The Evidence for Achieving Glycemic Control With Incretin Mimetics

Learning Objectives

- Identify at least 1 benefit and 1 barrier to each of the 6 classes of antihyperglycemic agents available prior to 2005.
- Describe the therapeutic indications for treatment with exenatide and discuss the research that led to these indications.
- List at least 1 benefit and 1 barrier to treatment with exenatide.
- Discuss the clinical use of incretin mimetics.

In this article, the efficacy and limitations of pharmacologic therapies for type 2 diabetes are briefly reviewed. In addition to the 6 classes of agents that were available for use in patients with type 2 diabetes prior to 2005, the new therapeutic class of incretin mimetics is also covered. Incretin mimetic therapies in development, as well as pivotal studies that led to the approval of exenatide (BYETTA®; Amylin Pharmaceuticals, Inc, San Diego, Calif), the first incretin mimic to be approved by the US Food and Drug Administration (US FDA), are described. Finally, the clinical use of exenatide and important educational issues are addressed, and an educational exenatide case study is presented.

Type 2 Diabetes Therapeutic Overview

There are a variety of treatments available for type 2 diabetes, including therapeutic lifestyle change, oral medications, and injectable therapies. Prior to 2005, there were 6 different classes of agents available for the
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treatment of type 2 diabetes: sulfonylureas (SUs), biguanides, thiazoladinediones (TZDs), meglitinides, \( \alpha \)-glucosidase inhibitors, and insulin. Each class addresses a different aspect of diabetes pathophysiology and has a different set of benefits and challenges associated with it. A summary of agents available before 2005 appears in Table 1.

Sulfonylureas

SUs, also called insulin secretagogues, work by stimulating the secretion of insulin from functioning \( \beta \) cells. SUs generally lower A1C by 1 to 2 percentage points. The most common adverse reaction to SU therapy is hypoglycemia, and allergic reactions may occur among people who have a sensitivity to sulfa drugs. Modest weight gain is also common with SU use.

Biguanides

The biguanide metformin works by improving insulin sensitivity in the liver and periphery and by reducing hepatic glucose output. Metformin has been shown to affect both fasting and postprandial plasma glucose levels and is often used as a first-line therapy. Biguanides reduce A1C by 1.5% to 1.8% and may also beneficially affect lipid profiles and weight. The most common adverse effects are gastrointestinal, and they are generally mild. There have been some reports of lactic acidosis with metformin use, although this effect is extremely rare. A recent comprehensive review revealed that SUs, TZDs, meglitinides, \( \alpha \)-glucosidase inhibitors, and insulin failed to show more benefit than metformin on glycemic control, body weight, or lipids.

Meglitinides

Drugs in this class are non-SU insulin secretagogues. Like SUs, they stimulate the secretion of insulin from functioning \( \beta \) cells. They generally lower A1C by 0.5% to 1.5%. Because these drugs are very rapid acting, they should be taken within 30 minutes prior to meals and are most appropriate for patients with normal fasting glucose but elevated postprandial glycemic levels. The most common side effects include hypoglycemia, allergic reaction, and weight gain. These effects are generally modest in nature.

Thiazoladinediones

TZDs are insulin sensitizers that work primarily by decreasing insulin resistance in muscle and adipose tissue. They have been shown to consistently lower both fasting and postprandial glucose concentrations and may affect lipid parameters and cardiovascular outcomes. They generally lower A1C by 0.7% to 1.75%. Potential adverse effects include edema, weight gain, and congestive heart failure (CHF), although CHF is rare.

\( \alpha \)-Glucosidase Inhibitors

This class of medications delays carbohydrate uptake by inhibiting \( \alpha \)-glucosidase, an enzyme that processes carbohydrates for absorption. As a result, \( \alpha \)-glucosidase inhibitors decrease postprandial hyperglycemia. These drugs have only a modest effect on A1C (0.5% to 1%) and are generally accompanied by gastrointestinal adverse effects such as flatulence and diarrhea. Although these drugs have been shown to have a clear effect on glycemic control and insulin levels, they provide no clear benefit on lipids or body weight.

