CALIFORNIA TECHNOLOGY ASSESSMENT FORUM℠

Insulin degludec (Tresiba) for the Management of Diabetes: Effectiveness, Value, and Value-Based Price Benchmarks

Final Background and Scope

November 19, 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%) has 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, in concert with other risk factors such as hypertension and hyperlipidemia, contributes to long-term adverse health outcomes such as 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).

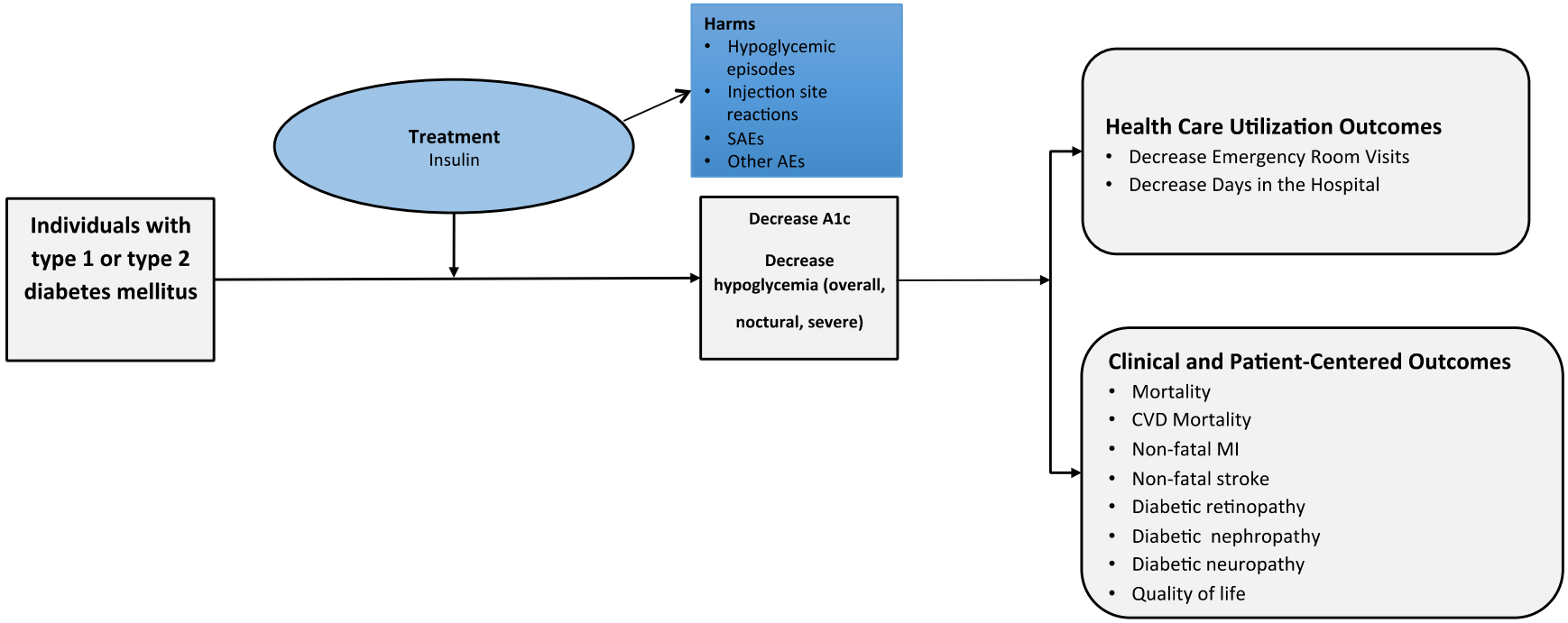
Scope of the Assessments:

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 and meta-analyses where available. We will also include real world observational data 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 Frameworks:

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

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 intervention of interest will be insulin degludec (Tresiba).

Comparators

The primary comparator will be long-acting insulin analogues (i.e., insulin glargine, insulin detemir).

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
- Other clinical parameters (e.g., weight, blood pressure, lipids)
- 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

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 use a validated and published simulation model, the UKPDS Outcomes Model version 2 (UKPDS OMv2)[2] to assess the cost-effectiveness of insulin degludec relative to other long-acting insulins. Separate analyses will be conducted for patients with type 1 DM and type 2 DM. Because the major trials of insulin degludec utilized non-inferiority designs, comparisons of glycemic control and corresponding extrapolations to downstream clinical events (e.g., micro- and macrovascular complications) will not be the primary focus of this analysis, although estimates of these outcomes will be produced using the UKPDS risk equations and the profile of patients enrolled in the clinical trials of insulin degludec. Primary analyses will 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. Sensitivity analyses will be considered in which point estimates for insulin degludec and its comparators are used for measures of effectiveness and safety. The time horizon will be

lifetime. 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 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 insulin degludec 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.
2. Hayes AJ, Leal J, Gray AM, Holman RR, Clarke PM. UKPDS outcomes model 2: a new version of a model to simulate lifetime health outcomes of patients with type 2 diabetes mellitus using data from the 30 year United Kingdom Prospective Diabetes Study: UKPDS 82. *Diabetologia.* 2013;56(9):1925-1933.