4 Diabetes Drugs Are Seen Raising Hope and Profit

Even as diabetes rates reach epidemic levels worldwide, four new drugs are generating optimism among doctors as well as Wall Street analysts.

New drugs alone will not reverse rising rates of Type 2 diabetes, a condition that affects about 20 million Americans and is closely tied to obesity and lack of physical activity. And doctors caution that for the foreseeable future, diabetes will remain a progressively worsening disease that can cause devastating complications.

But doctors say the new drugs are important additions to the treatment arsenal because they work differently from existing diabetes medicines and have relatively mild side effects.

One of the four treatments, Byetta, given by injection, is already on the market. Another, Exubera, an inhalable form of insulin, has been approved and will reach pharmacies next month. The other two, Galvus and Januvia, both taken as pills, are awaiting approval from the Food and Drug Administration, which analysts expect by early next year.

Byetta, introduced in June 2005, has stirred especially high hopes. The drug causes significant weight loss in many patients — in contrast to most existing diabetes treatments, which cause weight gain that can potentially worsen the disease. In addition, some data in animal studies hints that Byetta may help the pancreas regrow the cells that produce insulin, a crucial process in slowing the course of diabetes.

Byetta has become so popular that its makers, Amylin Pharmaceuticals and Eli Lilly, are having trouble meeting demand for it. Last week, the companies began asking doctors not to start patients on Byetta until a new manufacturing plant goes into operation, a process that may take several months.

The new drugs will probably cost $1,500 to $2,000 a year per patient, more than existing treatments, analysts say. Still, Byetta, won coverage relatively easily from most insurers, and Galvus and Januvia will probably follow because the complications of diabetes are so expensive, making drug treatment relatively cost-effective, said Richard Evans, an analyst at the Sanford C. Bernstein & Company investment bank.

Mr. Evans said that Exubera might have a harder time winning insurance coverage, since it was merely a new form of an existing treatment. Injectable insulin typically costs about $1,200 a year per patient.

Patients with Type 2 diabetes slowly lose the ability to produce insulin, a hormone secreted by the pancreas that controls the amount of sugar in the blood, even as their bodies grow steadily more resistant to the insulin they do make. The complications of late-stage diabetes can be devastating, including blindness and amputations.

Current diabetes drugs work by lowering blood sugar, either by sensitizing the body to insulin or by encouraging the pancreas to make more insulin. But over time, the conventional therapies tend to lose their effectiveness, and most patients must eventually inject themselves with insulin. That is why the new drugs, with their new approaches, are generating such interest.

Galvus, from the Swiss drug company Novartis, and Januvia, from Merck, raise the levels of a naturally occurring hormone that is released in the stomach and intestines during eating. The hormone, called GLP-1, causes the pancreas to produce more insulin while simultaneously discouraging the liver from producing sugar.

Both Galvus and Januvia, which are sometimes called gliptins, appear to have few side effects and work well with existing diabetes drugs, according to papers presented at the A.D.A. conference. While the F.D.A. has still to finish its review of the drugs, they are almost certain to be approved, Mr. Evans of Sanford Bernstein said. Doctors are optimistic, too.

Galvus and Januvia do not appear to be quite as potent at lowering blood sugar as metformin, the existing first-line diabetes drug. But because of their mild side effects, they will probably be given as an adjunct to metformin, replacing an older group of diabetes drugs — known as sulfonylureas — that are given to patients as a second- or third-line treatment, Dr. Zonszein and other doctors said.

The sulfonylureas cause weight gain in many patients and have a high risk of hypoglycemia, or low blood sugar, a potentially dangerous condition that can occur when insulin levels rise too quickly.

The fourth new drug is Exubera, Pfizer's inhalable insulin, which the F.D.A. approved in January and Pfizer plans to begin marketing this month. Insulin, the standard treatment for late-stage diabetes since the 1920's, is the most potent method of controlling blood sugar and is used by about five million Americans every day.

But until now it has been available only via injection. Pfizer argues that Exubera will attract patients who should be taking insulin but have not wanted to inject themselves.

"No other medicine can get all patients to their goals as insulin can," said Dr. Michael Berelowitz, a senior vice president of Pfizer who is an endocrinologist.

Still, some other doctors and analysts say that Exubera's benefits have been overstated, especially because clinical trials have shown that the drug slightly reduces patients' ability to breathe.

"Patient and doctor will have to weigh very carefully what the benefit and the risk really is," Dr. Buse said.

The success of Byetta, meanwhile, has caused some doctors to question whether diabetes patients fear injections as much as Pfizer claims. Like insulin, Byetta must be injected. But unlike insulin, Byetta causes significant weight loss in many patients and seems to pose very little risk of causing hypoglycemia. Byetta's most common side effect is nausea, which can be severe.

Eli Lilly and Amylin, which jointly manufacture Byetta, have not advertised Byetta to consumers, instead marketing it directly to doctors. Still, demand for the drug has soared since last year, growing faster than either analysts or the companies had expected. About 200,000 patients now take Byetta, the companies say, and analysts expect sales of close to $400 million this year.

Meanwhile, the companies are testing a version of Byetta that would need to be injected only once a week, instead of daily. If approved, that drug, currently called exenatide LAR, will easily top $1 billion in annual sales, analysts say.

Dr. Alan Garber, a professor of medicine at Baylor University, said that patients do not mind injecting Byetta to benefit from its weight loss effects. In addition, some animal studies appear to show that Byetta may cause the pancreas to regrow beta cells, which produce insulin, Dr. Garber said. Dr. Garber has not consulted for Lilly or Amylin.

"I'd love to have the data that conclusively shows that this has long-term benefits on people's beta cell function and mass," he said. For now, the theory remains unproved, he said.

Still, Dr. Garber, the Baylor professor, said he hoped that Byetta, especially when given to patients with relatively early-stage diabetes, might be able to halt the progression of the disease or even reverse its course.

"That has the potential to fundamentally change the diabetes paradigm," he said.