Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Novel Insulin Delivery Devices***
-August 2015-

Background:
In August 2015, the Indian Health Service (IHS) National Pharmacy and Therapeutic Committee (NPTC) reviewed novel insulin therapies in the treatment of Type 2 Diabetes Mellitus (T2DM), evaluating the safety and efficacy of insulin and its utilization within the agency. This class of medications was last reviewed in 2010 when insulin detemir, insulin aspart, NPH, regular insulin and insulin aspart protamine and insulin aspart (70/30) mix were added to the National Core Formulary (NCF). The 2015 review included subcutaneous insulin products (human and analog), inhaled insulin (Afrezza®) and a transdermal insulin delivery device (V-Go®). The discussion resulted in **retaining the current NCF insulin products** and the **addition of insulin pen devices** for insulin detemir (Levemir®), insulin aspart (NovoLog®) and insulin aspart protamine and insulin aspart (NovoLog® 70/30 Mix).

Discussion:
Insulin therapy remains the most effective treatment for lowering blood glucose (decreases HbA1c 1.5%-3.5%) and as beta cell function declines, many diabetic patients eventually require insulin treatment to reach and maintain their glycemic goals[1-4]. According to 2015 guidelines from the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE), when starting insulin therapy in T2DM, a basal insulin should be initiated first then either a bolus (rapid-acting) or glucagon-like peptide-1 receptor agonists should be added for prandial glucose reduction if needed[3,4]. No preferential recommendations are given on which basal or rapid-acting insulin are given, however, the AACE recommends using basal and prandial analogs over NPH, regular and mixed insulin due to the increased incidence of hypoglyemia[4].

Long-acting insulin analogs are equally efficacious in treating T2DM, however insulin detemir may require twice daily dosing to achieve similar glycemic control[1,5]. Concerns with insulin use often include the incidence of hypoglycemia and weight gain[5]. Long-acting insulin analogs have a similar rate of symptomatic and nocturnal hypoglycemia and these effects are lower than that with NPH[1,5]. Weight gain is more common with insulin glargine than once daily insulin detemir but similar when insulin detemir is given twice daily[1,5].

Despite its proven efficacy, patients are often reluctant to start insulin out of fear of needles, injections or lack of perceived convenience[7-12]. Patient preference is an important factor in adherence to insulin therapy. Utilizing insulin pen devices has been shown to reduce barriers to insulin use and improve adherence[7-12]. Insulin pens have been associated with decreased overall healthcare costs, decreased emergency department and hospitalization rates, decreased physician visits and improved glycemic control[10-15]. Additionally, IHS-specific utilization data illustrate that procurement of pen devices is prevalent across the agency for both basal and bolus insulin pens[16].

In 2014, the FDA approved a second-generation inhaled insulin, Afrezza® Technosphere insulin. Afrezza® is a dry powder, orally inhaled rapid-acting insulin used prior to meals for prandial glucose control[6]. Trials of inhaled insulin (T1DM and T2DM) demonstrated less favorable or non-inferior outcomes to comparator antidiabetic medications[17]. Afrezza® is contraindicated in patients with chronic lung disease (COPD, asthma), active lung cancer and should not be used in patients who are smoking or recently quit smoking (within the last 6 months) [6]. Inhaled insulin was found to lack key clinical advantages and/or cost-effectiveness compared with currently available NCF insulin products.

Studies of the recently-approved, disposable insulin delivery device (V-Go®) were evaluated. Small sample size, drop-out rates and short duration of studies limited the quality and interpretation of most clinical trial results[18]. Significant clinical outcomes in the studies presented were not consistently demonstrated with the V-Go® device.

Findings:
Insulin detemir is the most commonly prescribed insulin within IHS representing 77% of all prescribed long-acting insulin. This review did not identify new literature indicating superiority in any one insulin medication. Utilizing insulin is an important factor in improving glycemic control and patient satisfaction and adherence are improved with insulin pen use showing decreases in overall healthcare costs. Furthermore, studies and subsequent outcomes from the other insulin delivery devices were limited and did not confer cost-effective advantages to the IHS patient population.

Patient characteristics where insulin pen devices may provide benefit over traditional vial and syringes include the following:

- manual/physical dexterity issues
- visual impairment
- extreme age categories (i.e., pediatrics, elderly)
- trypanophobia (fear of needles and injections)
- small insulin dosage requirements
- lack of social acceptance
- poor (prior) adherence to insulin with vials and syringes

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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