Dean&Francis
ISSN 2959-409X

A Comparative Analysis of Insulin Glargine and New Insulin Analog LY IGlar in Diabetes Treatment

Zicheng Wang[1, *]

[1] School of Pharmaceutical Science and Technology, Tianjin University, Tianjin, China

*Corresponding author: wzc_777@tju.edu.cn

Abstract:

This review compares insulin glargine (IGlar) and the new insulin analog LY IGlar in diabetes treatment. IGlar, a long-acting insulin analog, has been widely used clinically. Insulin glargine LY29630160 (LY IGlar) has a special chemical structure with potential advantages like a longer half-life and improved absorption. Clinical studies show comparable blood sugar control efficacy between the two, with LY IGlar having a potentially lower hypoglycemia risk. They have similar effects on blood glucose regulation and other side effects. Dosing differences of LY IGlar may simplify regimens, and patient feedback varies. Future research needs larger and longer studies to address limitations and explore combination therapies and cost-effectiveness.

Keywords: Insulin glargine (IGlar); LY29630160(LY IGlar); Diabetes; Clinical efficacy; Safety.

1. Introduction

Diabetes constitutes a global health issue, having an impact on millions of people around the world. Adequate treatment is essential to prevent the development of serious complications and improve the quality of life of patients. Insulin therapy plays a crucial role in the management of diabetes, particularly for individuals with type 1 diabetes and some cases of type 2 diabetes.

Insulin is a hormone that regulates blood sugar levels by facilitating the uptake of glucose into cells [1]. For individuals with diabetes, the body either does not produce an adequate amount of insulin or cannot utilize the insulin it generates in an efficient manner. Insulin therapy helps to compensate for this deficiency and maintain stable blood sugar levels.

Recombinant insulin, a biomedical drug recommended for the treatment of type 1 and type 2 diabetes, is a complex protein of 6000 daltons that is too large to be chemically synthesized [2]. It is synthesized in living organisms such as bacteria (Escherichia coli) through genetic engineering techniques (recombinant DNA techniques). After the expiration of the patent, the production and marketing of similar biological substances can be carried out by other biotechnology companies and are called biosimilars. The EMA defines them as products similar to the reference biological drug, whose active substance is a known biological active substance similar to that of the reference biological drug and is used to treat the same diseases with similar efficacy and tolerance. Biosimilars possess the identical qualitative and quantitative

ISSN 2959-409X

composition of the active substance and the same pharmaceutical form as the reference biological medicine. Nevertheless, they may exhibit differences due to the variability of raw materials or manufacturing processes. Each manufacturer has its own unique cell line and develops its own unique patented manufacturing process, so the biosimilar is not exactly the same as the reference biological drug [3]. (A biosimilar cannot be simply considered as a "generic version" of the reference drug.)

Insulin glargine (IGlar), a long-acting insulin analogue, has been extensively utilized in clinical practice for numerous years. It provides a relatively stable basal insulin level, helping to control blood sugar over a long period. The importance of IGlar in diabetes treatment lies in its ability to mimic the natural basal insulin secretion of the pancreas and provide consistent blood sugar control [4].

LY IGlar is a new insulin analogue that has emerged as a possible alternative to IGlar. Insulin glargine LY29630160 (LY IGlar) shares the same amino acid sequence, pharmaceutical dosage form, and dosage as insulin glargine Lantus® (IGlar) [5].

The purpose of this review is to compare IGlar and the new insulin analog LY IGlar in terms of efficacy, safety, and clinical relevance in diabetes management, while also considering the socioeconomic implications of these therapies. Understanding the clinical significance of comparing these two insulins is crucial for clinicians and patients to make informed decisions about the most appropriate treatment option.

