



CALIFORNIA TECHNOLOGY ASSESSMENT FORUMSM

Insulin Degludec (Tresiba[®]) for the Management of Diabetes: Effectiveness, Value, and Value-Based Price Benchmarks

Draft Background and Scope

October 13, 2015

Background:

The Centers for Disease Control and Prevention (CDC) estimates that 29.1 million Americans have diabetes and 1.7 million adults are newly diagnosed with diabetes mellitus (DM) each year.¹ The majority of the population with diabetes (~95%) have type 2 diabetes, which is characterized by resistance of tissues in the body to the effects of insulin. The remaining 5% of patients have type 1 diabetes in which the body's immune system destroys the cells in the pancreas that produce insulin and is characterized by very low levels of insulin production. The direct medical costs of diabetes were estimated to be \$176 billion in 2012.¹ Diabetes is characterized by elevated blood glucose, which over time leads to premature heart disease, strokes, blindness, and kidney failure. Approximately 6 million Americans use insulin therapy as part of their treatment plan to control their blood glucose level.¹ Insulin degludec (Tresiba[®]) is a new, ultralong-acting insulin for use in both Type 1 and Type 2 DM.

Report Aim:

This project will evaluate the health and economic outcomes of insulin degludec (Tresiba) and the combination of insulin degludec and insulin aspart (Ryzodeg[®]).

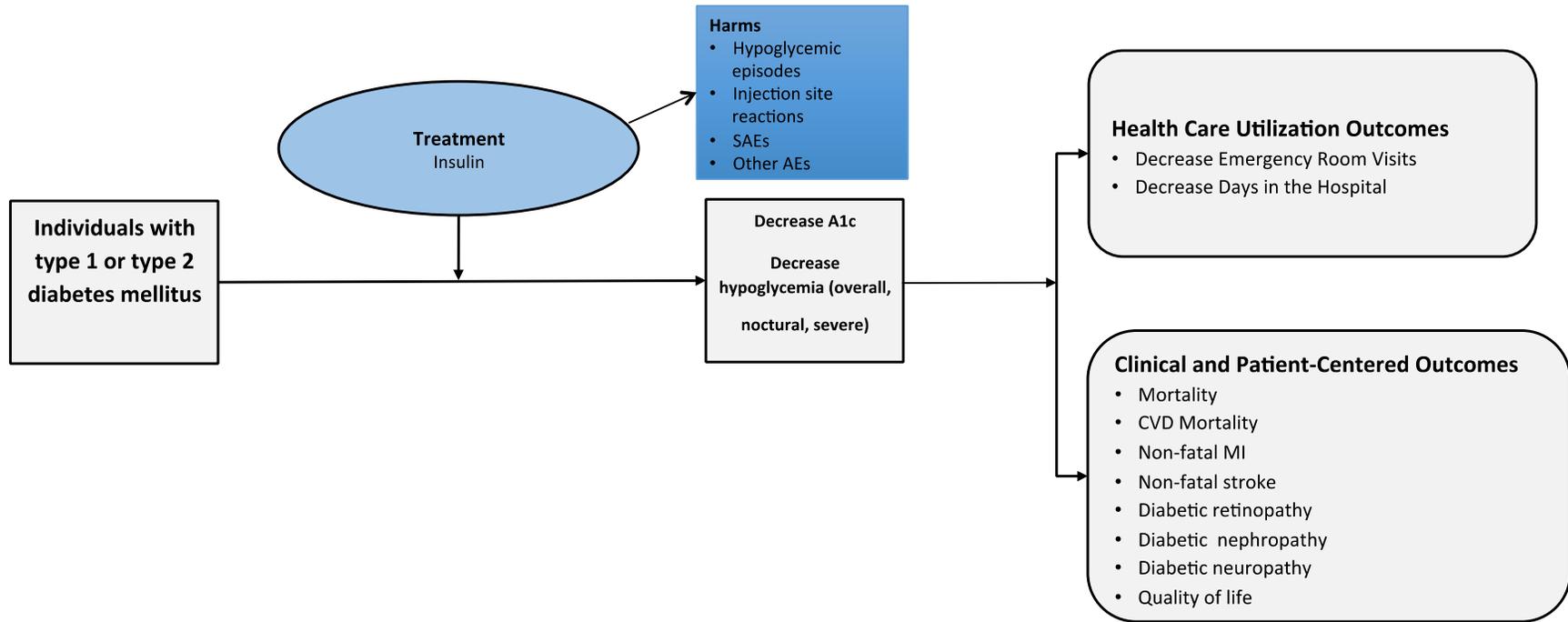
Scope of the Assessment:

