Budget impact model for dasiglucagon in the prevention and treatment of hypoglycemia in pediatric patients with congenital hyperinsulinism in the United States

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INTRODUCTION

- CHI is an ultra-rare disease impacting approximately 1:25,000–50,000 newborns (1, 2).
- Unregulated insulin secretion causes hypoglycemia in infants, with potential consequences including seizures, brain damage, and death (3, 4).
- Medical interventions include continuous glucose infusions, diazoxide, somatostatins, and surgery (4-7).
- Diazoxide, the only approved treatment for hyperinsulinism-induced hypoglycemia, is ineffective in up to 60% of cases, necessitating the off-label use of other medications, including somatostatins (8).
- Surgical interventions pose risks, including potential long-term consequences, such as insulin-dependent diabetes.
- Dasiglucagon, an anti-hypoglycemic agent, is currently being investigated as a potential CHI treatment by Zealand Pharma.
- No CHI-specific US economic analyses or treatment sequencing algorithms have been previously published.

OBJECTIVES

- To develop the first known US-specific budget impact model (BIM) for congenital hyperinsulinism (CHI), aiming to assess the financial implications of current and future CHI treatments.
- To assess how the introduction of dasiglucagon for CHI affects treatment variances and subsequent shifts in healthcare resource utilization.

ABBREVIATIONS
AE, adverse event; BIM, budget impact model; CHI, congenital hyperinsulinism; FDA, Food & Drug Administration; mTOR, mammalian target of rapamycin.

DISCLOSURES
Dasiglucagon is under review with the US Food & Drug Administration (FDA). The poster will be presented prior to regulatory approval, and therefore, we cannot claim first- or second-line treatment as per label.

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METHODS

A 5-year BIM was created from a US commercial perspective, assessing CHI newborns and children up to 18 years of age.

A targeted literature review was conducted to inform the clinical inputs, pharmacy, medical, surgical, and adverse event (AE) costs used in the model.

The model's framework is founded on a generic patient pathway. While CHI is treated on an individualized patient level, the creation of a generic pathway was necessary to establish a standardized pathway for use within the BIM.

The current patient pathway was developed by incorporating clinical guidelines and US clinical expert opinions (Figure 1). Subsequently, it underwent adjustments to illustrate the potential outcomes of employing dasiglucagon as either a first- or second-line treatment, as depicted in the model structure.

Currently, diazoxide serves as the primary treatment for patients with suspected CHI. However, considering if dasiglucagon is approved as a first-line option allows patients to receive either dasiglucagon or diazoxide until genetic test results are available. If patients discontinue dasiglucagon or do not respond to diazoxide, they will switch to an alternative second-line treatment.

For patients with diagnosed focal disease, treatment with dasiglucagon or diazoxide continues until a lesionectomy. If the surgery resolves hypoglycemia, no further treatment is needed; if not, they will either continue first-line treatment or may have another lesionectomy.

Patients with diffuse disease responding to dasiglucagon (or diazoxide) continue treatment. If hypoglycemia persists, they will try another medical therapy; if unsuccessful, partial or subtotal pancreatectomy is considered.

RESULTS

The BIM predicts that the introduction of dasiglucagon will lower medical costs by reducing hospitalization, surgery, AE management, and insulin-requiring diabetes (Figure 2 and Figure 3).

Hospitalization costs

Newborns incur hospitalization costs for first- and second-line treatments. Those on first- line treatment stay for monitoring and genetic testing. If not responsive to or discontinuing treatment, patients remain in hospital for initiation of alternative treatments.

Dasiglucagon as a potential first-line treatment lowers the need for second-line treatment. This is because the model predicts that a greater proportion of patients will continue with dasiglucagon when administered as the initial treatment, compared with if diazoxide were used first. Consequently, hospitalization costs are reduced.

When dasiglucagon is second-line treatment, diazoxide is the first-line treatment for all patients. Consequently, there is no change in the proportion of patients requiring second-line treatment in hospital, and thus no further reduction in hospitalization costs. Once dasiglucagon is introduced, the expectation is that fewer patients will proceed to third-line therapy and eventually pancreatectomy.

Surgery costs

Surgery involves lesionectomy and pancreatectomy for focal and diffuse patients,respectively.

As the model assumes all newborns with focal disease undergo lesionectomy, lesionectomy surgery costs remain unchanged with or without dasiglucagon as a first- or second-line treatment.

Diffuse patients undergo a pancreatectomy after multiple treatment failures. The model predicts the majority of patients using dasiglucagon will not require an alternative treatment, ultimately reducing the number of pancreatectomies and their associated costs.

Management of insulin-requiring diabetes costs

The BIM also considers the incidence of insulin-requiring diabetes that occurs within 1 year post-pancreatectomy.

