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This activity is jointly sponsored by Embryon and Medical Education Collaborative (MEC). MEC is a nonprofit organization that has been certifying quality educational activities since 1988.

Purpose Statement

The purpose of this project is to provide a vehicle for educating a large number of family practice physicians about the role and appropriate use of insulin analogs.

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Target Audience

Primary care practitioners (PCP)/General/Family practitioners

Learning Objectives

- Discuss the benefits that the appropriate insulin analogs provide when treating fasting and postprandial hyperglycemia
- Categorically present the various treatment options that are available for T2DM
- Present advantages and disadvantages of the various therapeutic options and what they address (i.e. fasting or postprandial hyperglycemia)
- Present studies that address combination therapies of insulin with newer agents with available data

Accreditation Statement

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Appropriate Use of Insulin Analogs in an Increasingly Complex Type 2 Diabetes Mellitus (T2DM) Therapeutic Landscape

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Because diabetes mellitus is a progressive disease, treatment should advance with the evolving needs of the patient. Within the last decade, newer insulin analogs have become available to replace standard insulin formulations and novel agents and delivery devices have been developed. Within this complex landscape of treatment options, physicians must develop treatment strategies that will enable patients to achieve glycemic goals.

The American Diabetes Association (ADA) recommends the following goals: glycosylated hemoglobin A1C (A1C) <7.0%; fasting plasma glucose (FPG) between 90 and 130 mg/dL; and peak postprandial glucose (PPG) <180 mg/dL.¹ Basing their recommendations on data from the United Kingdom Prospective Diabetes Study, which demonstrated that the risk for macrovascular and microvascular complications begins to increase at A1C >6.5%, the American Association of Clinical Endocrinologists (AACE) recommends even stricter targets: A1C <6.5%; FPG <110 mg/dL; and PPG <140 mg/dL. Thus, although differing somewhat on the exact treatment goals, both the ADA and AACE affirm the importance of glycemic control.² This article will provide an overview of insulin analogs and newer antidiabetes agents and evaluate their utility in the treatment of type 2 diabetes mellitus (T2DM).



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TABLE 1

OADs used in the treatment of T2DM⁴

OAD Class	Mechanism of Action	A1C Reduction From Baseline	Example(s)
Sulfonylureas and nonsulfonylurea secretagogues	Stimulates insulin secretion	1.5%-2.0%	Glimepiride, nateglinide
Biguanides	Reduces glucose production by the liver	1.5%-2.0%	Metformin
Thiazolidinediones	Improves insulin sensitivity	0.75%-2.0%	Pioglitazone, rosiglitazone
Alpha-glucosidase inhibitors	Delays carbohydrate absorption in the intestine	0.5%-1.0%	Acarbose, miglitol

A1C= glycosylated hemoglobin A1C, OAD = oral antidiabetic drug, T2DM = type 2 diabetes mellitus.

Progression of Therapy in T2DM

■ Lifestyle modifications

A healthy diet and exercise plan constitute the foundation of T2DM treatment. Patients with mild to moderate disease may initially utilize diet and exercise alone to restore effective glycemic control. As diabetes progresses, however, most patients will require pharmacologic intervention. A proactive, target-oriented approach to reaching glycemic goals is essential if patients are to avoid the comorbidities associated with prolonged hyperglycemia.³

■ Oral antidiabetes drug therapy

Pharmacologic therapy for T2DM is typically initiated with an oral antidiabetic drug (OAD). Various types of OADs with differing mechanisms of action are available, and their efficacy is well documented (TABLE 1, THIS PAGE).⁴ As these agents typically lower A1C levels by 0.5% to 1.5%, they are most appropriate for patients with a baseline A1C \leq 9.0%.⁵ Importantly, patients with severe hyperglycemia at initial diagnosis should be treated initially with insulin; upon resolution of the hyperglycemia, OAD therapy may be initiated.

As T2DM progresses, the majority of patients will require more than one agent to control hyperglycemia (FIGURE 1, PAGE 3). In some instances, the use of a second OAD can restore glycemic control. However, OADs cannot compensate for the decline

in pancreatic β -cell function observed in T2DM, and thus most patients will eventually require the addition of exogenous insulin, which is the only therapeutic agent to address the dual defects of diabetes (insulin resistance and insulin deficiency).⁴

■ Insulin therapy

Insulin is acknowledged as a highly effective anti-diabetes medication for lowering hyperglycemia.⁶ Although investigators initially speculated that hyperinsulinemia contributed to atherogenesis and the development of cardiovascular disease (CVD) or other symptoms of metabolic syndrome, more recent evidence suggests that the insulin-resistant state, not insulin itself, contributes to CVD.⁷⁻¹⁰ Specifically, the anti-inflammatory effects of insulin may help control glycemia, dyslipidemia, and epigenetic cellular phenomena and thereby counteract CVD progression.^{9,11-13}