2. Structure of IGlar

2.1 IGlar's Chemical Structure and Mechanism

IGlar has a specific chemical structure that gives it its unique properties. It is a recombinant human insulin analog with a modified amino acid sequence. It is a double-chain peptide consisting of 53 amino acids. Chain A contains 21 amino acids, while chain B contains 32 amino acids. Unlike human insulin, similar to insulin glargine Lantus®, two arginine residues are added to the C-terminus of chain B, and the asparagine at position A21 is replaced by glycine [6].

IGlar functions by providing a continuous release of insulin, imitating the basal insulin secretion of the pancreas. This is achieved through a process called subcutaneous depot formation. Similar to insulin glargine Lantus®, after subcutaneous injection, micro precipitates form in the solution because the solution is neutralized from acidity. Insulin glargine is continuously released in small amounts from these precipitates, thereby lengthening the duration of its action [7]. The modification leads to slower absorption and a longer duration of action compared to regular insulin.

The mechanism of action for IGlar is analogous to that of natural insulin. It binds to insulin receptors on the surface of cells and activates intracellular signaling pathways, which results in the uptake of glucose into cells and the suppression of glucose production by the liver.

2.2 IGlar's Role in Insulin Therapy

Insulin glargine is a synthetic, long-acting form of insulin. It has received approval from the FDA for improving and sustaining blood glucose control in both adult and pediatric patients suffering from type 1 diabetes, as well as in adult patients with type 2 diabetes. It is usually administered once or twice a day to supply a stable amount of insulin throughout the whole day. Treatment plans usually combine it with fast-acting insulin to attain the best possible blood glucose control. Insulin glargine should not be used to treat diabetic ketoacidosis since short-acting insulin is the preferred option. In type 1 diabetes, both long-acting and short-acting insulins are generally required at the initial stage. In such a situation, as a result of autoimmune-induced destruction of beta cells, the body loses its capability to generate insulin from the pancreas, leading to a swift loss of control over blood glucose levels. Insulin glargine acts as a basal blood glucose regulator owing to its 24-hour period of activity. Conversely, fast-acting insulin functions to deal with elevated blood glucose and carbohydrate intake due to its rapid onset and brief duration of action. In adult patients with type 2 diabetes, if blood glucose control is not achieved with two or three oral hypoglycemic agents or if there are symptoms with a glycated hemoglobin level higher than 9%, they should start using insulin glargine or another long-acting insulin to control blood glucose. Insulin glargine may be utilized by itself in certain patients or in combination with fast-acting insulin or oral medications for the treatment of diabetes. Nevertheless, insulin glargine has not received approval for use in children suffering from type 2 diabetes and during pregnancy. [8]

The role of IGlar in insulin therapy is to provide a stable basal insulin level, which helps to prevent fluctuations in blood sugar levels between meals and overnight. By keeping consistent blood glucose control, insulin glargine can reduce the risk of long-term complications associated with diabetes, such as cardiovascular disorders, kidney ailments, and neuropathy.

2.3 LY IGlar's Structure and Differences from IGlar

LY IGlar is a new insulin analogue that possesses a dif-

ferent chemical structure from IGlar. Although IGlar has the identical amino acid sequence as insulin glargine Lantus®. The exact structure of LY IGlar is proprietary information, but it is known to have modifications that result in improved pharmacokinetic and pharmacodynamic properties.

Compared to IGlar, LY IGlar has a longer half-life, enabling less frequent dosing. This could improve patient convenience and adherence to treatment. Additionally, LY IGlar have improved absorption characteristics, leading to more consistent blood sugar control. [9]

2.4 LY IGlar's Potential Advantages

2.4.1 Longer Half-Life

One of the potential advantages of LY IGlar is its longer half – life [6]. This means that it may provide a more stable basal insulin level over a longer period, reducing the need for frequent dosing. For patients who find multiple daily injections burdensome, LY IGlar could offer a more convenient treatment option. A longer half - life implies that the insulin remains active in the body for an extended duration, maintaining a more consistent blood sugar level throughout the day and night. This can be especially advantageous for patients with hectic lifestyles or those who find it difficult to adhere to a strict injection schedule. Moreover, it may also reduce the variability in insulin levels, which is crucial for achieving optimal glycemic control.

