



# Are you up-to-date on DIABETES MEDICATIONS?

Learn how the newest weapons in the arsenal of antihyperglycemic drugs can help your patient manage her disease.

By Donna Scemons, RN, FNP, CNS, MSN



OUR POPULATION is under attack. About 20 million people in the United States have been diagnosed with diabetes mellitus, the fifth leading cause of death in this country. Another 20% are at risk for this deadly disease.<sup>1</sup> (Criteria for diagnosing diabetes appear in *Testing 1, 2, 3.*)

Untreated or improperly treated diabetes is the number one cause of new blindness, renal failure leading to dialysis, and nontraumatic leg amputations. Each of these complications is due to microvascular and macrovascular changes that may be prevented or reduced with appropriate glycemic control.

Medications play a key role in helping patients with diabetes manage hyperglycemia, but keeping up with the latest drugs can be daunting. In this article, I'll discuss the importance of tight glycemic control in patients with diabetes and detail the drugs available to attain it, with special emphasis on the latest additions.

## Diabetes in review

Diabetes mellitus is a chronic systemic disease. The American Diabetes Association (ADA) divides it into four clinical classes<sup>2</sup>:

**Type 1** diabetes is an autoimmune disease possibly triggered by genetic and environmental factors. It's caused by the destruction of pancreatic beta cells that produce insulin. Totally insulin-deficient, the patient needs exogenous insulin to survive.

**Type 2** diabetes, accounting for 90% to 95% of all diabetes in the United States, involves a decreased ability to use the insulin produced in the pancreas.<sup>1</sup> The beta cells maintain some function but become progressively desensitized to blood glucose levels. Decreased insulin sensitivity in the liver and peripheral tissues adds to the problem.

**Gestational** diabetes develops during pregnancy.

**Other types** have various specific causes, such as genetic defects in beta cell function or insulin action, pancreatic disease, or adverse drug reactions.

## Aiming for a target

Large research studies have shown that maintaining blood glucose levels within specific ranges significantly reduces comorbidities and secondary complications of diabetes and improves quality of life. Targeting ranges for fasting and postprandial blood glucose levels and frequently monitoring them help your patient monitor glycemic control throughout the day. The ADA and American College of Endocrinology (ACE) also recommend monitoring hemoglobin A1C (A1C) levels to gauge long-term control.

The ADA recommends that someone with diabetes maintain her A1C level below 7%; the ACE recommends keeping it at 6.5% or less for optimal control.<sup>2,3</sup> (*Aiming for healthy targets* provides details on all recommended ranges.) The patient should have A1C testing at least every 3 months if she's changing therapy or hasn't reached target. Once she's on target, testing twice a year is usually sufficient.

Your patient should work with her diabetes care provider to set goals. Although tight blood glucose control is

recommended for most patients with diabetes, it isn't recommended for children, most older adults with diabetes, or anyone who can't recognize and respond to signs and symptoms of hypoglycemia. Less-intensive glycemic targets may be appropriate for these patients. Tight control is suggested for women with diabetes who become pregnant or women with gestational diabetes, to reduce the incidence of birth defects and other problems.

### Medications to help meet goals

Although some people with type 2 diabetes reach target blood glucose levels with careful meal planning, exercise, and weight management, most also rely on medications. According to the Centers for Disease Control and Prevention, 57% of adults with diabetes manage their disease with oral medications, 12% use both oral medications and insulin, and 16% use insulin only. The rest take neither type.<sup>1</sup> "Managing Diabetes with 'Agent Oral'" and "Unlock the Mysteries of Insulin Therapy" (*Nursing2004*, March) provide a comprehensive review of these drugs.\*

Let's review the traditional drugs used to manage diabetes, then take a close look at recent additions.