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Table 1

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Site of Action</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>Pancreatic ( \beta ) cell</td>
<td>Hypoglycemia, weight gain</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Pancreatic ( \beta ) cell</td>
<td>Hypoglycemia, weight gain</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Liver, muscle</td>
<td>Gastrointestinal distress, lactic acidosis</td>
</tr>
<tr>
<td>( \alpha )-Glucosidase inhibitors</td>
<td>Intestine</td>
<td>Gastrointestinal distress</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Liver, muscle, fat</td>
<td>Weight gain, edema</td>
</tr>
<tr>
<td>Insulin</td>
<td>Liver, muscle, fat</td>
<td>Hypoglycemia, weight gain</td>
</tr>
</tbody>
</table>

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Insulin

There are a variety of different types of insulin currently available. Insulin types are categorized according to their onset of action: rapid acting (onset of less than 15 minutes), short acting (onset of 0.5 to 2 hours), intermediate acting/long acting (onset 2-4 hours). Common insulin types and their action profiles appear in Table 2. Frequently, patients may need to take more than 1 type of insulin (eg, a rapid-acting insulin and an intermediate- or long-acting insulin). Some types of insulin (eg, insulin glargine [Lantus®; Aventis Pharmaceuticals Inc, Kansas City, Mo]) should not be mixed with other types of insulin. When mixing insulin is required, there are 2 options currently available to patients: manually mixing different types of insulin or using premixed insulin formulations. Premixed insulin formulations afford greater convenience but do not allow as much flexibility in terms of dosing. Frequent adverse effects of insulin include weight gain and hypoglycemia.

Treatment Challenges in Type 2 Diabetes

Because of the numerous antihyperglycemic agents available, there is no clear consensus on the most optimal treatment paradigm for type 2 diabetes. One suggested treatment algorithm is shown in Figure 1. Although there are many options available for the treatment of type 2 diabetes, there also are many challenges. Many of the available therapies target only 1 aspect of the underlying pathophysiology of type 2 diabetes, and multiple agents are often needed to achieve glycemic targets. Furthermore, type 2 diabetes is a progressive disease, making therapy a progressive endeavor. Treatment is further complicated by the adverse effects associated with various therapies, including hypoglycemia and weight gain. Weight gain is particularly problematic among people with type 2 diabetes who may already be struggling with issues related to weight, including concomitant insulin resistance and dyslipidemia. Accordingly, there is a great need for a therapy that targets multiple aspects of the underlying physiology, is more durable, and limits side effects that may interfere with patient adherence.

The Potential of Incretin-Based Therapies

The incretin hormone glucagon-like peptide 1 (GLP-1) has a number of beneficial effects on glucose metab-
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olism and weight. Although individuals with type 2 diabetes show an impairment in GLP-1 secretion, the ability of GLP-1 to exert effects on glucose metabolism and weight is preserved.\(^1\)\(^7\)\(^8\) Research has demonstrated that increasing exposure to GLP-1 affects a number of different targets: it normalizes glucose levels, promotes glucose-dependent insulin secretion, suppresses postprandial glucagon secretion, promotes feelings of satiety, and reduces weight among people with type 2 diabetes.\(^1\)\(^9\)-\(^2\)\(^1\) GLP-1 also improves \(\beta\)-cell function in animal models and in human islets studied in vitro.\(^2\)\(^2\)-\(^2\)\(^1\) Accordingly, incretin-based therapies show great promise for the treatment of type 2 diabetes.

### Incretin-Based Therapies Approved for Clinical Use

Currently, exenatide is the only incretin-based therapy that has been approved by the US FDA for the treatment of type 2 diabetes. It is indicated for use among people with type 2 diabetes inadequately controlled with metformin, an SU, or combination therapy with metformin and SU.\(^2\)\(^4\) A series of 3 pivotal studies (AC2993: Diabetes Management for Improving Glucose Outcomes [AMIGO]) led to the submission of exenatide to the US FDA for regulatory approval. All 3 of the AMIGO studies included patients with type 2 diabetes whose hyperglycemia was not adequately controlled by their present therapies. The following sections describe the AMIGO studies.