As dasiglucagon reduces the need for pancreatectomy, fewer patients develop insulin-requring diabetes, therefore lowering associated management costs.

AE costs

Treating more patients with dasiglucagon, especially as a first-line option, significantly reduces the costs associated with managing AEs.

Treating patients with dasiglucagon can reduce patients experiencing costly AEs, such as pulmonary hypertension, neutropenia, and hypertrichosis with diazoxide.

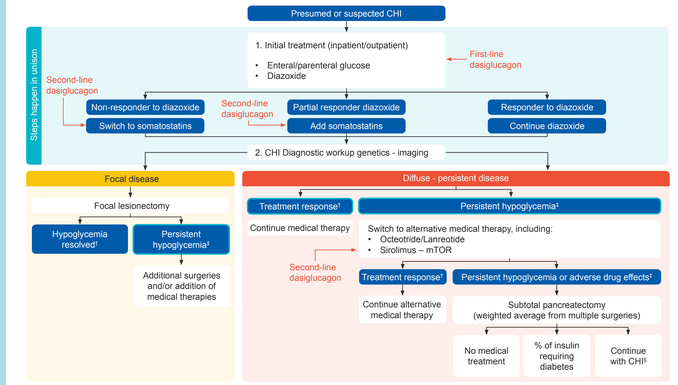

Figure 1: Current simplified treatment pathway for CHI patients
† responders; ‡ non-responder; § medical therapy to maintain CHI

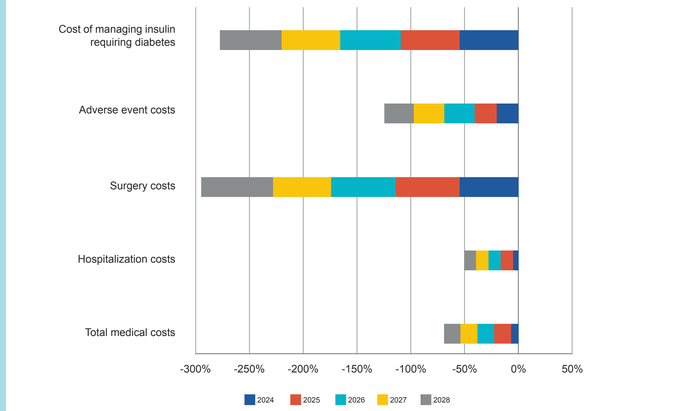

Figure 2: The proportional change in costs between the scenario with and the scenario without dasiglucagon in first-line

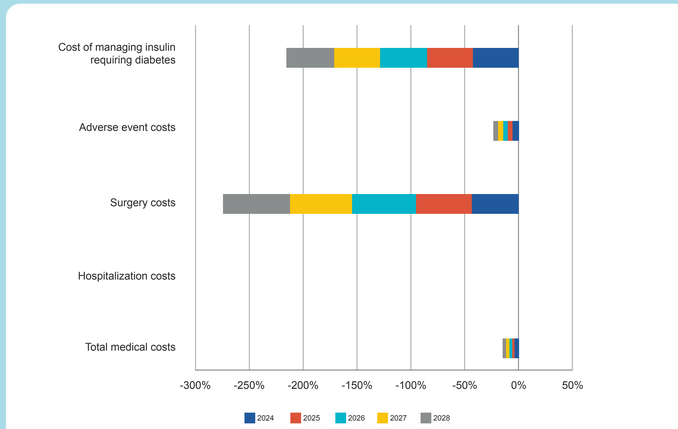

Figure 3: The proportional change in costs between the scenario with and the scenario without dasiglucagon in second-line

CONCLUSIONS

The introduction of dasiglucagon may lead to improved patient treatment response. This BIM predicts a reduced need for subsequent treatment.

The model predicts that introducing dasiglucagon as a first- or second-line treatment reduces the need for additional medical or surgical interventions, lowering the risk of long- term consequences and their associated costs.

The greatest cost reduction occurred when dasiglucagon was used as a first-line treatment, compared with second-line.

The BIM's strengths lie in its *de novo* design, which includes a novel treatment sequencing algorithm, clinical data, costs, and published literature, whilst accommodating uncertainty through sensitivity and scenario analyses.

While the BIM does not account for the potential enhanced glycemic control of dasiglucagon, it is anticipated that dasiglucagon will expedite hospital discharge and reduce resource utilization.

The generic pathway does not consider concomitant use of dasiglucagon and diazoxide which may be used in future clinical practice

Future cost-effectiveness analyses should encompass the broader long-term benefits of dasiglucagon, including potential avoidance of neurodevelopmental damage, exocrine pancreatic insufficiency, and the incidence of insulin-requiring diabetes that may occur years after pancreatectomy.

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