Basaglar

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Introduction

In December 2015, the U.S. Food and Drug Administration (FDA) approved Basaglar, a 100 units/mL long-acting human insulin analog. Basaglar is the first follow-on biologic insulin approved in the United States; its comparator agent is insulin glargine (Lantus). It is available in a prefilled pen (KwikPen) that can deliver 1–80 units per injection (1).

Indications

Basaglar is indicated to improve glycemic control in adult and pediatric patients with type 1 diabetes and in adults with type 2 diabetes (1).

Limitations of Use

Basaglar is not recommended for the treatment of diabetic ketoacidosis or in patients with a hypersensitivity to Basaglar or any of its excipients (1).

Mechanism of Action

Insulin glargine lowers blood glucose by stimulating peripheral glucose uptake and inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis and enhances protein synthesis. Basaglar has a duration of action of ~24 hours and no pronounced peak (1).

Potential Advantages

One of the expected benefits of follow-on biologics is decreased cost. Basaglar is currently ~15% less expensive than Lantus (2). Basaglar is available in a pen device, which can ease administration for patients with poor vision or dexterity.

Potential Disadvantages

Like all insulin products, Basaglar has the risk of hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema, and weight gain (1). Basaglar and Lantus cannot be freely substituted for each other. No crossover studies between Lantus and Basaglar have been published. Because of this, these biologics are not currently approved as interchangeable by the "Orange Book," the FDA's resource for therapeutic equivalence. Insulin has a narrow therapeutic window, and even small changes between products can be clinically meaningful. Therefore, transitioning a patient from one product to another requires close glucose monitoring (1).

Cost

Basaglar is supplied in a 3-mL prefilled pen. The wholesale acquisition cost for a box of five pens (1,500 units) is $316. In comparison, Lantus costs $372 for the same quantity of pens (SoloSTAR) (2). Biologic products have more complex manufacturing processes and thus are more expensive to produce than medications with simple chemical structures. Because of the higher production costs, manufacturers may not be able to reduce the net pricing of similar biologic products to that of generic medications (3).

Commentary

Unlike other biologics, insulin is regulated under the Food, Drug, and Cosmetic Act rather than the

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Public Health Service Act. Because the term "biosimilar" is limited to agents that are highly similar to those approved through the Public Health Service Act, similar insulin products are referred to as "follow-on biologics" rather than biosimilars. Basaglar was approved through the 505(b)(2) pathway, which partially relied on the FDA's previous findings of the safety and effectiveness of its comparator agent, Lantus (4). Basaglar has the exact same amino acid sequence as Lantus but is manufactured by a different process. Because of the complexity of biologically derived insulin products and the many production processes involved in manufacturing a biologic product, the final biologic product may have small variations from the comparator agent. Two phase 3 trials, one in patients with type 1 diabetes and the other in patients with type 2 diabetes, found Basaglar to be similar to Lantus in terms of efficacy and safety.

The ELEMENT 1 study (5) compared Basaglar to Lantus in 535 patients with type 1 diabetes. During the randomized, open-label, 52-week trial, patients received either Lantus or Basaglar in addition to their bolus insulin regimen. The average age of patients was 41 years. The mean BMI was 26 kg/m^2. The average basal insulin dose was 0.33 units/kg/day, and the average prandial insulin dose was 0.40 units/kg/day. The mean baseline A1C was 7.7%. At 52 weeks, the average basal insulin doses were similar between Basaglar and Lantus (0.38 and 0.36 units/kg/day, respectively, P >0.05). No significant difference was found in change in A1C from baseline to 24 weeks (Basaglar –0.35% vs. Lantus –0.46%, P >0.05). At 52 weeks, there were no differences in any of the safety outcomes analyzed, including adverse events, allergic reactions, hypoglycemia, weight change, and insulin antibodies.

The ELEMENT 2 study (6) was a 24-week, randomized, double-blind study that compared Basaglar to Lantus in 756 patients with type 2 diabetes. Patients were all taking ≥2 oral antihyperglycemic medications and had failed to achieve adequate glycemic control. About 40% of patients were on Lantus, and the remainder were insulin naive. The primary efficacy outcome was change in A1C from baseline to 24 weeks. The average age of the patients was ~59 years. All patients had an A1C between 7 and 11%, with an average A1C of 8.3%. The average duration of diabetes was 12 years. The mean BMI was 32 kg/m^2. Results showed both treatment groups had significant decreases in A1C from baseline to 24 weeks, but no significant differences were found between the groups (Basaglar –1.29% vs. Lantus –1.34%, P >0.05). There were no treatment differences (P >0.05) in fasting plasma glucose, proportion of patients reaching an A1C <7%, or insulin dose at 24 weeks. Adverse events, allergic reactions, weight change, hypoglycemia, and insulin antibodies were similar between treatment groups.

The results of these trials show that the two products have similar effects on blood glucose control and frequency of adverse effects. However, crossover studies to determine the interchangeability of Lantus and Basaglar have not been published. Because of this, they are not currently rated as therapeutic equivalents by the FDA's "Orange Book," and therefore cannot be substituted for each other without a prescriber's authorization (7). For patients who are switching between Lantus and Basaglar, it is recommended to use the same daily insulin dosage and monitor patients' blood glucose closely. For patients who are switching from twice-daily NPH or insulin glargine 300 units/mL to Basaglar, it is recommended that the dose of Basaglar be 80% of the previous total daily insulin dose.

Clinical Implications

As the first follow-on biologic insulin, Basaglar opens a new chapter in diabetes management. Basaglar provides an effective and less expensive alternative to other insulin glargine products. Providers who are switching patients from Lantus to Basaglar should use an equivalent dose and monitor patients' blood glucose levels closely after transition.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

References

1. Basaglar [prescribing information]. Indianapolis, Ind., Eli Lilly/Boehringer Ingelheim, 2016

2. Truven Health Analytics. Micromedex Solutions [Internet]. Available from http://www.micromedexsolutions.com/micromedex2/librarian/CS/8685A3/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/2827FF/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/redbook.FindRedBook?navitem=topRedBook&isToolPage=true. Accessed 1 March 2017

3. Peters AL, Pollom RD, Zielonka JS, Carey MA, Edelman SV. Biosimilars and new insulin versions. Endocr Pract 2015;21:1387–1394

4. U.S. Food and Drug Administration. FDA approves Basaglar, the first "follow-on" insulin glargine product to treat diabetes. Available from https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm477734.htm. Accessed 1 March 2017

5. Blevins TC, Dahl D, Rosenstock J, et al. Efficacy and safety of LY2963016 insulin glargine compared with insulin glargine (Lantus®) in patients with type 1 diabetes in a randomised controlled trial (the ELEMENT 1 study). Diabetes Obes Metab 2015;17:726–733

6. Rosenstock J, Hollander P, Bhargava A, et al. Similar efficacy and safety with LY2963016 insulin glargine and insulin glargine (Lantus®) in patients with type 2 diabetes who were insulin-naive or previously treated with insulin glargine: a randomized, double blind controlled trial (the ELEMENT 2 study). Diabetes Obes Metab 2015;17:734–741

7. U.S. Food and Drug Administration. Electronic Orange Book. Available from http://www.fda.gov/cder/ob/default.htm. Accessed 15 March 2017