The proposed scope for these assessments is described below using the PICOTS (Population, Intervention, Comparators, Outcomes, Timing, and Settings) framework. Evidence will be culled from Phase II or III randomized controlled trials and comparative cohort studies as well as high-quality systematic reviews where available. We will also include case series that meet certain quality criteria (e.g., sample retention, consecutive patients, clearly-defined entry criteria). The majority of the pivotal randomized trials submitted for FDA approval of insulin degludec use a non-inferiority design compared to available insulin therapy. Both arms of the trials adjust insulin dosing to achieve pre-breakfast blood glucose levels of 70-90 mg/dL and to have equivalent hemoglobin A1c levels.

Analytic Framework:

The analytic framework for this assessment is depicted in Figure 1 on the following page.

Figure 1. Analytic Framework: Diabetes Management with Insulin



Note: SAEs: severe adverse effects; AEs: adverse effects; MI: myocardial infarction

Populations

The population of focus for the reviews of both interventions will include adults ages 18 years and older with type 1 or type 2 DM. We will consider type 1 and type 2 DM as separate populations. Within the population of individuals with type 2 DM, we will consider patients starting on insulin for the first time separately from patients already on insulin therapy.

Interventions

The interventions of interest will be insulin degludec (Tresiba) and the combination insulin degludec/aspart (Ryzodeg).

Comparators

The primary comparator will be long-acting insulins (i.e., insulin glargine, insulin detemir) and combinations of long-acting and short-acting insulins.

Outcomes

This review will examine clinical and health care utilization outcomes related to both interventions. Listed below are the outcomes of interest:

- Macrovascular outcomes (myocardial infarction, stroke, death from cardiovascular disease)
- Microvascular outcomes (retinopathy, nephropathy, neuropathy)
- DM-related hospitalizations and emergency room visits
- Hypoglycemic events (overall, nocturnal, and severe)
- Hemoglobin A1c as a measure of glycemic control
- Measures of functional status, and/or health-related quality of life
- Short- and long-term complications and adverse events of treatment
- Costs and cost-effectiveness of insulin degludec and insulin degludec/insulin aspart

Timing

Evidence on intervention effectiveness and harms will be derived from studies of any duration.

Settings

All relevant settings will be considered, including inpatient, clinic, and outpatient settings.

Simulation Models:

We will develop simulation models to assess the cost-effectiveness of insulin degludec relative to other long-acting insulins and insulin degludec/insulin aspart relative to other combinations of long-acting insulin with a short-acting insulin. Separate analyses will be conducted for patients with Type 1 and Type 2 DM. Because the major trials of insulin degludec with or without insulin aspart utilized non-inferiority designs, comparisons of glycemic control and corresponding extrapolations to downstream clinical events (e.g., micro- and macrovascular complications) would not be appropriate in this setting. The model will therefore focus on the avoidance of hypoglycemic episodes and other adverse events, along with associated costs (e.g., emergency room visits and/or hospitalizations) and corresponding reductions in health-related quality of life. The time horizon will be limited to 5 years, as the adverse events of interest

would likely be observed relatively quickly after treatment initiation. Results will be expressed primarily in terms of the cost per quality-adjusted life year (QALY) gained.

We will also assess the budgetary impact of insulin degludec and insulin degludec/insulin aspart over a 5-year time horizon, utilizing information on treatment costs and cost offsets from reduced rates of adverse events. Budgetary impact analyses will assume a specific product “uptake” rate over the 5-year period. Finally, we will develop a “value-based price benchmark” for both insulin degludec and insulin degludec/insulin aspart in each of the populations of interest; this benchmark represents a “policy trigger” for managing the cost of new interventions with a budgetary impact that exceeds the level of growth in the overall US economy.

More information on ICER’s methods for estimating product uptake and calculating value-based price benchmarks can be found at: <http://www.icer-review.org/wp-content/uploads/2014/01/Slides-on-value-framework-for-national-webinar1.pdf>.

References:

1. Centers for Disease Control and Prevention. *National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014*. 2014.