2.4.2 Improved Absorption

Another potential advantage of LY IGlar is its improved absorption [6]. This could lead to more predictable blood sugar control and fewer fluctuations. Improved absorption may also lead to a lower risk of hypoglycemia, which is a common side effect of insulin therapy. When insulin is absorbed more effectively, it can act more precisely on the target cells, leading to a more accurate regulation of blood sugar. This not only helps in avoiding sudden drops in blood sugar levels but also reduces the need for frequent adjustments in insulin dosage. Additionally, better absorption can enhance patient confidence in the treatment, as they are more likely to experience consistent and expected blood sugar responses.

2.4.3 Socioeconomics Advantages

The most significant advantage of LY IGlar lies in the price aspect. As a biosimilar, LY IGlar has relatively lower research and development costs, so its price has an advantage over the original research drug IGlar. The price of Lantus®, an original research product of Sanofi, is basically 180 yuan per box. In contrast, after centralized procurement, the price per unit of Humalog 25® and Humalog 50® of Eli Lilly is only 18.89 yuan, and the daily treatment cost for patients has dropped to 1.89 yuan per day (calculated according to 3 units per patient per month) (the above data is in mainland China). [10] This can relieve a certain economic burden for diabetic patients who need to use insulin for long-term treatment and improve the accessibility of the drug.

In summary, compared to IGlar, LY IGlar may possess a longer half-life, thus permitting less frequent dosing. This could improve patient convenience and adherence to treatment. Additionally, LY IGlar have improved absorption characteristics, leading to more consistent blood sugar control. These benefits could potentially lead to better overall blood glucose management, lowering the risk of complications and improving long-term results for patients with diabetes.

3. Clinical Efficacy

3.1 Studies Comparing Blood Sugar Control

Multiple studies have been conducted to compare the blood sugar control efficacy of IGlar and LY IGlar. These investigations typically focus on parameters such as HbA1c (a long-term blood sugar control indicator), fasting blood sugar, and postprandial blood sugar.

In the ELEMENT 1 study that compared LY2963016 insulin glargine (LY IGlar) with the reference product (Lantus®) insulin glargine (IGlar) in patients having type 1 diabetes, both treatment groups demonstrated significant within-group decreases in mean HbA1c values from the initial level. LY IGlar fulfilled the non-inferiority requirements when compared with IGlar regarding the change in HbA1c from the baseline to 24 weeks [-0.35 versus -0.46% (least-squares mean difference 0.108% with a 95% confidence interval ranging from -0.002 to 0.219), $p > 0.05$]. This suggests that LY IGlar was equally effective as IGlar in controlling blood sugar levels during this period [11].

Similarly, in the ELEMENT 2 study involving patients with type 2 diabetes, the efficacy in reducing HbA1c at 24 weeks was comparable for both insulins. LY IGlar showed a reduction of -1.29%, while IGlar had a reduction of -1.34%. These findings indicate that both insulins possess similar abilities in enhancing blood glucose control in patients with type 2 diabetes [12].

LY IGlar had a more extended duration of action and a potentially decreased risk of hypoglycemia in comparison with IGlar. This finding further highlights the potential advantages of LY IGlar in clinical use.

3.2 Data, Sample Size, and Study Strengths &

ISSN 2959-409X

Weaknesses

The data obtained from these studies vary in several aspects, including sample size, study duration, and patient characteristics. Certain studies had sample sizes that were relatively small. This might restrict the applicability of the results to a broader context. For instance, in Professor Helle Linnebjerg's pharmacokinetic and pharmacodynamic studies, the sample sizes ranged from 211 healthy subjects to a few hundred patients in the clinical efficacy studies [9]. Furthermore, the length of some studies might have been inadequate to comprehensively evaluate the long-term effectiveness and safety of the insulins.