■ Basal insulin therapy

Early addition of insulin to oral therapy, easily initiated with a simple basal insulin regimen providing 24-hour control of FPG, has been shown to improve A1C levels significantly in patients with T2DM (FIGURE 2, PAGE 5).^{3,14} As formulations of insulin vary in timing of onset and duration of action, the dose and number of injections required depend on the formulation used and the level of glycemic

control needed.¹⁵⁻¹⁷ The ideal basal insulin replacement should approximate physiologic insulin secretion as closely as possible and have a duration of action lasting 24 hours, without any periods of pronounced peak activity.

Neutral protamine Hagedorn insulin

Neutral protamine Hagedorn (NPH) insulin is an intermediate-acting insulin with a duration of action of approximately 13 hours (TABLE 2, PAGE 4).¹⁵ NPH insulin is dosed twice daily, which may impact convenience and increase the risk for nocturnal or morning hyperglycemia, thereby potentially decreasing compliance. Additionally, NPH insulin is associated with intersubject pharmacodynamic variability.¹⁵ Newer basal insulin analogs, which require fewer daily doses and are associated with a lower risk of hypoglycemia, are a convenient and effective alternative to NPH insulin. Two insulin analogs are currently available, insulin glargine and insulin detemir.

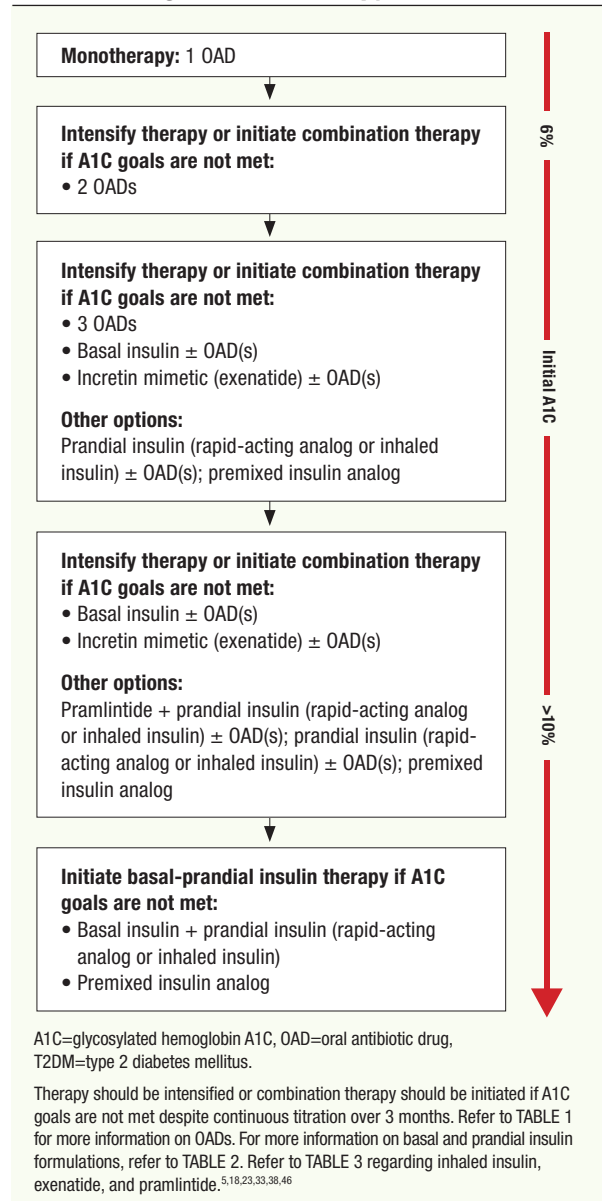
Insulin glargine

Insulin glargine, which can be titrated using a simple algorithm and administered with simple once-daily dosing (TABLE 3, PAGE 6), has an activity profile similar to physiologic insulin secretion.¹⁸ It has no pronounced peak, a 24-hour duration of action, and less intersubject variability than NPH insulin (TABLE 2, PAGE 4).^{15,18} Several trials evaluated insulin glargine versus NPH insulin added to existing OAD therapy. Results found that treatment with either agent resulted in similar improvements in glycemic control, with the majority of patients in both the insulin glargine and NPH insulin groups achieving A1C goals.¹⁸⁻²⁰

Insulin glargine is associated with less nocturnal hypoglycemia compared with NPH insulin, likely due to its 24-hour pharmacokinetic profile.¹⁸⁻²⁰ Furthermore, a meta-regression analysis revealed that at equivalent rates of hypoglycemia, insulin glargine is associated with significantly lower A1C levels compared with NPH insulin.²¹ Consequently, the insulin glargine dose can be increased as needed to achieve target A1C goals with reduced hypoglycemic risk.