### Exenatide Plus Sulfonylurea

The efficacy of exenatide therapy on glycemic control among patients failing therapy with SU treatment was examined in 1 of the 3 AMIGO studies.\(^2\)\(^5\) In this triple-blind, placebo-controlled 30-week study, 377 adults with type 2 diabetes were randomly assigned to 1 of 3 groups: placebo, 5 \(\mu\)g exenatide twice daily, or 10 \(\mu\)g exenatide twice daily. There was a 4-week, single-blind placebo lead-in period for all participants. Following the lead-in period, all patients assigned to either exenatide arm were placed on a 4-week exenatide acclimation period, during which time all patients randomized to either exenatide treatment arm received 5 \(\mu\)g exenatide twice daily. After that 4-week period, patients assigned to the 10-\(\mu\)g group had their dose increased to 10 \(\mu\)g twice daily, and patients assigned to the 5-\(\mu\)g group remained on that dose. Previous research showed that nausea associated with exenatide treatment could be attenuated by dose-escalation techniques.\(^2\)\(^6\) In addition to treatment with exenatide or placebo, all patients continued SU therapy. To standardize SU use, all patients were escalated to the maximally effective dose of their SU prior to the initial lead-in period. In the event of a documented episode of hypoglycemia, progressive 50% reductions in SU dose were recommended in the study protocol. Primary study end points included measures of glycemic control and adverse events.

Of the 377 patients randomized to treatment, 260 completed the study. On average, the patient population was predominantly male (60%), middle-aged (mean = 55 years), overweight or obese (mean body mass index [BMI] = 33 kg/\(\mu\)m\(^2\)), and had suboptimal glycemic control (mean A1C = 8.6%). At the end of the 30-week study period, a significant improvement in A1C was observed in both exenatide arms compared with placebo. At study completion (30 weeks), A1C was decreased by 0.86% in the 10-\(\mu\)g group and by 0.46% in the 5-\(\mu\)g group, compared with an increase of 0.12% in the control group.
Of participants with an A1C > 7% at baseline (n = 237), more achieved an A1C < 7% in the 10-µg exenatide (41%) and 5-µg exenatide (33%) groups compared with placebo (9%, P < .001). Fasting plasma glucose decreased in the 10-µg exenatide group compared with placebo (P < .05). Treatment with exenatide was also associated with weight loss of 1.6 kg in the 10-µg group (P < .05 compared with placebo).

The most frequent adverse event was nausea, experienced by 51% of patients in the 10-µg exenatide group, 39% of patients in the 5-µg exenatide group, and 7% of patients in the placebo group. Most episodes of nausea were mild or moderate in intensity. Nausea was most notable when therapy was initiated; subsequent rates of nausea were lower.

Mild-to-moderate hypoglycemia was experienced by 36% of patients in the 10-µg exenatide group, 14% of patients in the 5-µg exenatide group, and 3% of patients in the placebo group. There were no occurrences of severe hypoglycemia. The increased incidence of hypoglycemia in patients treated with exenatide does not appear to be caused directly by exenatide. Rather, the susceptibility to hypoglycemia that is observed with SU treatment may be increased as patients’ ambient glycemic levels dropped.

**Exenatide Plus Metformin**

The efficacy of exenatide on glycemic control among patients not optimally controlled on metformin monotherapy was also examined. This triple-blind, randomized, placebo-controlled trial enrolled 336 adult patients with type 2 diabetes who were taking metformin at maximally tolerated doses. The study design was comparable to the study testing the efficacy of exenatide therapy used in conjunction with SU. Participants were randomized to 1 of 3 conditions: placebo, 5 µg of exenatide twice daily, or 10 µg of exenatide twice daily. After a 4-week placebo period, both of the experimental groups received 5 µg of exenatide twice daily for 1 month. After 1 month, patients assigned to the 10-µg group had their dose increased. All participants continued on their prestudy dose of metformin. Primary end points included glycemic control and adverse events. Secondary end points included percentage of patients achieving an A1C < 7%, fasting and postprandial glucose concentrations, and body weight.

As in the SU study, participants in this study were predominantly middle-aged (mean age = 53 years), overweight or obese (average BMI = 34.2 kg/m²), and did not have optimal glycemic control (mean A1C = 8.2%). After 30 weeks, there was a significant improvement in A1C in both exenatide treatment groups. The 10-µg group had a 0.78% reduction in A1C, and the 5-µg group had a 0.40% reduction, compared with 0.08% increase in A1C observed in the placebo group (adjusted P < .002). After 30 weeks, 46% of patients in the 10-µg group and 32% of patients in the 5-µg group achieved an A1C < 7%, compared with 13% of patients in the placebo group (P < .01 vs placebo). Postprandial plasma glucose levels in response to a standardized meal tolerance test also improved for both exenatide-treated groups compared with placebo (P < .006). Subjects on exenatide also showed dose-dependent weight loss by the end of the study, with the 10-µg group losing 2.8 kg and the 5-µg group losing 1.6 kg (P < .001 vs placebo; Figure 3).

