cqyv) Injection
New Molecular Entity: bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for treatment of relapsed or refractory multiple myeloma in adults who have failed at least four prior lines of therapy

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