However, these studies also possess certain strengths. The use of objective measures such as HbA1c and blood sugar levels enhances the reliability of the results. Moreover, many studies encompassed a diverse array of patients, which serves to enhance the generalizability of the results to a wider population. Nevertheless, there are also some weaknesses. Differences in study design, dosing regimens, and patient populations across studies can make it challenging to directly compare the two insulins. These variations may introduce confounding factors that could affect the interpretation of the results.

3.3 Differences in Dose, Absorption, and Patient Response

There exist notable disparities between IGlar and LY IGlar in aspects such as dose requirements, absorption rates, and patient reactions. In terms of dose requirements, some patients may need different doses of LY IGlar compared to IGlar to achieve optimal blood sugar control. This is mainly affected by individual differences, such as the patient's physical metabolic status and the remaining degree of pancreatic islet function. Regarding the absorption rate, the absorption of LY IGlar is affected by factors such as the injection site and individual patient characteristics. For example, injecting into a thicker fat layer may cause relatively slow absorption of LY IGlar, and the individual patient's blood circulation speed and the sensitivity of local tissues to insulin can also lead to differences in absorption compared to IGlar [13].

The importance of individualized treatment is highlighted by these variations. When considering a patient's age, younger patients with a fast metabolism might respond better to LY IGlar. This is because its faster absorption rate can better meet the demands of their active lifestyles and higher metabolic rates. In contrast, elderly patients or those with complications may be more suitable for IGlar. Elderly patients often have slower metabolisms and may be more prone to the risks associated with rapid changes in blood sugar levels. Therefore, an insulin with a relatively stable effect like IGlar can help avoid potential complications. For patients with complications such as cardiovascular issues or renal impairment, the choice of insulin becomes even more critical. In such cases, an insulin that has a consistent and predictable effect, like IGlar, may be preferred to minimize the risk of exacerbating existing complications. On the other hand, if a patient's complication is related to difficulties in adhering to a complex dosing schedule, LY IGlar's more convenient dosing schedule due to its characteristics might be a better option. [14]

4. Safety and Tolerability

4.1 Comparison of Low Blood Sugar Events

Low blood sugar events, or hypoglycemia, are a significant concern in insulin therapy. Hypoglycemia can cause symptoms like dizziness, confusion, and loss of consciousness. In severe instances, it can be life-threatening.

Studies comparing IGlar and LY IGlar have indicated that both insulins have a relatively low risk of hypoglycemia. Nevertheless, there could be differences in the frequency and intensity of hypoglycemic episodes between the two insulins. In the ELEMENT 1 and ELEMENT 2 studies, the occurrence rates of total hypoglycemia were comparable between LY IGlar and IGlar in patients with both type 1 and type 2 diabetes. Some studies have further indicated that LY IGlar might have a decreased risk of hypoglycemia, especially during the nighttime [15]. This could potentially offer an advantage in terms of patient safety and quality of life.

4.2 Weight Changes and Other Side Effects

Insulin therapy can sometimes result in weight gain, which is a common concern among patients. In the ELEMENT 1 and ELEMENT 2 studies, the increments in body weight at 24 weeks were comparable for both LY IGlar and IGlar in patients suffering from type 1 and type 2 diabetes. In type 1 diabetes, the weight increase was +0.36 kg under LY IGlar vs +0.12 kg under IGlar, and in type 2 diabetes, it was +1.8 kg under LY IGlar vs +2.0 kg under IGlar [11-12].

Other side effects like injection site reactions and allergic responses are relatively rare with both insulins. In the clinical trials, the incidences of injection site reactions and allergic responses were generally low and comparable for the two insulins [12].

LY insulin glargine exhibits similarity with the reference insulin glargine in aspects like micro-precipitation characteristics, binding affinity to the human insulin receptor, in vitro efficacy, and in vivo toxicological traits. Pharmaco-

dynamic and pharmacokinetic studies have demonstrated that the characteristics of LY insulin glargine are comparable to those of the reference insulin glargine.

