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

Final Background and Scope

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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

- **Individuals with type 1 or type 2 diabetes mellitus**
- **Treatment Insulin**
- **Decrease A1c**
- **Decrease hypoglycemia (overall, nocturnal, severe)**
- **Harms**
  - Hypoglycemic episodes
  - Injection site reactions
  - SAEs
  - Other AEs

- **Health Care Utilization Outcomes**
  - Decrease Emergency Room Visits
  - Decrease Days in the Hospital

- **Clinical and Patient-Centered Outcomes**
  - Mortality
  - CVD Mortality
  - Non-fatal MI
  - Non-fatal stroke
  - Diabetic retinopathy
  - Diabetic nephropathy
  - Diabetic neuropathy
  - Quality of life

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.

References:
