

INHALED INSULIN

Breathing new life into diabetes therapy

FERNANDO LOPEZ, 49, was diagnosed with type 2 diabetes 5 years ago. At 5 feet 11 inches (178 cm), he weighs 242 pounds (110 kg) and has a body mass index (BMI) of 33.7 kg/m² (30 kg/m² or more indicates obesity). He takes metformin (Glucophage) and glyburide (Glynase) twice a day, but his fasting blood glucose levels range from 165 to 195 mg/dL (recommended range for adults with diabetes, 90 to 130 mg/dL). His hemoglobin A1C (A1C) level is 9.9% (target range for someone with diabetes, 7% or less). His health care practitioner has been urging Mr. Lopez to start insulin therapy, but he doesn't want to give himself daily injections.

Now he has reason to reconsider. The introduction of inhaled short-acting human insulin (Exubera) gives adults with diabetes mellitus an injection-free option for managing their disease. In this article, we'll explain what you need to know about this new insulin form so you can give Mr. Lopez the information he needs to make educated decisions about his therapy.

Replacing injected doses, supplementing other therapies

Many patients with type 2 diabetes need to take exogenous insulin, either alone or with other therapies, to help maintain their blood glucose levels within the normal

Get up to snuff on this new treatment so you can help patients with diabetes explore all their options.

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range. This helps prevent microvascular and macrovascular complications of hyperglycemia, including peripheral and autonomic neuropathy, retinopathy, and nephropathy. Everyone with type 1 diabetes needs exogenous insulin to survive. Until the introduction of inhaled insulin, exogenous insulin had to be injected or infused to reach the bloodstream.

Approved for use before meals by people age 18 or older with type 1 or type 2 diabetes, inhaled short-acting insulin can be used in conjunction with injected intermediate- or long-acting insulin, with oral glucose-lowering drugs, or alone with dietary changes. An adult with type 1 diabetes must always use it in conjunction with longer-acting injected insulin.¹

Unique form, new challenges

Supplied as a white powder, inhaled insulin is administered through a special inhaler. A primary difference between this form and injected insulin is dosing, which poses patient-teaching chal-

lenges and a risk of errors.

Inhaled insulin is packaged in "blisters" containing unit doses of 1 mg or 3 mg. The 1-mg dose is equivalent to about 3 international units of subcutaneously injected regular insulin; the 3-mg dose is equivalent to about 8 international units. Carefully teach your patient how to calculate doses and make sure he understands the differences between the two types. (See *Guide to initial premeal inhaled insulin dosing* for details.) Emphasize that he must use the blister packets exactly as prescribed to prevent dosing errors. For example, he could get an overdose if he uses three 1-mg blisters in place of one 3-mg blister.

The onset of action for inhaled insulin is 10 to 20 minutes, which is more rapid than that of either regular or lispro subcutaneous insulin, so the patient should take it no more than 10 minutes before meals to prevent hypoglycemia. (See *Why absorption is rapid.*) Inhaled insulin reaches peak effectiveness within 2 hours and remains effective for about 6 hours.

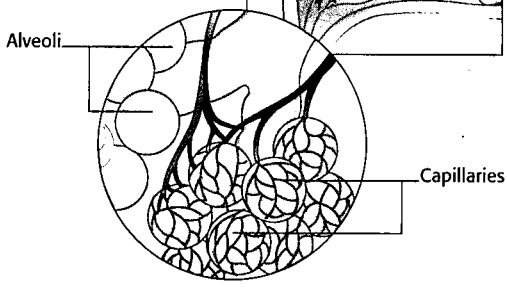
Safe glycemic control

Clinical trials of 2,500 patients have shown comparable glycemic control when inhaled insulin was substituted for subcutaneous injections of short-acting insulin or taken with oral agents.¹ Scientific studies examining the safety of

Why absorption is rapid

Inhalation is a good way to get insulin into the bloodstream. The large surface of the alveoli—comparable in size to a tennis court—is rich with capillaries and perfused by 5 liters of blood each minute. Thin alveolar membranes allow rapid transport of insulin into the blood without excessive breakdown by enzymes.

However, in smokers the alveolar capillary membrane is more permeable, so insulin is absorbed more rapidly. Patients who smoke or who've stopped smoking in the past 6 months have two to five times more drug exposure and a significant risk of developing hypoglycemia.⁷



inhaled insulin therapy in patients with type 1 and type 2 diabetes have produced these findings:

- Patients with *type 1 diabetes* taking twice-daily doses of medium- or long-acting insulin and using inhaled insulin before meals achieved glycemic control comparable to that of patients using basal injections and premeal injections of short-acting insulin.²
- Patients with *type 2 diabetes*

pulmonary disorder (forced expiratory volume in 1 second [FEV₁] less than 70% of predicted value) shouldn't use it because it may reduce pulmonary function. Anyone who smokes or quit smoking within the past 6 months isn't an appropriate candidate either because smokers absorb inhaled insulin faster, which raises the risk of hypoglycemia.

To detect undiagnosed pul-

monary disease before a patient starts inhaled insulin therapy and to monitor for decreased pulmonary function during long-term use, the Food and Drug Administration recommends pulmonary function testing before he starts therapy, 6 months later, and then annually. He should be tested more frequently if he develops signs and symptoms such as cough, dyspnea, or wheezing.