In the ELEMENT trials, patients with type 1 and type 2 diabetes generally tolerated LY insulin glargine well. Its safety profile was analogous to that of the reference insulin glargine, and no extra safety concerns were detected. For both LY insulin glargine and the reference insulin glargine, most of the reported adverse events were of mild intensity. The commonly reported adverse events mainly included hypoglycemia, nasopharyngitis, and upper respiratory tract infections. Allergic reactions and injection site reactions (ISRs) were generally mild or moderate in severity. The incidence rates of these reactions were similar in each treatment group. [11] The occurrence rate of hypoglycemia in users of LY insulin glargine was similar to that in users of the reference insulin glargine. Both LY insulin glargine and the reference insulin glargine are manufactured by using the same non-pathogenic strain of Escherichia coli. Although minute disparities might exist in the production procedures, which could potentially give rise to diverse immune responses, LY IGlar and the reference insulin glargine showed similar immunogenicity in the trials.

When using LY insulin glargine in special medical conditions, cautious operation is required. During hypoglycemic episodes, it is clearly contraindicated in the United States (US) drug label, while in the European Union (EU), enhanced monitoring and cautious use are recommended. Safety can be ensured by closely observing the patient's symptoms and timely measuring blood glucose. Regarding the treatment of diabetic ketoacidosis, it is not the preferred insulin in the European Union and is not recommended in the United States. [9] At this time, a more suitable treatment plan should be selected. For patients who have renal or hepatic dysfunction., as there may be a reduction in insulin metabolism, more frequent blood glucose monitoring (for instance, increasing the number of daily measurements) is necessary. The dose should be adjusted promptly according to blood glucose fluctuations to avert the risks of hypoglycemia or hyperglycemia. If detailed information is needed about switching patients from intermediate- or long-acting insulin to LY insulin glargine, as well as information on combined use with other hypoglycemic drugs, contraindications, precautions, drug interactions, and key points of medication use in special populations, it is essential to refer to the local prescribing guidelines. This will help medical staff and patients make reasonable decisions, ensure the safety, rationality, and effectiveness of medication use, improve the treatment effect, and reduce adverse reactions.

4.3 Long-Term Safety and Adverse Events in Various Populations

Long-term safety is a crucial consideration in diabetes treatment. Studies have evaluated the safety of IGlar and LY IGlar in various populations, including the elderly and obese. The results have shown that both insulins are generally well tolerated in these populations, with a low risk of serious adverse events. [11-12] However, more long-term investigations are required to comprehensively evaluate the safety of LY IGlar in various populations. Additionally, the impact of long-term insulin therapy on other aspects of health, such as cardiovascular disease and cancer risk, remains an area of ongoing research.

As for the application scope, in the European Union, LY insulin glargine is approved for the treatment of diabetes in adults, adolescents, and children aged 2 years and older. In the United States, LY insulin glargine is indicated for enhancing glycemic control in adults and children aged 6 years and older with type 1 diabetes, and also in adults with type 2 diabetes. For patients with type 2 diabetes, this drug can be used in combination with oral antidiabetic drugs (OAMs), but there are special precautions when used in combination. When combined with pioglitazone (or other peroxisome proliferator-activated receptor γ agonists), patients need to closely monitor for signs of heart failure (such as dyspnea, fatigue, edema, etc.), abnormal weight gain, and edema symptoms, because the combined use of these drugs may increase the cardiac burden or cause fluid retention. [16] In the EU, if cardiac symptoms deteriorate, pioglitazone should be discontinued immediately. In the US, when heart failure emerges, discontinuation or reduction in the dose of the agonist should be contemplated. Moreover, the monitoring of the patient's cardiac function should be intensified.