FIGURE 1

Progression of therapy in T2DM



Insulin detemir

Insulin detemir activity peaks at approximately 8 hours, has a mean residence time of approximately 14 hours in adults, and exhibits less pharmacokinetic variability compared with NPH insulin (TABLE 2, PAGE 4).²² Addition of NPH insulin or insulin detemir twice daily to existing OAD treatment in patients with T2DM resulted in similar improvements in A1C levels. Furthermore, insulin detemir was associated with

TABLE 2

Basal and prandial insulin formulations used in the treatment of T2DM

Insulin Formulation	Coverage	Duration of Action	Dosing	Special Considerations
NPH insulin ¹⁵	Basal	13 hours	Twice daily	Nocturnal hypoglycemia; morning hyperglycemia; intersubject variability
Insulin glargine ^{15,51}	Basal	24 hours	Once daily	Less risk of hypoglycemia (overall and nocturnal) compared with NPH insulin; once-daily dosing
Insulin detemir ^{22,23,28}	Basal	14 hours	Once or twice daily	Less nocturnal hypoglycemia and less weight gain compared with NPH insulin; most patients require twice-daily dosing
RHI ²⁹	Prandial	6-8 hours	30 minutes premeal	Limited mealtime flexibility
Insulin lispro ³⁰	Prandial	3-4 hours	Up to 15 minutes premeal or immediately postmeal	
Insulin aspart ²⁹	Prandial	3-4 hours	Up to 15 minutes premeal or immediately postmeal	
Insulin glulisine ^{30,31,52}	Prandial	3-4 hours	Up to 15 minutes premeal or up to 20 minutes postmeal	Only rapid-acting agent evaluated in conjunction with a dosing algorithm

NPH = neutral protamine Hagedorn, RHI = regular human insulin, T2DM = type 2 diabetes mellitus.

less nocturnal hypoglycemia and less weight gain compared with NPH insulin.²³ Data comparing the pharmacokinetics and efficacy of insulin glargine and insulin detemir are conflicting.²⁴⁻²⁷ Jungmann recently demonstrated that patients receiving once-daily insulin glargine achieved lower levels of blood glucose compared with patients receiving once- or twice-daily insulin detemir.²⁶ In contrast, Rosenstock et al observed that treatment with either insulin glargine or insulin detemir resulted in similar decreases in A1C levels, a similar proportion of patients achieving goal (A1C <7.0%), and comparable relative risk of overall and nocturnal hypoglycemia.²⁷

When choosing a basal insulin, dosing is one important factor to consider; once-daily dosing may aid in compliance, especially in insulin-naive patients with T2DM. Patients taking NPH insulin or insulin detemir may require 2 injections, typically before breakfast and in the evening within 1 hour before dinner, to achieve clinical efficacy.^{23,28}

■ Prandial insulin therapy

If overall glycemic control or if PPG target levels are not achieved with basal insulin therapy, therapy

with a rapid-acting insulin can be added. Prandial insulin is typically initiated with 1 injection at the largest meal of the day; if necessary, additional injections can be added at other mealtimes to obtain glycemic control. The ideal profile for prandial insulin replacement would blend a rapid onset with a short duration of action, similar to physiologic insulin secretion at mealtimes. Regular human insulin (RHI) has a relatively long onset and must be injected 30 minutes prior to a meal.²⁹ As a result, patients are at increased risk for hypoglycemia if they deviate from their scheduled mealtimes.

Newer rapid-acting insulin analogs, such as insulin glulisine, insulin lispro, and insulin aspart, provide greater dosing flexibility, with an onset of action of approximately 15 minutes, a peak near 60 minutes postdose, and a duration of action of 3 to 4 hours (TABLE 2, THIS PAGE).^{29,30} Insulin glulisine and insulin lispro are both approved for premeal or postmeal administration.²⁹ Additionally, insulin glulisine can be titrated using a simple dosing algorithm: patients receive a fixed dose of mealtime glulisine that is adjusted weekly by 1, 2, or 3 units, depending upon premeal glucose patterns. Patients using this

algorithm achieved similar glycemic control with less symptomatic hypoglycemia compared with patients using the gold standard, carbohydrate counting, which many patients find complex.³¹

