Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***New Long-Acting Basal Insulins***
-August 2017-

Background:

In August 2017, the Indian Health Service (IHS) National Pharmacy & Therapeutics Committee (NPTC) reviewed two newer, long-acting basal insulin therapies for the management of Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) and evaluated their safety, efficacy and utilization within the agency. The NPTC last reviewed novel insulin delivery devices (including basal insulins) in August 2015 which resulted in the addition of pen devices to National Core Formulary (NCF) insulin products. *Current insulins on the NCF include insulin aspart (NovoLog®), regular insulin (NovoLIN®), insulin NPH (NovoLIN® N), insulin detemir (Levemir®), and the combination products insulin aspart / insulin aspart protamine (NovoLog® 70/30 Mix) and insulin NPH / regular insulin (NovoLIN 70/30®)*. The 2017 NPTC review included the subcutaneous insulin products insulin degludec (Tresiba®) and insulin glargine (Basaglar®). Based on the NPTC review and committee discussion, **no modifications were made to the NCF**.

Discussion:

Insulin therapy is the most effective treatment for lowering blood glucose for patients with type 2 diabetes mellitus (T2DM) and is the only treatment option for patients with type 1 diabetes mellitus (T1DM).[1-3] The 2017 guidelines from the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) recommend starting insulin therapy with a basal insulin but offer no recommendations as to the selection of a specific insulin product upon initiation.[2,3] The AACE recommends basal insulin analogs over neutral protamine Hagedorn (NPH) due to concerns for increased risk of hypoglycemia with NPH.[3]

In 2015, the FDA approved the ultra-long-acting insulin, Tresiba® (insulin degludec) in both 100 units/mL and 200 units/mL concentrations.[4] The efficacy and safety of Tresiba® was studied in a series of open-labeled, randomized controlled trials that were designed to test for non-inferiority of Tresiba® versus insulin glargine or insulin detemir.[5-11] The primary endpoint for each study was percent change in hemoglobin A1c from baseline, and secondary endpoints included reduction in fasting blood glucose (FBG) and achievement of an A1c less than 7%. The studies also observed episodes of hypoglycemia, including overall hypoglycemia and nocturnal hypoglycemia. Three studies were conducted in patients with T1DM, and four studies were conducted in patients with T2DM.

In terms of efficacy, all seven studies demonstrated non-inferiority between Tresiba® and insulin glargine or insulin detemir in reduction of A1c and FBG.[4-11] The primary safety endpoint, overall episodes of hypoglycemia, was not significantly different, however four studies did report a statistically significant benefit with Tresiba® in episodes of nocturnal hypoglycemia. Despite absolute risk reductions (favoring Tresiba®) ranging from 0.1% to 7% in multiple studies[5,7-9], the impact in improved patient safety is not likely to be deemed clinically significant.

Current data regarding the use of Tresiba® has focused primarily on benefits in terms of the efficacy and safety surrounding blood glucose management. The DEVOTE trial was a double-blinded, treat-to-target study of cardiovascular outcomes comparing Tresiba® to insulin glargine. The primary composite outcome included major cardiovascular events (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) in patients with T2DM at high risk for cardiovascular events. Tresiba® was shown to be non-inferior to insulin glargine in the incidence of major cardiovascular events (HR, 0.91; 95% confidence interval, 0.78 to 1.06; $p<0.001$ for non-inferiority).[12]

In 2015, the FDA approved the long-acting insulin analog, Basaglar® (insulin glargine) as a “follow-on” product.[13] Studies of Basaglar® demonstrated non-inferiority to insulin glargine (Lantus®) in A1c reduction, adverse events, allergic reactions, weight change, hypoglycemia and insulin antibodies in patients with T1DM and T2DM.[14,15]

Findings:

Insulin detemir is the most commonly prescribed basal insulin within IHS, representing approximately 76% of all prescribed long-acting basal insulins over the past 24 months. Currently, there is limited data comparing the efficacy of Tresiba® and Basaglar® beyond A1c reduction. Additionally, the majority of studies have targeted non-inferiority to the parent products and appear to offer little, if any, appreciable safety benefit over established products. Based on the available data, neither product demonstrated significant advantages over NCF insulins in terms of patient-specific clinical factors or cost-effectiveness to the IHS.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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