INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Ultra-Long Acting Insulins***
-August 2022-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of ultra-long acting insulins. Although the NPTC regularly reviews insulin products and classes, this is the first focused review of the ultra-long acting insulins products, insulin degludec and insulin glargine. Currently, the IHS National Core Formulary includes insulin products from the rapid-acting, short-acting, intermediate-acting and long-acting (or basal) classes, in addition to combination insulin products as well. Following a comprehensive clinical review and analysis, the NPTC **made no modifications** to the IHS National Core Formulary.

Over 37 million Americans are currently diagnosed with diabetes, with roughly 1.5 million being newly diagnosed annually.[1] Diabetes is the 7th leading cause of death in the U.S. and costs the U.S. healthcare system over $327 billion annually in both direct and indirect medical costs.[2,3] American Indians and Alaska Natives are 2.4 times more likely to be diagnosed with diabetes compared to non-Hispanic white populations. Additionally, death and kidney failure due to diabetes are roughly 2 times more likely in this population and cardiovascular disease is 3–8 times higher as well.[2] Treatment goals for diabetes focus on delaying the progression of disease, preventing micro/macrovascular complications, and managing comorbidities such as hypertension and dyslipidemia.[4] Goals such as optimizing a healthy lifestyle including weight loss, exercise, and nutrition are key.[5]

Discussion:

As there are many types of insulin, one factor considered when determining which insulin regimen or specific insulin to use with diabetic patients is duration of action.[4,5] Rapid- and short-acting insulins are useful for covering meal time needs and need to be dosed multiple times daily, whereas intermediate-acting insulins last longer and require less frequent dosing. Basal insulins cover a longer duration of action, typically 24 hours, and require only once or twice daily dosing while providing steady coverage. These basal formulations help to form the backbone of most patient's insulin regimen. However, certain patient factors such as large basal doses or doses that don't last a full 24 hours may be an indication to initiate an ultra-long acting insulin.[4,5]

Ultra-long acting insulins typically last >24 hours and provide less variability in coverage compared to standard basal insulins.[4,5] Insulin glargine U-300 is available in the U.S. and is the ultra-long acting form of insulin glargine U-100.[6] The higher concentration offers an extended half-life and increases the duration of action up to 32 hours compared to U-100's 19 hours. The other ultra-long acting insulin is insulin degludec which is available in U-100 and U-200 concentrations and provides a half-life of 42 hours.

Trade Name (type of insulin)	Manufacturer	Appearance	Initial Onset of Action	Peak Activity	Duration of Action
LONG ACTING					
LANTUS® (insulin glargine U-100)	Sanofi	Clear	4 – 6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Toujeo® (insulin glargine U-300)	Sanofi	Clear	4 – 6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Basaglar® (insulin glargine U-100)	Eli Lilly	Clear	4 – 6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
SEMGLEE™ (insulin glargine U100	Viatris	Clear	4 – 6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Levemir® (insulin detemir)	Novo Nordisk	Clear	1 – 2 hours	2 – 12 hours (mild, varies by dose)	Up to 24 hours (depends on injected dose)
Tresiba® (insulin degludec U-100 or U-200)	Novo Nordisk	Clear	1 – 2 hours	About 12 hours	≥42 hours

**modified chart provided at childrenwithdiabetes.com (Jan 19, 2022)*

Many guidelines support the use of a combination basal/bolus insulin regimen for advanced type 2 diabetes and as a cornerstone of care for type 1 diabetes; however, do not specifically address the use of a preferred ultra-long acting insulin.[4,5] Both the American Association of Clinical Endocrinology and the U.K. National Institute for Health and Care Excellence guidelines promote the use of ultra-long acting insulins to help prolong the duration of action of basal regimens and minimize the risk of nocturnal hypoglycemia.[4]

A series of meta-analyses and systematic reviews have assessed the use of ultra-long acting insulins compared to standard basal insulin regimens. A 2021 systematic review examined the use of ultra-long acting insulins in relation to hypoglycemia and fracture risk for adult patients with type 1 and type 2 diabetes.[7] The review found that use of ultra-long acting insulins demonstrated less risk of hypoglycemia compared to standard basal insulins, specifically a 23% reduction with insulin degludec vs. insulin glargine U-100 (RR 0.77, 95% CI: 0.43 to 1.37) and 68% reduction with insulin glargine U-300 vs. insulin glargine U-100 (RR 0.62, 95% CI: 0.44 to 0.88).[7]

A 2021 systematic review and a 2019 meta-analysis both examined the use of ultra-long acting insulins' effect on A1c, hypoglycemia, and weight gain compared to standard basal regimens.[8,9] The reviews found that ultra-long acting insulins resulted in equivalent A1c reduction among all agents, lower rates of hypoglycemia compared to NPH, lower rates of nocturnal hypoglycemia compared to standard basal insulins, and greater weight gain with degludec compared to insulin detemir.[8,9]

Findings:

Diabetes mellitus disproportionately affects American Indian and Alaska Native populations and requires a treatment plan tailored to address individual patient needs. Ultra-long acting insulins, such as the insulin formulations glargine U-300 and degludec, have been shown to be as safe and effective as other long-acting insulins and may result in less nocturnal hypoglycemia. Use of ultra-long acting insulins should be considered for a subset of insulin-requiring patients who; (1) have current basal insulin regimens that do not provide adequate 24-hour coverage, (2) have erratic work schedules that make insulin administration difficult or inconvenient, (3) require large doses of basal insulin, and/or (4) experience nocturnal hypoglycemia. Currently, there is insufficient evidence to support the addition of ultra-long acting insulins to the IHS National Core Formulary.

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.

References:

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