Premixed insulin formulations

Premixed insulin or insulin analog formulations combine an intermediate- or long-acting insulin with a short-acting insulin in a fixed-dose regimen and can provide convenience with regard to the number of injections needed for basal-prandial coverage. However, the requirement for strict adherence to mealtimes and exercise schedules and the increased risk of hypoglycemia are important considerations when evaluating their clinical utility.³²

Newer therapeutic options

Inhaled human insulin

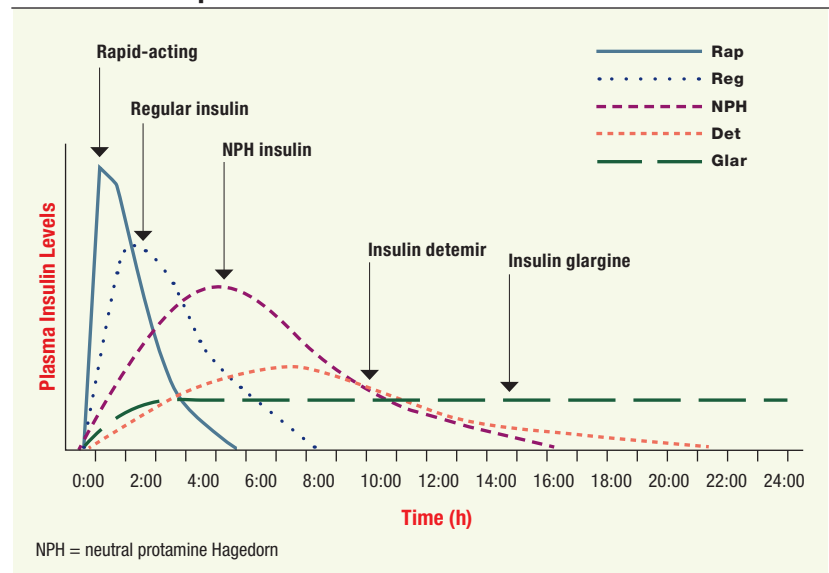
Human insulin inhalation powder was approved in 2006 for prandial coverage in adults with T1DM or T2DM (TABLE 4, PAGE 8). Inhaled insulin can be used in combination with oral agents or basal insulin.³³ Similar to rapid-acting insulin analogs, inhaled insulin has a rapid onset of action and a duration of action comparable to subcutaneously administered RHI and thus may be most appropriate for control of prandial glucose excursions.³³ In a 24-week randomized trial evaluating the safety and efficacy of adding inhaled human insulin or metformin to existing sulfonylurea therapy in patients with T2DM, inhaled insulin treatment resulted in a mean reduction in A1C of -2.17% from baseline in patients with baseline A1C $>9.5\%$ and -1.94%

in patients with baseline A1C $\leq 9.5\%$.³⁴ Hypoglycemia and increased cough were more common in the inhaled-insulin group, while other adverse events and changes in pulmonary function parameters were similar between groups.³⁴ No data are available comparing the efficacy of inhaled insulin with rapid-acting insulin analogs.

Important considerations when using inhaled insulin include dosing, convenience, and patient satisfaction. Inhaled insulin, available as a 1-mg (equivalent to ~ 3 IU subcutaneous RHI) or 3-mg (equivalent to ~ 8 IU subcutaneous RHI) dose, should be titrated based on patient blood glucose monitoring results.³³ Inhaled insulin is contraindicated in patients who smoke, who discontinued smoking within 6 months of initiating therapy, or who have underlying lung disease. In addition, the forced expiratory volume (FEV) should be assessed in all patients prior to initiating therapy. Inhaled insulin is not recommended in patients with a baseline FEV $<70\%$ of predicted value.³³ Some patients may find the inhalation device preferable to injection; however, active patients or those who

FIGURE 2

Time profiles of available insulin formulations¹⁵⁻¹⁷



NPH = neutral protamine Hagedorn
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TABLE 3

A simple algorithm for the titration of insulin glargine

Start with 10 IU/d bedtime basal insulin and adjust weekly	
Mean of Self-Monitored FPG Values from Preceding 2 Days (mg/dL)	Increase in Insulin Dose (IU/d)
≥180	8
≥140 but <180	6
≥120 but <140	4
100-120	2

The treat-to-target FPG was ≤100 mg/dL. Exceptions to this algorithm were 1) no increase in dosage if plasma-referenced glucose <72 mg/dL was documented at any time in the preceding week, and 2) in addition to no increase, small insulin dose decreases (2-4 IU/d per adjustment) were allowed if severe hypoglycemia (requiring assistance) or plasma-referenced glucose <56 mg/dL were documented in the preceding week.

