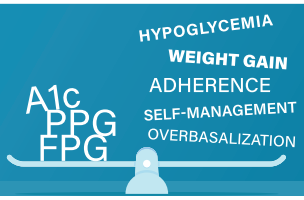

Ask the Faculty

1. Patient affordability has become increasingly important when considering insulin therapy. What's the approximate cost of these products? Does insurance, particularly Medicare, cover any of them?

Answer:

As with most medications, the cost of insulin products can vary greatly depending on where the insulin product is purchased and insurance coverage. The case prices (July 2018 data) for the products are shown below (source: GoodRx.com). Note that the follow-on insulin glargine Basaglar is the least expensive basal insulin.

NPH 3 mL Kwikpen	$119
Degludec (Tresiba) 3 mL Flextouch pen	$115
Detemir (Levemir) 3 mL Flextouch pen	$105
Glargine U-100 (Basaglar) 3 mL Kwikpen	$83
Glargine U-100 (Lantus) 3 mL Solostar pen	$98
Glargine U-300 (Toujeo) 1.5 mL pen	$154
Degludec/Liraglutide (Xultophy 100/3.6) 3 mL pen	$249
Glargine/Lixisenatide (Soliqua 100/33) 3 mL Solostar pen	$165

Regarding insurance coverage, there is great variability in out-of-pocket cost depending on whether the product is on the payer's formulary. Even if it is, it is subject to deductibles and copays. Medicare Part B covers the cost of insulin, but only if it is administered via pump (subject to $183 deductible with 20% copay).[1] Insulin that is self-administered using a needle is covered under Medicare Part D, subject to the plan's deductible and copay.

Manufacturers provide assistance to patients who meet eligibility requirements. Further information may be found at the following:

Degludec (Tresiba): https://www.tresiba.com/savings-and-coverage/prescription-assistance.html

Detemir (Levemir): https://www.levemir.com/savings-and-co-pay.html

Glargine U-100 (Basaglar): https://www.basaglar.com/savings-support

Glargine U-100 (Lantus): https://www.lantus.com/sign-up/savings-and-support

Glargine U-300 (Toujeo): https://www.toujeo.com/toujeo-savings-card-coupon-and-support

Degludec/Liraglutide (Xultophy 100/3.6): https://www.xultophy10036.com/savings-coverage/how-much-is-my-copay.html

Glargine/Lixisenatide (Soliqua 100/33): https://www.soliqua100-33.com/savings-and-support

2. I am relatively comfortable initiating treatment with basal insulin, but much less comfortable titrating it for fear the patient might experience an episode of severe hypoglycemia. How do I know when I should stop increasing the dose of basal insulin and add another medication?

Answer:

Hypoglycemia is certainly a concern, especially with the older basal insulin products.[2] Basal insulin products primarily lower the fasting plasma glucose, with much less effect on the postprandial glucose. Therefore, if the glycated hemoglobin (A1c) is above target (<7.0% for most patients) and the fasting plasma glucose is in the normal range, increasing the basal insulin dose is unlikely to be of any benefit in further lowering the A1c. On the other hand, the incidence and severity of hypoglycemia are likely to be increased.[3] The rule of thumb is to avoid, or at least proceed with great caution with close blood glucose monitoring, total daily basal insulin doses >0.5 units/kg.[4] The most likely reason the A1c remains above target is because the postprandial

glucose remains elevated. This can be verified by checking the blood glucose level multiple times per day over several days. Beyond confirming postprandial hyperglycemia, this would also identify unexpectedly large fluctuations in the blood glucose level, which, if present, should result in further investigation, including the patient's eating [habits] and physical activity. Another indicator suggesting the need for adding a medication rather than increasing the total daily dose of basal insulin is a BeAM value greater than 45-55 mg/dL.[5] The BeAM value is calculated by subtracting the fasting plasma glucose level from the bedtime glucose level. Therefore, a BeAM value >45 to 55 mg/dL suggests unresolved postprandial hyperglycemia.

3. Clinical trials have investigated the cardiovascular safety of the individual components in the fixed-ratio basal insulin/glucagon-like peptide-1 receptor agonist combination products. Have similar trials been conducted with the fixed-ratio combination products?

Answer:

No, similar cardiovascular outcomes trials have not been conducted with the fixed-ratio basal insulin/glucagon-like peptide-1 receptor agonist combination products. To summarize, cardiovascular outcomes trials showed both glucagon-like peptide-1 receptor agonists liraglutide and lixisenatide do not increase cardiovascular risk compared with placebo as part of standard therapy.[6,7] Additionally, liraglutide, but not lixisenatide, reduced cardiovascular risk compared with placebo. With respect to the basal insulin components, the ORIGIN trial showed the cardiovascular safety of glargine to be similar to standard care,[8] while the DEVOTE trial showed the cardiovascular safety of degludec to be similar to glargine.[9]

With respect to both fixed-ratio basal insulin/glucagon-like peptide-1 receptor agonist combination products, post hoc analyses have demonstrated benefits in cardiovascular risk markers–not cardiovascular events. Separate analyses of the DUAL II and DUAL V randomized, controlled trials showed that, compared with degludec or glargine, the fixed-ratio combination of degludec/liraglutide resulted in significantly greater reductions in systolic blood pressure, total cholesterol, and low-density lipoprotein cholesterol.[10] Similarly, analysis of the Lixi-Lan-L trial showed a significantly smaller increase in fasting triglycerides with glargine/lixisenatide 100/33 compared with glargine.[11]

REFERENCES

1. Centers for Medicare and Medicaid Services. Current Medicare coverage of diabetes supplies. August 16, 2018. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/SE18011.pdf. Accessed January 24, 2019.
2. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm- 2018 Executive Summary. ***Endocr Pract***. 2018;24(1):91-120.
3. Reid T, Gao L, Gill J, et al. How much is too much? Outcomes in patients using high-dose insulin glargine. ***Int J Clin Pract***. 2016;70(1):56-65.
4. American Diabetes Association. Standards of Medical Care in Diabetes-2019. ***Diabetes Care***. 2019;42(Suppl 1):S1-S193.
5. Zisman A, Morales F, Stewart J, Stuhr A, Vlajnic A, Zhou R. BeAM value: an indicator of the need to initiate and intensify prandial therapy in patients with type 2 diabetes mellitus receiving basal insulin. ***BMJ Open Diabetes Res Care***. 2016;4(1):e000171.
6. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. ***N Engl J Med***. 2016;375(4):311-322.
7. Pfeffer MA, Claggett B, Diaz R, et al. Lixisenatide in patients with type 2 diabetes and acute coronary syndrome. ***N Engl J Med***. 2015;373(23):2247-2257.
8. Gerstein HC, Bosch J, Dagenais GR, et al. Basal insulin and cardiovascular and other outcomes in dysglycemia. ***N Engl J Med***. 2012;367(4):319-328.
9. Marso SP, McGuire DK, Zinman B, et al. Efficacy and safety of degludec versus glargine in type 2 diabetes. ***N Engl J Med***. 2017;377(8):723-732.
10. Vilsboll T, Bode B, Agner B, et al. IDegLira improves cardiovascular risk markers in patients with type 2 diabetes uncontrolled on basal insulin: analyses of DUAL II and DUAL V. Abstract 113. European Association for the Study of Diabetes; September 12-15, 2017; Lisbon, Portugal.
11. Giorgino F, Shaunik A, Liu M, Saremi A. The effect on lipid profiles of iGlarLixi versus iGlar in the LixiLan-L trial. Abstract 810. European Association for the Study of Diabetes; September 12-15, 2017; Lisbon Portugal.