As with the exenatide and SU study, the most frequent adverse event was nausea, and it was generally mild to moderate in nature. Nausea was reported by 36% of patients in the 5-µg group and by 45% of the 10-µg group, compared with 23% of the placebo group. In this study, there were no observed differences in hypoglycemia observed between exenatide-treated patients...
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and control patients, supporting the hypothesis that exenatide does not cause hypoglycemia; rather, it increases susceptibility to hypoglycemia caused by SU use at lower ambient glycemic levels.

**Exenatide Plus Metformin and Sulfonylurea**

The goal of this study was to test the efficacy of exenatide on glycemic control among people with type 2 diabetes inadequately controlled with metformin-sulfonylurea combination therapy. A total of 733 subjects were enrolled in this 30-week, double-blind, placebo-controlled study. As in the other 2 AMIGO studies, participants in this study were overweight or obese adults who were not in good glycemic control. Prior to study enrollment, all participants were being treated with metformin and SU. Participants were randomly assigned to receive placebo twice daily, 5 μg exenatide twice daily, or 10 μg exenatide twice daily. Again, a 4-week lead-in period was used, and dose escalation was employed for participants assigned to the 10-μg twice-daily dose. All participants continued on their prestudy dose of metformin. In terms of SU use, participants were randomized to receive either maximal recommended SU dose or minimally effective SU dose. Primary study end points included glycemic control and adverse events. A variety of secondary end points was also examined.

At 30 weeks, A1C decreased by 0.80% in the 10-μg group and by 0.60% in the 5-μg group, whereas A1C increased by 0.20% in the placebo group (adjusted $P < .0001$ vs placebo). A glycemic target of A1C <7% was more likely to be met by participants in the exenatide groups (34% in the 10-μg group and 27% in the 5-μg group) than by participants in the placebo group (9%, $P < .0001$). A dose-dependent effect for weight loss was also observed. Participants in the exenatide groups lost more weight than their placebo counterparts did (2.8 kg in the 10-μg group and 1.6 kg in the 5-μg group; $P < .01$ vs placebo). The most frequently reported adverse events were mild-to-moderate gastrointestinal symptoms. No severe hypoglycemia was reported, and incidence of mild-to-moderate hypoglycemia was low and comparable across treatment arms. For SU dosing, the effects on glycemic control were similar between the 2 groups, but there was a decrease in hypoglycemia observed in the minimally effective SU dose group, supporting the reduction in SU dose when used in conjunction with exenatide.

**Summary**

The 3 AMIGO studies showed that exenatide therapy effectively improves glycemic control among patients inadequately controlled with SU, metformin, or combination therapy with SU and metformin. A summary of clinical trial data on exenatide appears in Table 3. The participants in the AMIGO studies were fairly typical patients with type 2 diabetes. On average, they were middle-aged and overweight or obese adults with poor glycemic control. The observed effect of exenatide on glycemic control is relatively durable in nature. Additional data have suggested that glycemic improvements seen with exenatide treatment are sustained over a period of 82 weeks.

In addition to improved glycemic control, a number of other important treatment-related findings emerged from these studies. First, unlike most other antihyperglycemic therapies, exenatide was associated with weight loss, rather than weight gain. In addition, treatment with exenatide did not appear to cause hypoglycemia; however, it was associated with increased hypoglycemia when used with an SU but not when used with metformin. Taken together, these findings suggest that exenatide treatment did not cause hypoglycemia. Rather, as exenatide treatment lowers glycemic levels, the risk of hypoglycemia due to concomitant SU use may increase. Consequently, SU dose may need to be decreased when initiating treatment with exenatide.