FPG = fasting plasma glucose.

Reprinted from Riddle MC, Rosenstock J, Gerich J; on behalf of the Insulin Glargine 4002 Study Investigators. The Treat-to-Target Trial: randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients.

FPG = fasting plasma glucose.

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travel extensively may find it cumbersome and difficult to transport discreetly owing to its large size relative to insulin pen devices.

Incretin mimetics and dipeptidyl-peptidase IV inhibitors

Incretin mimetics and dipeptidyl-peptidase IV (DPP-IV) inhibitors are 2 new classes of antidiabetes agents. Incretin mimetics promote insulin secretion, decrease glucagon secretion, delay gastric emptying and promote satiety.³⁵ Glucagon-like peptide-1 (GLP-1) is an incretin with a relatively short half-life and is rapidly degraded in the body. One strategy being used to exploit the incretin effect in diabetes treatment is the development of a GLP-1 analog that is resistant to enzyme degradation. A second strategy is to inhibit DPP-IV, the peptidase responsible for GLP-1 degradation. Clinical studies have shown that patients with T2DM have reduced concentrations of active GLP-1, and preliminary study results suggest that both classes of agents may improve β-cell function.³⁶

Exenatide

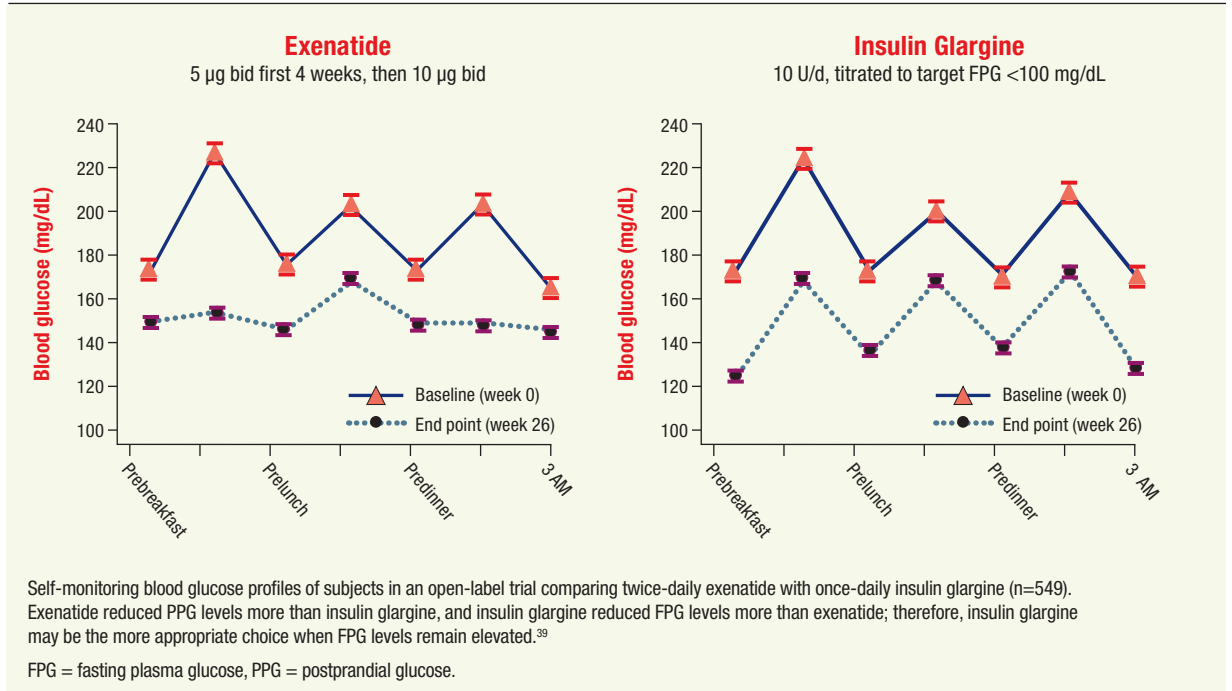
The GLP-1 analog exenatide has a prolonged duration of action compared with endogenous GLP-1 (**TABLE 4, PAGE 8**).^{37,38} Exenatide is indicated for adjunctive therapy in patients with T2DM inadequately controlled with metformin and/or a sulfonylurea and is administered through subcutaneous injection 60 minutes prior to breakfast and dinner.³⁸