**Oral medications.** A person with type 2 diabetes typically begins therapy with one of five classes of oral drugs. Her physiologic characteristics, the drug's site of action, and her response to therapy all help determine which medication is right for her. Over time, the number and type of drugs she takes will change, and she may require insulin therapy as her diabetes progresses. (Learn about current options in *Diabetes drugs and how they work.*)

**Insulin therapy for type 1 diabetes.** Someone with type 1 diabetes requires multiple insulin doses each day. Her regimen may consist of administering a rapid-acting insulin (such as insulin aspart or lispro) or short-acting regular insulin with an intermediate-acting

### Testing 1, 2, 3

A nonpregnant adult in any of these three groups meets the ADA's criteria for diagnosis of diabetes:

1. signs and symptoms of diabetes, such as polyuria, polydipsia, and unexplained weight loss  
+  
a plasma glucose level of 200 mg/dL or greater tested at any time of day without regard to meals
2. a plasma glucose level of 126 mg/dL or greater after fasting 8 hours or more
3. a 2-hour postprandial glucose level of 200 mg/dL or greater during a standard oral glucose tolerance test.

Source: American Diabetes Association.<sup>2</sup>

insulin (such as NPH). Following this regimen, she takes a rapid- or short-acting insulin before the first meal of the day, another before her evening meal, and a dose of NPH at bedtime.

To simulate a more physiologic process, the patient may learn to base her insulin doses on the amount of carbohydrates she consumes at meals, her daily activity, and her total insulin intake over 24 hours. The regimen typically consists of taking aspart or lispro insulin with meals and NPH or glargine at bedtime. Before starting this type of regimen, the patient may record her fasting, premeal, postprandial, and bedtime blood glucose levels and communicate them to her diabetes care provider.

Educate your patient about target

### Aiming for healthy targets

Most adults with diabetes should aim for the following targets to reduce the risk of complications:

- A1C, less than 7%
- capillary plasma glucose level:
  - before meals, 90 to 130 mg/dL
  - peak postprandial level, less than 180 mg/dL
- BP, less than 130/80.

Source: American Diabetes Association.<sup>2</sup>

blood glucose levels, blood glucose monitoring, measuring carbohydrate intake, the effects of carbohydrates and activity on insulin dosing, insulin/carbohydrate ratios, insulin sensitivity, and how all this affects her on a daily basis. "Nutrition for Diabetes—All in a Day's Work" (*Nursing2006*, June) explains how to count carbohydrates and other measures to help her achieve her goals.\*

### Insulin therapy for type 2 diabetes.

Optimal management of blood glucose is the goal of treatment with once- or twice-daily insulin doses or flexible insulin use to meet the needs of active people, such as marathon runners. Once-a-day use in combination with oral agents is appropriate for some patients with type 2 diabetes, but it lacks a basal-bolus cycle. (The duration of action for basal insulin is 14 to 24 hours; for bolus insulin, it's 4 to 10 hours.)

Combination "biphasic" products containing either rapid-acting or short-acting insulin with intermediate-acting insulin are commonly used with type 2 diabetes. NPH or glargine in the evening or combination 70/30 NPH/regular (70% intermediate action/30% short action) before the evening meal is the most common regimen in this type of management.

Even if a patient with type 2 diabetes meets her target with combination oral and insulin therapy, she'll eventually require more exogenous insulin as the pancreatic beta cells continue to deteriorate. Her once-a-day insulin dose will progress to twice a day as she continues oral medications.

Yet another option is to administer rapid- or short-acting insulin before the first meal of the day and NPH before bedtime to manage overnight glucose production. The patient's blood glucose levels during the evening and early morning will determine which schedule is appropriate. Closely monitoring blood glucose levels to individualize treatment is neces-

\*Individual subscribers can access these articles free online at <http://www.nursing2007.com>.

