

RX CARE Fred Gebhart, Contributing Editor

Inhaled insulin appears to be on the rebound



Inhaled insulin may be on the way back.

That's the hope at MannKind, a California-based biopharmaceutical company developing a rapid-acting inhaled insulin called Afrezza (insulin human rDNA origin). The company has a New Drug Application under review by FDA and hopes to receive marketing approval toward the end of 2010. The only inhaled insulin to be approved for the U.S. market was withdrawn in 2007 for lack of interest.



Peter Richardson

"Being inhaled instead of injected is a real convenience for the patient, but it's also a means to an end," said MannKind Corporate Vice President and Chief

Scientific Officer Peter Richardson, MRCP. "The pharmacokinetics are vastly improved over regular rapid-acting insulins."

Afrezza is an ultra-rapid mealtime insulin delivered with a high-resistance inhalation device about the size of a whistle. A single-dose cartridge is loaded into the inhaler and taken at the beginning of a meal. Peak serum levels are reached in 12 to 14 minutes, Dr. Richardson noted, which mimics the release of endogenous insulin in healthy individuals. About 80% of Afrezza is metabolized within 3 hours of administration compared to 30% of injected rapid-acting insulin. The rapid onset and disappearance of active drug are responsible for improved clinical response.

"Standard mealtime insulin therapies are effective in managing blood sugars but are known to cause weight gain and severely low blood-sugar levels," said Philip Raskin, chair of biomedical research, University of Texas Southwestern Medical School, Dallas, speaking at the American Association of Clinical Endocrinologists annual meeting earlier this year. "Our

study shows that treatment regimens incorporating Afrezza offer glycemic control comparable to convention regimens with the added benefits of weight loss and less incidence of hypoglycemia."

Whether potential weight loss and lower risk for hypoglycemia will bring FDA approval and commercial success are still unknown. Clinical trial data show similar reductions in hemoglobin A_{1c} levels between Afrezza and conventional insulin following a 2-year prospective study. But the improvements in weight and hypoglycemic events were small.

Patients showed a statistically significant difference in weight with a loss of 0.59 kg for Afrezza versus a 1.38-kg gain for standard therapy. Afrezza patients had a 61.8% incidence of hypoglycemic events versus 66.05% for patients on standard therapy.

MannKind is hoping the clinical advantages of its inhaled product are enough to overcome memories of Exubera, one of the biggest flops the diabetes world has seen. The inhaled product was introduced by Pfizer with great fanfare in 2006 and withdrawn

a year later because of poor sales. Novo Nordisk and Eli Lilly stopped their own inhaled insulin development projects in 2008 and 2009 respectively. That left MannKind as the last company standing in the world of inhaled insulin.

Assuming that Afrezza receives FDA approval, the company plans to launch with 2 doses, 4- and 8-unit equivalents. Higher doses will follow if the initial submission is approved. Most patients need the equivalent of 4 to 16 units, Dr. Richardson said.

The biggest initial market for Afrezza is likely to be patients with type 2 diabetes who still have endogenous insulin production. The ultra-rapid action means patients do not need to titrate dosing as closely as with injected insulin and do not need to count carbs to maintain glycemic control.

Patients with type 1 diabetes must maintain a background level of insulin and titrate mealtime insulin. An insulin pump plus Afrezza is the most effective combination, he said.

Pricing has not been set, Dr. Richardson added, but will be comparable to that of other rapid-acting insulins. **DT**