In clinical trials, treatment with exenatide 5 µg or 10 µg twice daily reduced A1C from baseline in patients treated with sulfonylurea (-0.46% and -0.86% for the 5 µg and 10 µg doses, respectively), metformin (-0.40% and -0.78%, respectively), or both (-0.6% and -0.8%, respectively).³⁷ Exenatide 10 µg twice daily compared with insulin glargine once daily resulted in similar reductions in A1C (1.1%), similar percentages of patients achieving A1C ≤7.0% (46%-48%), and a similar incidence of hypoglycemia in patients with T2DM who were inadequately controlled with metformin and a sulfonylurea (**FIGURE 3, PAGE 7**).³⁹ In evaluating glucose levels, patients receiving insulin glargine achieved lower FPG values, while patients receiving exenatide achieved lower PPG values; thus exenatide may be best utilized for prandial control.³⁹

Exenatide should be initiated at 5 µg twice daily and can be increased to 10 µg twice daily.³⁸ Positive aspects of exenatide treatment include weight loss and the availability of a fixed dose.³⁷⁻³⁹ Potential limiting factors include cost, the need for twice-daily dosing, gastrointestinal side effects, the increased risk of hypoglycemia, particularly when used in conjunction with a sulfonylurea, and the potential for interactions with oral contraceptives and oral antibiotics.³⁷⁻³⁹ It is unknown whether exenatide will be effective in patients with advanced disease because residual insulin secretion is necessary for exenatide to exert its effects. Exenatide is not a substitute for insulin in insulin-requiring patients, and preliminary data suggest that substitution of basal insulin with exenatide may result in deterioration of glycemic control.^{38,40} Additionally, exenatide is not approved for use in conjunction with insulin, but studies addressing the safety and efficacy of combination therapy are under

FIGURE 3

Open-label trial comparing twice-daily exenatide with once-daily insulin glargine



Adapted with permission from Heine RJ et al. *Ann Intern Med.* 2005;143:559-569. American College of Physicians is not responsible for the accuracy of the translation.

way and suggest that exenatide may allow for a reduction in the insulin dose in some patients.^{40,41}

Liraglutide

Phase 3 trials began in February 2006 for liraglutide, a long-acting GLP-1 analog that has a longer pharmacokinetic half-life relative to exenatide (14 hours vs 2.4 hours, respectively), and its effects on blood glucose are sustained for 24 hours, suggesting that once-daily dosing may be possible.^{35,42} Initial data indicate that treatment with liraglutide results in improved glycemic control and modest weight loss.⁴²

Sitagliptin and Vildagliptin

The oral DPP-IV inhibitor, sitagliptin, was approved in October 2006 and is indicated for use as monotherapy or in combination with metformin or a thiazolidinedione in patients with T2DM. In clinical trials, sitagliptin 100 mg once daily provided significant improvements in A1C, FPG, and PPG levels

($P < 0.001$ vs placebo). Additionally, combination therapy with sitagliptin ± metformin or sitagliptin ± pioglitazone was superior to monotherapy with either metformin or pioglitazone. The overall incidence of adverse events was similar between the sitagliptin and placebo groups.^{36,43}

Vildagliptin, also an oral DPP-IV inhibitor, is in late-stage clinical development and has been shown to improve insulin secretion and sensitivity and glycemic control in patients with diabetes (**TABLE 4, PAGE 8**).⁴⁴ Added to existing metformin treatment in patients with T2DM, vildagliptin 50 mg once daily reduced A1C 0.5% to 0.6% from baseline after 12 weeks, with improvement maintained to week 52.^{44,45} Moderate hypoglycemia occurred in 4 of 56 vildagliptin-treated patients, and body weight did not significantly change in the vildagliptin group during the 12-week trial.⁴⁵

GLP-1 analogs and DPP-IV inhibitors may be dependent on residual insulin secretion to exert their