## Diabetes drugs and how they work

Medication, administration route	Mechanism of action	Types
<b>insulin</b> • subcutaneous injection • I.V. infusion • inhalation	replaces or supplements the body's own insulin	<i>Rapid-acting</i> • insulin lispro • insulin aspart • insulin glulisine <i>Short-acting</i> • regular <i>Intermediate-acting</i> • NPH • Lente  <i>Long-acting</i> • ultralente • insulin glargine • insulin detemir <i>Premixed insulins, %</i> • 70/30 NPH/regular • 50/50 NPH/regular • 75/25 lispro protamine/lispro • 70/30 aspart protamine/aspart
<b>sulfonylureas</b> oral	insulin secretagogues: stimulate insulin secretion by the pancreatic beta cells	<i>First generation</i> • acetoheamide • chlorpropamide • tolazamide • tolbutamide  <i>Second generation</i> • glyburide • glipizide • glimepiride
<b>meglitinides</b> oral	insulin secretagogues	• repaglinide • nateglinide
<b>biguanide</b> oral	• reduces glucose production in the liver • enhances tissue response to insulin • improves glucose transport into cells	• metformin
<b>thiazolidinediones</b> oral	increase insulin receptor site sensitivity	• rosiglitazone (See <i>Using Avandia with caution.</i> ) • pioglitazone
<b>alpha-glucosidase inhibitors</b> oral	limit carbohydrate digestion	• acarbose • miglitol
<b>synthetic analogue of human amylin</b> subcutaneous injection	decreases gastric emptying	• pramlintide acetate
<b>incretin mimetic</b> subcutaneous injection	stimulates insulin production in type 2 diabetes	• exenatide

sary for appropriate control and health.

**Continuous insulin infusion.** A patient with diabetes who's hospitalized may require intravenous (I.V.) infusions of regular insulin to maintain glycemic control. Intravenous insulin may be administered preoperatively and postoperatively to maintain tight glucose control in specific situations. For example, it may be administered to a patient undergoing cardiac surgery to reduce the risk of complications and morbidity.

Several studies have shown that keeping blood glucose levels at or near target range during hospitalization improves patient outcomes through reduced nosocomial infection rates, more rapid resolution of infections when they occur, fewer cardiac events, and reduced length of stay.

When your patient is receiving I.V.

insulin, follow facility protocol to monitor her blood glucose level (as frequently as every 15 minutes to every 4 hours) and select the appropriate insulin dosage for infusion. Once her blood glucose levels reach target, she may be switched to subcutaneous insulin injections. If her hyperglycemia

was caused by a transient problem, insulin may be discontinued altogether and she may be discharged on her previously prescribed medication regimen.

**Continuous subcutaneous insulin infusion (CSII).** Used to manage type 1 and type 2 diabetes, CSII is often considered if a patient hasn't achieved ade-

### Using Avandia with caution

As this article went to press, the FDA announced a potential safety issue related to the use of rosiglitazone (Avandia).

Data from clinical trials have shown a potentially significant increase in the risk of myocardial infarction (MI) and cardiac-related deaths in patients taking Avandia, although the FDA hasn't confirmed the clinical significance of the reported risks. Other published and unpublished data from long-term clinical trials of Avandia provide contradictory evidence.

Switching from one diabetes treatment to another also poses risks. The FDA recommends that patients who are taking Avandia, especially those with underlying cardiac disease or a high risk of MI, talk with their diabetes care provider about whether to continue therapy with this medication.

quate glycemic control despite the appropriate use of insulin injections, oral hypoglycemic drugs, and lifestyle changes. A patient who's motivated and capable can learn to use an external insulin pump for intensive diabetes management with more lifestyle flexibility. Most patients using an insulin pump administer a rapid-acting insulin such as insulin aspart.

**Inhaled insulin.** The Food and Drug Administration (FDA) has approved short- or rapid-acting recombinant human insulin in powder form for inhalation by adults. It can be used in conjunction with longer-acting insulin injections to manage type 1 diabetes. For type 2 diabetes, it can be used as monotherapy or in combination with oral hypoglycemic drugs or longer-acting insulins.

Because inhaled insulin is absorbed in the lungs, these patients *shouldn't* use it:

- anyone with an underlying respiratory disease such as asthma, chronic bronchitis, or emphysema, because inhaled insulin may reduce pulmonary function
- anyone who smokes or quit smoking within the last 6 months, because smoking increases drug absorption and the risk of hypoglycemia
- anyone under age 18 because safety and effectiveness haven't been determined for this age-group.

The FDA recommends baseline tests for lung function before a patient starts inhaled insulin therapy, after 6 months of treatment, and then annually. She should also be willing to tell her health care provider if she starts smoking, or intends to, or if she has any problems after starting treatment.

