

## Brief Therapeutics Update from PES Drugs and Therapeutics Committee

### New Ready-to-Use Glucagon Preparation: Zegalogue

Zegalogue (dasiglucagon) is a ready-to-use injectable glucagon preparation approved in 2021 for treatment of severe hypoglycemia in adults and children over 6 years with diabetes mellitus. Both Zegalogue and Gvoke are ready-to-use glucagon preparations for injection that do not require reconstitution and are stable in solution. Baqsimi is another FDA-approved, ready-to-use glucagon product that is administered as a dry powder intranasally [1]. Zegalogue comes as a 0.6 mg/0.6 mL autoinjector or pre-filled syringe. Zegalogue is manufactured by Zealand Pharma and supplied in one- or two-dose packs. The recommended dose is 0.6 mg administered subcutaneously. If no response is observed after 15 minutes, a second 0.6-mg dose from a new device may be administered [2].

Dasiglucagon is a glucagon analog that has seven amino acid substitutions compared with endogenous glucagon that increase stability in aqueous solution. [3]. In a randomized, double-blind study of adults with type 1 diabetes, dasiglucagon exhibited peak plasma concentrations at 35 minutes, increased plasma glucose to  $\geq 70$  mg/dL within 6-10 minutes, and had a longer-lasting and greater effect on plasma glucose when compared to reconstituted glucagon. Specifically, there was a statistically significant increase in glycemic response over 6 hours at all doses of dasiglucagon when compared to glucagon. This could reduce recurrence of hypoglycemia, but requires further investigation for clinical relevance. Overall, both treatments reached goal endpoints within 30 minutes [4]. Another randomized trial in adults demonstrated that dasiglucagon 0.6 mg performed similarly to reconstituted glucagon 1 mg with 99% and 95% plasma glucose recovery within 15 minutes, respectively, for the two preparations [3].

Zegalogue was also studied in pediatric patients with diabetes ages 6-17 years in a randomized placebo-controlled trial (Trial C, NCT03667053). It was found to be safe and effective for treatment of severe hypoglycemia in children with diabetes who are at least 6 years of age (n=42). Mean time to plasma glucose recovery was 10 minutes, which is similar to reconstituted glucagon formulations [2, 5]. Common side effects included nausea, vomiting, headache, and pain at the injection site. Refrigeration allows use through the expiration date and, if stored at 68-77°F (room temperature), Zegalogue can be used for up to 12 months [2].

Glucagon has a well-established history of use in children and adults with diabetes complicated by insulin-induced hypoglycemia. The evolution of formulations to include ready-to-use medications promotes safe, effective, simplified and rapid intervention for all caregivers during a hypoglycemic emergency. Stability at room temperature also allows for use and storage across multiple environments. Further, this may allow for evolving indications beyond emergency use, such as progress in the development of the dual-hormone artificial pancreas system and treatment of children with congenital hyperinsulinism [6, 7].

#### References:

1. <https://pedsendo.org/wp-content/uploads/2020/08/Glucagon.pdf>
2. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2021/214231s0001bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214231s0001bl.pdf)
3. Pieber TR, et al. Dasiglucagon: A Next-Generation Glucagon Analog for Rapid and Effective Treatment of Severe Hypoglycemia Results of Phase 3 Randomized Double-Blind Clinical Trial. *Diabetes Care*. Apr 2021, dc202995; DOI: 10.2337/DC20-2995
4. Hövelmann U, et al. Pharmacokinetic and Pharmacodynamic Characteristics of Dasiglucagon, a Novel Soluble and Stable Glucagon Analog. *Diabetes Care*. Mar 2018, 41 (3) 531-537; DOI: 10.2337/dc17-1402

5. Battelino, T, et al. Dasiglucagon, a next-generation ready-to-use glucagon analog, for treatment of severe hypoglycemia in children and adolescents with type 1 diabetes: Results of a phase 3, randomized controlled trial. *Pediatr Diabetes*. 2021; 22( 5): 734– 741.  
<https://doi.org/10.1111/pedi.13220>
6. Hawkes CP, et al. Novel Preparations of Glucagon for the Prevention and Treatment of Hypoglycemia. *Curr Diab Rep*. 2019 Sep 6;19(10):97. doi: 10.1007/s11892-019-1216-4. PMID: 31493043; PMCID: PMC6951434.
7. Xu B et al. Dasiglucagon: an effective medicine for severe hypoglycemia. *Eur J Clin Pharmacol*. 2021 Jul 5. doi: 10.1007/s00228-021-03183-0. Epub ahead of print. PMID: 34223944

*Prepared on behalf of the PES Drugs and Therapeutics Committee by*  
Kristal Matlock, MD, Dania Al-Hamad, MD, Vandana Raman, MD and Amit Lahoti, MD