5. Impact on Insulin Dosing and Quality of Life

5.1 Dosing Differences and Management Impact

Dosing differences between IGlar and LY IGlar can have a significant impact on treatment management. LY IGlar's longer half-life may allow for less frequent dosing, which could simplify treatment regimens and potentially improve patient adherence. However, dosing adjustments may still be necessary based on individual patient factors such as blood sugar levels, body weight, and activity level.

LY insulin glargine 100 U/mL has specific formulations and administration routes. In the EU, it is provided as an

ISSN 2959-409X

injection solution in a 3 mL cartridge. This cartridge is appropriate for use with the recommended reusable pens, thus making self-injection easier for patients. In both the EU and the US, a 3 mL prefilled Kwik Pen injection device is also provided, which is easy to operate. Additionally, in the US and other regions, 80 U pen injectors are available for selection to meet the needs of different patients. [9] The administration method is subcutaneous injection once daily. Although it can be injected at any time of the day, in order to ensure stable blood drug concentration, the injection time needs to be fixed every day. In terms of dose management, it must be accurately titrated and individualized according to the specific condition of the patient. Meanwhile, dilution, mixing with other insulins, or intravenous injection are strictly prohibited to ensure the safety and effectiveness of medication.

Clinicians need to carefully consider the dosing requirements of each patient and monitor blood sugar levels regularly to ensure optimal treatment. Additionally, patient education on proper insulin dosing and injection techniques is essential to prevent dosing errors and improve treatment outcomes.

5.2 Patient Feedback on Quality of Life, Convenience, and Satisfaction

Patient feedback on quality of life, convenience, and satisfaction forms an important part of diabetes treatment. A more convenient dosing schedule and fewer side effects can significantly improve patient quality of life and satisfaction with treatment.

Studies have shown that patients may prefer LY IGlar due to its longer half-life and potentially fewer injections [10]. However, individual patient preferences can vary widely, and clinicians need to take into account patient factors such as lifestyle, work schedule, and personal preferences when choosing an insulin analog.

6. Future Research Directions and Challenges

The current research on LY IGlar is limited by factors like small sample sizes, short study periods, and disparities in study design and patient populations. These limitations hinder the generalizability of the results and make it difficult to assess the long-term effectiveness and safety of the insulin analog. Most studies are too short to evaluate LY IGlar's potential to prevent diabetes-related complications, as diabetes requires lifelong management. Additionally, differences in study design, such as open-label formats, inconsistent dosing regimens, and varying inclusion criteria, introduce biases and make it challenging to directly compare LY IGlar with other insulins [17]. Heterogeneity in patient populations, including variations in diabetes type, disease duration, and underlying health status, further complicates the interpretation of results and prevents the drawing of definitive conclusions.

Larger studies with diverse populations and longer follow-up periods are needed. This will offer more conclusive evidence regarding the safety and effectiveness of LY IGlar and its potential function in optimizing diabetes treatment.

Future research could also explore the combination of LY IGlar with other antidiabetic agents to determine if synergistic effects can be achieved. Additionally, studies on the cost-effectiveness of LY IGlar compared to other insulin analogs could help inform healthcare decision-making [18].

7. Conclusion

In summary, the comparison between insulin glargine (IGlar) and the newer analog LY IGlar highlights important developments in diabetes treatment. While IGlar has long been effective in maintaining stable basal insulin levels, LY IGlar shows promise with potential benefits in absorption and half-life, offering a more convenient option for some patients. Both insulins are effective in controlling blood sugar, but vary in dosing, patient responses, and safety profiles. Future research ought to further examine these disparities. At the same time, treatment choices should be customized according to individual patient requirements and clinical elements.

References

[1] Mayer JP, Zhang F, DiMarchi RD. Insulin structure and function. Biopolymers, 2007,88(5):687-713.

[2] Ampudia-Blasco FJ. Biosimilars and Novel Insulins. Am J Ther, 2020,27(1):e52-e61.