Treatment with exenatide was associated with mild-to-moderate gastrointestinal effects, particularly during treatment initiation. Additional research has demonstrated that dose titration can reduce these effects. Accordingly, patients should be started on the 5-μg dose, which can be increased after a month if needed and well tolerated. Because exenatide potently inhibits gastric emptying and glucagon secretion, it is more effective at controlling postprandial hyperglycemia. Finally, the durable nature of the treatment to date, combined with the results from animal and in vitro studies, suggests that treatment with exenatide may affect the underlying pathophysiologic defects present in type 2 diabetes. In short, exenatide treatment offers numerous benefits for the treatment of type 2 diabetes, including weight loss...
instead of weight gain, durable treatment effects, ability to work in a glucose-dependent fashion and improve postprandial hyperglycemia, and the ability to affect multiple therapeutic targets.

**Incretin-Based Therapies in Development**

A number of other incretin-based therapies are currently in development. Among them are the GLP-1 analog liraglutide, which has been shown to have beneficial effects on glycemic control and a modest reduction in body weight. The dipeptidyl peptidase IV (DPP-IV) inhibitor vildagliptin (formerly LAF327; Novartis International AG, Basel, Switzerland) has also shown favorable effects in clinical research. DPP-IV inhibitors increase the body’s exposure to GLP-1 by blocking DPP-IV, the enzyme that degrades GLP-1. When added to metformin monotherapy, treatment with vildagliptin prevented glycemic deterioration over the course of 1 year, with no changes in lipid parameters or body weight. Although it does not promote weight loss, it is also not associated with the same gastrointestinal effects as treatment with GLP-1 receptor agonists. In addition, this therapy has the added benefit of being orally available.

**The Clinical Use of Incretin-Based Therapies**

Because exenatide is currently the only FDA-approved incretin-based therapy, this section will focus on the clinical use of exenatide. Exenatide is indicated as adjunctive therapy for patients with type 2 diabetes who are not achieving adequate glycemic control with metformin, SU, or combination therapy with metformin and SU.

**Dosing and Administration**

Unlike insulin, exenatide does not need to be altered for food intake or exercise. Accordingly, it is available in fixed-dose prefilled pens, which are available in 5-μg-per-dose or 10-μg-per-dose versions. Each pen dispenses 60 doses per pen (a 30-day supply). After the initial pen setup is complete, priming the pen before each use is not necessary. The exenatide pens are pictured in Figure 4.

In terms of integrating exenatide into a patient’s existing treatment regimen, no dose alterations need to be made for patients taking only metformin. A dose reduction of 50% is recommended for patients taking SUs. Use of exenatide does not require patients to perform any additional self-monitoring of blood glucose, although monitoring in the postprandial state may be a beneficial way for patients to gauge exenatide effectiveness.

As previous research has demonstrated, mild-to-moderate nausea may accompany initiation of exenatide therapy. However, if patients are started at the lowest recommended dose and then increased after a month if necessary, nausea is less likely to occur. Accordingly, exenatide therapy should be initiated at the 5-μg dose, and patients should remain on that dose for 1 month. After a 1-month period, patients can be advanced to the 10-μg dose if the 5-μg dose is well tolerated and additional glycemic control is needed. A schematic representation of exenatide dosing appears in Figure 5.

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**Table 3**

**US Clinical Trials of Exenatide: Summary of Selected Outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Study With Metformin</th>
<th>Study With Maximal Dose of Sulfonylurea</th>
<th>Study With Metformin Plus Sulfonylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in A1C</td>
<td>–0.9</td>
<td>–1.0</td>
<td>–1.0</td>
</tr>
<tr>
<td>(placebo adjusted), %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight change, kg</td>
<td>–1.3 to –2.5</td>
<td>–0.3 –1.0</td>
<td>–0.7</td>
</tr>
<tr>
<td>(placebo vs 10 μg), %</td>
<td>23 vs 45</td>
<td>7 vs 51</td>
<td>21 vs 49</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(placebo vs 10 μg), %</td>
<td>2 vs 4</td>
<td>2 vs 5</td>
<td>1 vs 3</td>
</tr>
<tr>
<td>Severe nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(placebo vs 10 μg), %</td>
<td>5 vs 5</td>
<td>3 vs 36</td>
<td>13 vs 28</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(placebo vs 10 μg), %</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Exenatide is administered as a twice-daily injection, and it should be given within 60 minutes before morning and evening meals. Injections may be given in the abdomen, thigh, or arm. Exenatide should not be taken after a meal. Patients who miss a dose should wait until the time of the next scheduled dose. A dose should never be doubled to make up for a missed dose. Exenatide should be kept refrigerated, and the pen should be discarded 30 days after the first use, even if there is some medication remaining in the pen. A summary of exenatide dosing and administration information appears in Table 4.