Most important, the patient needs to understand the differences between dosage units of inhaled insulin (milligrams) and other forms (international units). Her diabetes care provider or diabetes educator must discuss a plan for a missed dose and the patient must understand this plan, as double doses

## Who should—and shouldn't—use pramlintide acetate?

According to the FDA, this medication should be prescribed only for patients who meet the following criteria:

- currently using insulin as prescribed but needing better glycemic control
- able to precisely follow the prescriber's instructions
- willing to make frequent follow-up visits with the prescriber
- willing to test blood glucose levels before and after meals and at bedtime
- able to understand how to adjust pramlintide acetate dosing to insulin dosing.

The following patients *shouldn't* use pramlintide acetate:

- anyone who's unaware of or unable to communicate the signs and symptoms of hypoglycemia
- anyone with gastroparesis.

can cause significant harm due to hypoglycemia.

Many drugs affect glucose metabolism and may require insulin dose adjustment and close monitoring of blood glucose levels. They include corticosteroids, diuretics, angiotensin-converting enzyme inhibitors, and beta-blockers. Refer to the package insert for a complete list of drug interactions.

To learn more about inhaled insulin therapy and the administration technique, see "Inhaled Insulin: Breathing New Life into Diabetes Therapy" and "Teach Your Patient to Administer Inhaled Insulin" (*Nursing2007*, January).\*

**Synthetic analogue of human amylin.** Injectable pramlintide acetate (Symlin) is a synthetic form of amylin, a neuroendocrine hormone secreted by the pancreatic beta cells that works with insulin to control postprandial blood glucose levels. It does this by slowing gastric emptying, suppressing glucagon secretion, and modulating appetite to regulate food intake.

Pramlintide acetate is approved for use with insulin in adults who have type 1 and type 2 diabetes. (See *Who should—and shouldn't—use pramlintide acetate?*) Administered subcutaneously, it may reduce the amount of insulin needed at mealtimes. However, it doesn't replace insulin and can't be mixed with any injectable medication, so the patient must take two injections before meals. Teach your patient these points about using this medication:

- To use it safely, she must consume at

least 250 calories or 30 grams of carbohydrate at her meal.

- She should tell her diabetes care provider if she's nursing or pregnant or she may become pregnant. Whether the drug is harmful to a fetus or excreted in breast milk isn't known. Her care provider can help her decide if the benefits outweigh the potential risks.
- If she misses a dose, she should wait and take the next regular premeal dose.
- She shouldn't use pramlintide acetate if the solution looks cloudy.
- She shouldn't take other drugs that could slow stomach emptying while on this medication. Opioids, antacids containing aluminum hydroxide, and lithium are examples.
- Because pramlintide acetate can cause hypoglycemia, she should always keep fast-acting sugar, such as glucose tablets, hard candy, or glucagon, on hand.
- At the start of therapy, she shouldn't drive, operate machinery, or participate in other activities requiring alertness until she learns how she responds to the medication.
- Advise her to avoid alcohol, which may increase the risk of hypoglycemia.
- She shouldn't take the medication if she can't eat or drink, such as before a medical procedure or when illness interferes with her normal meal patterns.
- Nausea is the most common adverse reaction to pramlintide acetate. She's most likely to develop nausea early in therapy, but it usually subsides within a few weeks. Other possible reactions include dizziness, decreased appetite, vomiting, stomach pain, fatigue, and

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indigestion. Advise her to discuss troublesome reactions with her diabetes care provider.

**Incretin mimetic hormone (exenatide).** This synthetic drug stimulates production of insulin in response to elevated fasting and postprandial blood glucose levels. It's specifically indicated for patients with type 2 diabetes who aren't currently using insulin and haven't reached goal or target blood glucose levels with oral medications and diet.

Exenatide (Byetta), available in pen injectors, is administered as a 5-mcg or 10-mcg dose before the first meal of the day and again before the evening meal. If your patient is about to start therapy, teach her these points:

- She may initially have mild to moderate nausea, but the frequency and severity should decrease with continued therapy.
- If she's also taking a sulfonylurea, the prescriber may reduce the sulfonylurea dose to reduce the risk of hypoglycemia.

- This new medication may reduce her appetite, food intake, and body weight, but she shouldn't change her drug regimen without first consulting the prescriber.

- Exenatide isn't a substitute for insulin if she requires insulin therapy.