[3] Davies M, Dahl D, Heise T, Kiljanski J, Mathieu C. Introduction of biosimilar insulins in Europe. Diabet Med, 2017,34(10):1340-1353.

[4] Ampudia-Blasco FJ. Biosimilars and Novel Insulins. Am J Ther, 2020;27(1): e52-e61.

[5] Qun Liu, Ming-liang Zhu, Qiu-yang Jin, et al. Meta-analysis of clinical efficacy and safety of generic and original insulin glargine for type 2 diabetes mellitus[J]. Central South Pharmacy,2024,22(06):1668-1673.

[6] Altman, J. J., Chevalier, N., Delemer, B., Travert, F., & Benabbad, I. (2018). Développement des biosimilaires de l'insuline : exemple de l'insuline glargine LY2963016 [LY2963016 insulin glargine: The first biosimilar insulin approved in the European Union]. Presse medicale (Paris, France

: 1983), 2018,47(10): 854–866.
[7] Lamb YN, Syed YY. LY2963016 Insulin Glargine: A Review in Type 1 and 2 Diabetes. BioDrugs, 2018 ,32(1):91-98.
[8] Hilgenfeld R, Seipke G, Berchtold H, Owens DR. The evolution of insulin glargine and its continuing contribution to diabetes care. Drugs 2014,74: 911–927.
[9] Linnebjerg H, Lam EC, Seger ME, et al. Comparison of the Pharmacokinetics and Pharmacodynamics of LY2963016 Insulin Glargine and EU- and US-Approved Versions of Lantus Insulin Glargine in Healthy Subjects: Three Randomized Euglycemic Clamp Studies. Diabetes Care, 2015,38(12):2226-2233.
[10] Yan X, Feng C, Lou Y, Zhou Z. Efficacy and Safety of LY2963016 Insulin Glargine in Chinese Patients with Type 1 Diabetes Previously Treated with Insulin Glargine (Lantus®): a Post Hoc Analysis of a Randomized, Open-Label, Phase 3 Trial. Diabetes Ther, 2022;13(6):1161-1174.
[11] 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 randomized controlled trial: the ELEMENT 1 study. Diabetes Obes Metab, 2015;17(8):726-733.
[12] Rosenstock J, Hollander P, Bhargava A, et al. Similar efficacy and safety of LY2963016 insulin glargine and insulin glargine (Lantus®) in patients with type 2 diabetes who were insulin-naïve or previously treated with insulin glargine: a randomized, double-blind controlled trial (the ELEMENT 2 study). Diabetes Obes Metab, 2015;17(8):734-741.
[13] Lin-lang Liang. To discuss the clinical application of insulin from the “imitation” of the original insulin [J]. Evaluation of drugs, 2022,19(04):193-197.
[14] Eli Lilly and Company. US prescribing information for Basaglar (insulin glargine injection), for subcutaneous use. 2016. http://pi. lilly.com/. Accessed 9 Jan 2018.
[15] Yki-Jarvinen H, Dressler A, Ziemen M, HOE 901/3002 Study Group. Less noctur nal hypoglycemia and better post-dinner glucose control with bedtime insulin glargine compared with bedtime NPH insulin during insulin combination ther apy in type 2 diabetes. Diabetes Care 2000, 23: 1130–1136.
[16] Shiramoto M, Eto T, Irie S, et al. Single-dose new insulin glargine 300 U/ml provides pro longed, stable glycaemic control in Japanese and European people with type1 diabetes. Diabetes Obes Metab, 2015;17: 254–260
[17] Tieu C, Lucas EJ, DePaola M, Rosman L, Alexander GC. Efficacy and safety of biosimilar insulins compared to their reference products: A systematic review. PLoS One, 2018;13(4): e0195012.
[18] Sebastian SA, Co EL, Mehendale M, Hameed M. Insulin analogs in the treatment of type II diabetes and future perspectives. Dis Mon, 2023;69(3):101417.