TABLE 4

Newer therapeutic options for the treatment of T2DM

Agent	Mechanism of Action	A1C Reduction from Baseline	Indication	Dosage
Inhaled human insulin ^{33,34}	Lowers blood glucose levels by stimulating peripheral glucose uptake and inhibiting hepatic glucose production	-1.94% and -2.17% after 24 weeks of treatment in patients with baseline A1C levels ≤9.5% and >9.5%, respectively	Monotherapy or in combination with OADs or basal insulin	Up to 10 minutes premeal
Exenatide ³⁷⁻³⁹	Incretin mimetic; enhances glucose-dependent insulin secretion	0.4%-1.1% after 26-30 weeks of treatment	Adjunctive therapy in patients inadequately controlled with metformin ± sulfonylurea	5-10 µg twice daily within 60 minutes before breakfast and dinner
Sitagliptin ⁴³	DPP-IV inhibitor; increases the half-life of the physiologic incretin GLP-1	0.6%, 0.7%, and 0.9% after 24 weeks of treatment monotherapy, +metformin, or as +pioglitazone, respectively	Monotherapy or adjunctive therapy in patients inadequately controlled with metformin or TZD	100 mg once daily
Vildagliptin ⁴⁵	DPP-IV inhibitor; increases the half-life of the physiologic incretin GLP-1	0.6% after 12 weeks of treatment	Awaiting FDA approval	50 mg once daily added to existing metformin treatment
Pramlintide ⁴⁶⁻⁵⁰	Amylin analog; suppresses postprandial glucagon secretion and regulates gastric emptying	0.6% after 52 weeks of treatment	Adjunctive therapy in patients inadequately controlled on prandial insulin ± sulfonylurea and/or metformin therapy	60-120 µg immediately premeal

A1C = glycosylated hemoglobin A1C, DPP-IV = dipeptidyl-peptidase IV, FDA = Food & Drug Administration, GLP-1 = glucagon-like protein-1, OAD = oral antidiabetic drug, T2DM = type 2 diabetes mellitus, TZD = thiazolidinedione.

physiologic effects and thus may not be appropriate for patients with advanced disease. Additionally, DPP-IV has physiologic activities beyond that of metabolic control. Early studies have implicated DPP-IV in the normal development and function of the immune system, and in vitro studies with DPP-IV inhibitors have shown inhibition of T-cell activity. Furthermore, DPP-IV acts on a number of substrates in vivo, including hormones, neuropeptides, and chemokines.³⁶ Additional studies are necessary to adequately evaluate the impact of DPP-IV inhibitors on physiologic pathways other than glucose control.

Pramlintide

Pramlintide is a synthetic analog of amylin (TABLE 4, THIS PAGE), a naturally occurring hormone secreted by pancreatic β-cells in response to food intake.^{46,47} Pramlintide complements the effects of insulin by suppressing postprandial glucagon secretion and reg-

ulating the rate of gastric emptying.⁴⁷ Administered through subcutaneous injection at mealtimes immediately prior to major meals, pramlintide is indicated for adjunctive therapy in patients with T1DM or T2DM inadequately controlled on prandial insulin with or without concurrent sulfonylurea and/or metformin therapy.⁴⁶

The addition of pramlintide to insulin therapy results in modest reductions in A1C levels: pramlintide 120 µg twice daily or 75 to 150 µg 3 times daily reduced A1C levels by 0.6% after 1 year of treatment in patients with T2DM treated with insulin.^{48,49} Pramlintide was also associated with weight loss and no overall increase in the rate of severe hypoglycemic events.⁴⁸⁻⁵⁰

In patients with T2DM, pramlintide should be initiated at a dose of 60 µg and titrated to a maintenance dose of 120 µg.⁴⁶ Patients should be monitored frequently, and dose reductions in

concomitant short-acting or fixed-mix insulin formulations should be made to minimize the risk of hypoglycemia.⁴⁶ Pramlintide may be most appropriate in obese patients who are insulin-deficient, although more data are needed.

Summary

Effective glycemic control can substantially reduce the micro- and macrovascular complications associated with diabetes. As evidenced by the recent consensus statement and treatment algorithm jointly issued by the ADA and the European Association for the Study of Diabetes, substantive evidence-based research supports the use of OAD regimens and insulin analogs for fasting and postprandial control of glucose. Furthermore, numerous studies have revealed the benefits of early, intensive treatment of hyperglycemia with insulin. Unlike incretin mimetics or DPP-IV inhibitors, treatment with insulin can address the dual physiologic defects of diabetes: insulin resistance and insulin deficiency.

Notwithstanding the promise that newer and emerging agents hold providing effective glycemic control, studies evaluating their long-term efficacy and safety (as monotherapy and in combination therapy), as well as head-to-head comparisons with existing treatments, are necessary to determine the role of these agents in the diabetes treatment algorithm.

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CME POSTTEST

THERE IS ONLY ONE CORRECT ANSWER TO EACH QUESTION.