### New weapons in the arsenal

As new weapons are added to the arsenal of diabetes medications, knowing when they're indicated and how they work will help you teach patients how to use them to achieve and maintain glycemic control. ♦♦

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The author has disclosed that she has no significant relationship with or financial interest in any commercial companies that pertain to this educational activity.

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### Are you up-to-date on diabetes medications?

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## Are you up-to-date on diabetes medications?

**GENERAL PURPOSE** To provide nurses with an overview of current medications available to treat type 1 and type 2 diabetes.

**LEARNING OBJECTIVES** After reading the preceding article and taking this test, you should be able to: **1.** Indicate signs and symptoms of diabetes. **2.** Identify the medications currently available to treat diabetes. **3.** Indicate the importance of tight glycemic control.

**1. Untreated or improperly treated diabetes is the primary cause of all the following complications except**

- a. new blindness.
- b. hepatitis.
- c. nontraumatic lower-extremity amputations.
- d. renal failure.

**2. Destruction of pancreatic beta cells that produce insulin causes**

- a. type 1 diabetes.
- b. type 2 diabetes.
- c. secondary diabetes.
- d. gestational diabetes.

**3. Which type of diabetes accounts for 90% to 95% of all cases in the United States?**

- a. type 1
- b. type 2
- c. gestational
- d. secondary

**4. Which blood test is recommended to gauge long-term glycemic control?**

- a. A1C
- b. fasting blood glucose
- c. random blood glucose
- d. postprandial blood glucose

**5. How often should a patient have A1C testing once she's reached target levels?**

- a. every 3 weeks
- b. every 6 weeks
- c. every 3 months
- d. every 6 months

**6. What capillary plasma glucose level should most adults with diabetes aim for?**

- a. 50 to 80 mg/dL before meals
- b. 90 to 130 mg/dL before meals
- c. 190 to 200 mg/dL peak postprandial
- d. 200 to 210 mg/dL peak postprandial

**7. Which of the following is a rapid-acting insulin?**

- a. regular insulin
- b. NPH
- c. insulin lispro
- d. Lente

**8. Which medication stimulates insulin secretion by the pancreatic beta cells?**

- a. metformin
- b. insulin lispro
- c. miglitol
- d. chlorpropamide

**9. Which medication reduces glucose production in the liver and improves glucose transport into the cells?**

- a. metformin
- b. pioglitazone
- c. acarbose
- d. pramlintide acetate

**10. What's the administration route for exenatide?**

- a. oral
- b. subcutaneous
- c. I.V.
- d. inhalation

**11. Which statement about continuous I.V. infusion of regular insulin during hospitalization is correct?**

- a. It may be used before and after surgery to control blood glucose levels.
- b. It improves patient outcomes but doesn't affect nosocomial infection rates.
- c. It requires monitoring blood glucose levels every 6 to 8 hours.
- d. The patient should be switched to subcutaneous pioglitazone injections once her blood glucose levels reach target.

**12. How is continuous subcutaneous insulin infusion typically used?**

- a. before insulin injections and administration of oral drugs
- b. by patients who want to avoid injections
- c. with a pump administering a long-acting insulin
- d. when insulin injections, oral drugs, and lifestyle changes are ineffective

**13. Which statement about inhaled insulin is correct?**

- a. It may reduce pulmonary function.
- b. It's recommended for patients under age 18.
- c. The patient should have baseline liver function tests before starting therapy.
- d. Cigarette smoking decreases drug absorption.

**14. Which statement about injectable pramlintide acetate (Symlin) is correct?**

- a. The solution is normally cloudy.
- b. It's mixed with injectable medications before meals.
- c. To use it safely, the patient must consume at least 250 calories at her meal.
- d. Double the premeal dose if a dose was missed.

**15. Which statement about exenatide is correct?**

- a. It's indicated for someone with type 1 diabetes who hasn't reached target goals with oral medications.
- b. It's administered in 1.5- to 2-mcg doses before each meal.
- c. It's a substitute for insulin in type 1 diabetes.
- d. Nausea should decrease with continued therapy.



### ENROLLMENT FORM *Nursing2007, July, Are you up-to-date on diabetes medications?*

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**C. Course Evaluation\***

- 1. Did this CE activity's learning objectives relate to its general purpose?  Yes  No
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