**Exenatide and Patient Education**

There are a variety of important educational issues surrounding exenatide use. Patients should be educated on proper administration, medication storage, and possible side effects. In this section, a case study on the use of exenatide is presented.

**Clinical Case Study**

Mr B is a 47-year-old man who has had type 2 diabetes for 8 years. He struggles with issues related to weight. Currently, he weighs 237 lbs (107.5 kg), and his BMI is 31.2 kg/m². The medications he is taking include 1000 mg of metformin administered twice daily and 10 mg glipizide with breakfast. He has experienced a few hypoglycemic episodes related to SU use. His glycemic control is suboptimal, with an A1C of 7.9%, a fasting plasma glucose range of 95 to 162 mg/dL (5.28-9.00 mmol/L), and a postprandial plasma glucose range of 192 to 243 mg/dL (10.7-13.5 mmol/L). He is not meeting glycemic targets despite being reasonably adherent with oral medications. His renal and liver function are both normal. In terms of his lifestyle, he has a sedentary job and a somewhat unpredictable schedule. He is not comfortable discussing his diabetes with other people and expresses a reluctance to start an injectable medication.

Because the patient was not meeting his glycemic targets, his physician made the decision to advance his therapeutic regimen. He was started on a twice-daily injection of exenatide at the 5-µg dose to reduce the likelihood of nausea. He was instructed to continue on the same dose of metformin, but his SU dose was decreased.
by 50%. In addition, he was referred to a diabetes educator to learn how to properly administer the exenatide injections and to address his concerns related to therapy advancement.

After the educator conducted a thorough assessment, education on exenatide was provided. The educator explained how exenatide therapy can provide benefits, including improved diabetes control and feelings of well-being. In addition, the educator clarified that exenatide is not insulin. Next, the educator provided instructions on proper exenatide administration technique. Details on proper dosing and administration of exenatide appear in Table 4. The educator also assisted Mr B in developing a schedule of treatment delivery and monitoring. Because of Mr B’s reluctance to discuss his diabetes with others, his treatment schedule was structured so that exenatide use occurs at home just prior to meals. Monitoring of postprandial blood glucose levels was also recommended. The educator also discussed side effects with Mr B, including possible nausea, sensations of fullness, and hypoglycemia because of concurrent SU use. Mr B was also informed that he could expect some small but consistent weight loss. The educator also tried to promote positive beliefs and address negative ones. Specifically, the importance of weight loss to diabetes control was addressed. Even though exenatide therapy will likely result in weight loss, physical activity is still an important part of treatment of type 2 diabetes. The importance of glycemic control for the prevention of diabetic complications was emphasized.

The patient followed up with his physician at 1 month after the initiation of exenatide injections. At that time, his weight had decreased by 3 lbs (1.4 kg). He reported that he experienced mild nausea and sensations of fullness during the first week of treatment but that it had since subsided. At that time, the exenatide dose was increased to 10 µg. The patient was able to schedule injections to be taken in the home, and he was much more comfortable with the idea of an injection after meeting with the educator. Finally, the patient reported increased energy with improved glycemic control, and his initial weight loss encouraged him to increase his physical activity. When his A1C was tested at 3 months, it had decreased to 7.5%, which further motivated him to continue treatment with exenatide and lifestyle change.

**Ask the Expert**

Q: Currently, exenatide is indicated for use among adult patients with type 2 diabetes who are not meeting targets on metformin, SU, or metformin and SU combination therapy. What other therapeutic combinations or patient groups are being explored?

A: Ongoing studies are examining the use of exenatide as monotherapy, as well as in combination with thiazolidinediones.

Q: Can exenatide be used in patients with gastroparesis or following gastric bypass surgery?

A: There is little clinical experience with exenatide in these scenarios. Hence, it should not be used, or if it is used, extreme caution should be applied.

Q: How should exenatide be used in a hospital setting?

A: There is little experience with exenatide in the hospital setting. It may be more prudent to use insulin in many patients who are hospitalized for acute diabetes management.

**References**