- 1. A healthy diet and lifestyle should be encouraged in which of the following?**
 - a. Only those patients with a baseline A1C level > 9.0%
 - b. Only those patients who are not compliant with therapy
 - c. Only those patients who fail oral antidiabetes therapy
 - d. All patients with type 2 diabetes mellitus (T2DM)
- 2. Pharmacologic therapy can be initiated in patients with T2DM using:**
 - a. An oral antidiabetes drug
 - b. An amylin analog (pramlintide)
 - c. An incretin mimetic (exenatide)
 - d. A dipeptidyl-peptidase IV (DPP-IV) inhibitor
- 3. The ideal basal insulin replacement would have:**
 - a. Once-daily dosing
 - b. A duration of action lasting 24 hours
 - c. No pronounced peak (flat) activity profile
 - d. All of the above
- 4. Which of the following statements regarding insulin glargine is FALSE?**
 - a. Insulin glargine has a 24-hour duration of action with no pronounced peak.
 - b. Insulin glargine was associated with less nocturnal hypoglycemia compared with NPH insulin in clinical trials.
 - c. Insulin glargine is dosed once daily.
 - d. None of the above
- 5. Which of the following statements regarding insulin detemir is TRUE?**
 - a. Insulin detemir is a short-acting insulin analog.
 - b. Insulin detemir causes excessive weight gain.
 - c. Many patients in clinical trials required twice-daily dosing with insulin detemir.
 - d. Insulin detemir is used for prandial glucose coverage.
- 6. Prandial insulin therapy:**
 - a. Can be added to basal insulin therapy if A1C goals are not at target despite adequate titration
 - b. Should NOT approximate physiologic insulin secretion at mealtimes
 - c. Should be initiated with long-acting insulin analogs
 - d. Should be initiated with 1 injection at the smallest meal of the day
- 7. Please select the FALSE statement:**
 - a. Exenatide is an incretin mimetic.
 - b. Exenatide is a good substitute for insulin in insulin-requiring patients.
 - c. Exenatide is administered by injection.
 - d. Exenatide is administered twice daily.
- 8. Which of the following statements regarding pramlintide is TRUE?**
 - a. Pramlintide is a synthetic analog of amylin.
 - b. Amylin is a naturally occurring hormone that suppresses postprandial glucagon secretion and regulates the rate of gastric emptying.
 - c. Pramlintide dosing ranges from 60 µg to 120 µg immediately prior to major meals in patients with T2DM.
 - d. All of the above
- 9. Please select the FALSE statement:**
 - a. Inhaled human insulin does not require any dosage titration once it is initiated.
 - b. Inhaled human insulin has a rapid onset of action.
 - c. Inhaled human insulin can be used in combination with oral agents or basal insulin.
 - d. Inhaled human insulin is indicated for prandial glucose coverage.
- 10. More data are needed regarding the newer agents AND:**
 - a. Their long-term efficacy and safety
 - b. Their use in combination with basal or prandial insulin analogs
 - c. Both of the above
 - d. Neither of the above

Appropriate Use of Insulin Analogs

in an Increasingly Complex Type 2 Diabetes Mellitus (T2DM) Therapeutic Landscape

POST-ACTIVITY Evaluation and Credit Application

Release date: January 2007

Expiration date: January 2008

To receive continuing education credit for this activity you must complete this Evaluation and Application for Continuing Education Credit

COURSE EVALUATION

I. Please evaluate this educational activity by checking the appropriate box:

Activity Evaluation

Circle the appropriate response
(1 = Excellent; 2 = Very Good; 3 = Good; 4 = Fair; 5 = Poor)

Faculty	1	2	3	4	5
Content	1	2	3	4	5
Facilities	1	2	3	4	5
How well did this activity avoid commercial bias and present content that was fair and balanced?	1	2	3	4	5
What is the likelihood you will change the way you practice based on what you learned in this activity?	1	2	3	4	5
Overall, how would you rate this activity?	1	2	3	4	5

II. Course Objectives

Were the following overall course objectives met? At the conclusion of this presentation, are you able to:

Objective	Yes	Somewhat	No
Discuss the benefits that the appropriate insulin analogs provide when treating fasting and postprandial hyperglycemia			
Categorically present the various treatment options that are available for T2DM			
Present advantages and disadvantages of the various therapeutic options and what they address (ie, fasting or postprandial hyperglycemia)			
Present studies that address combination therapies of insulin with newer agents with available data			

III. Additional Questions

a. Suggested topics and/or speakers you would like for future activities

b. Additional comments

CREDIT APPLICATION

Instructions:

- Applications will only be accepted through January 31, 2008.
- Please anticipate 6-8 weeks to receive your certificate.
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ACCME (Physician)

I certify that I participated in Appropriate Use of Insulin Analogs in an Increasingly Complex Type 2 Diabetes Mellitus (T2DM) Therapeutic Landscape

ATTENDANCE: Please fill in the number of actual hours that you spent on this activity. _____

Date of participation: _____

Number of hours (Max 0.75 hrs) _____

Signature _____

Please submit completed application to:
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