Pulmonary status plays a vital role

Although an amazing breakthrough in diabetes therapy, inhaled insulin isn't for everyone. Its effectiveness and safety in patients under age 18 haven't been established.

And anyone with a

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Mr. Lopez, who quit smoking 2 years ago and doesn't have a history of pulmonary problems, is thinking about starting inhaled insulin therapy and undergoes pulmonary function testing. His FEV₁ is 85%, so he can safely administer insulin into his lungs.

Mr. Lopez's serum A1C levels have been tested periodically to gauge his glycemic control. The most accurate way to assess long-term control, the A1C level measures average blood glucose over a 2- to 3-month period. The American Diabetes Association recommends maintaining the A1C level below 7% as the optimal level for someone with diabetes.⁴

However, both the American College of Endocrinologists and the International Diabetes Federation recommend keeping the A1C level below 6.5% for optimal control.^{5,6} At 9.9%, Mr. Lopez's A1C level reflects inadequate glycemic control and the need for better treatment. He agrees to start inhaled insulin therapy.

His health care practitioner discontinues glyburide and pre-

Guide to initial premeal inhaled insulin dosing

Patient weight (kg)	Patient weight (lbs)	Initial dose/meal	1-mg blisters (number)	3-mg blisters (number)	Approximate equivalent dose, subcutaneous insulin (international units)
30 - 39.9	66 - 87	1 mg	1	—	3 units
40 - 59.9	88 - 132	2 mg	2	—	6 units
60 - 79.9	133 - 176	3 mg	—	1	8 units
80 - 99.9	177 - 220	4 mg	1	1	11 units
100 - 119.9	221 - 264	5 mg	2	1	14 units
120 - 139.9	265 - 308	6 mg	—	2	16 units

Source: Exubera package insert.¹

scribes 5 mg of inhaled insulin (based on his weight) 10 minutes before each meal and metformin, 1,000 mg, twice daily. He advises Mr. Lopez to self-monitor his blood glucose levels before meals and record the results.

He also recommends consultation with a dietitian for nutritional analysis and encourages Mr. Lopez to exercise at least 30 minutes a day. He should return for follow-up in 4 weeks.

Preparing your patient for a new world

To enter the world of inhaled insulin therapy, Mr. Lopez must understand the implications and demonstrate his ability to safely

signs and symptoms. Remind him that because inhaled insulin takes effect so fast, he could become hypoglycemic if he doesn't eat within 10 minutes of taking a dose.

- Assess his ability to solve problems, such as adapting insulin doses in response to hypoglycemia, hyperglycemia, illness, stress, and missed meals.
- Teach him that he'll need to have periodic pulmonary function tests to make sure the therapy isn't causing lung problems.
- Inform him that a cough is a common adverse reaction to inhaled insulin, but it should improve as therapy progresses.¹ Other adverse reactions include sinusitis and dry mouth. Tell him

Anyone with a pulmonary disorder shouldn't use inhaled insulin, and anyone who smokes or quit smoking within the past 6 months isn't an appropriate candidate either.

administer doses. Safeguard his approach to therapy with the following measures:

- Teach him the proper technique for using the insulin inhaler. (For a step-by-step review, see "Teach Your Patient to Administer Inhaled Insulin," starting on the next page.)
- Go over the prescribed dosage with him and emphasize the need to use the blisters as prescribed. For Mr. Lopez, the prescribed dose calls for one 3-mg blister and two 1-mg blisters before each meal. He should continue taking his oral medication as prescribed.
- Have him demonstrate his ability to monitor his blood glucose level and interpret the results. Explain that initially, he should monitor more frequently than usual and adjust his insulin doses accordingly.
- Teach him that hypoglycemia is the most common adverse reaction to inhaled insulin and review the

to report any new, unusual, or bothersome signs and symptoms to his health care practitioner.

- Caution your patient not to smoke while on inhaled insulin therapy. Tell Mr. Lopez to immediately contact his practitioner if he starts smoking again so a different medication can be prescribed.

If you care for a woman with diabetes who's pregnant or planning to become pregnant, she should inform her practitioner right away. The safety of inhaled insulin in pregnancy hasn't been fully established and it's excreted in breast milk. Her practitioner may prescribe adjustments in her injected insulin dosing, food plan, and exercise regimens instead.

Motivated by improvement

Four weeks after starting inhaled insulin therapy, Mr. Lopez sees his health care practitioner for follow-

up. Weighing 238 pounds (108 kg), he reports fasting blood glucose levels ranging from 150 to 185 mg/dL. A check of his A1C level indicates 9.2%. His glycemic control has improved, but it's still far from ideal.

The practitioner recommends that he continue therapy with metformin and inhaled insulin along with the dietary changes and exercise regimen he's been following. Mr. Lopez will monitor his blood glucose level before each meal and may reconsider adding injected basal insulin to his treatment plan after his next scheduled visit. Thanks to inhaled insulin therapy, he's improved his glycemic control and gained motivation to better manage his diabetes. ◀▶

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