new & improved meds

Pharmacy shelves and the approval pipeline are packed with new medications for all types of diabetes, according to our experts.

BY **Hope S. Warshaw, R.D., CDE**
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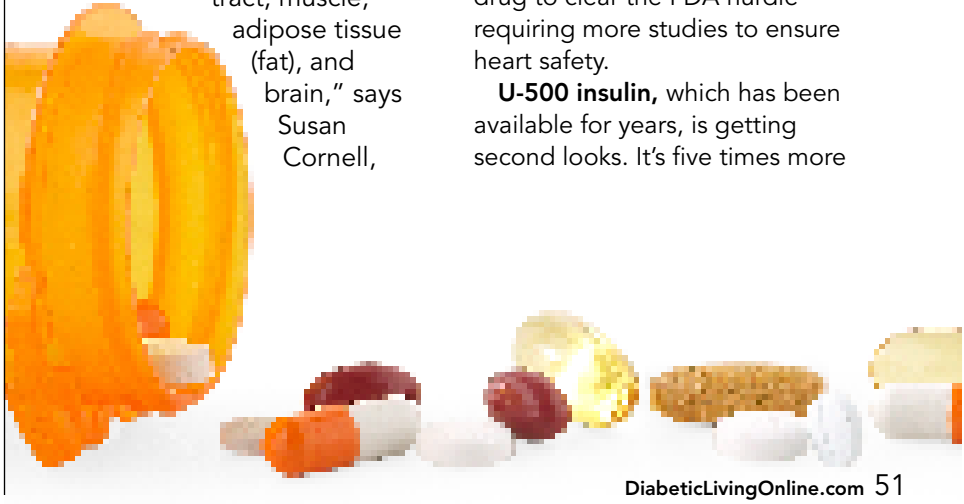
"Efforts to develop and approve blood glucose-lowering medicines for type 2 diabetes are at an unprecedented high," says Kelly L. Close, PWD type 1, president of Close Concerns, Inc., a health care information company, and editor-in-chief of e-newsletter *diaTribe* (**diatribe.us**). "No surprise—so are the numbers of people with type 2 and the need for new therapies."

The need, the numbers, and the understanding that type 2 is more than just a glucose and insulin problem have revved the drug-development engines, with some likely benefits for type 1 diabetes, too. "We now know that six or more organs are involved in glucose control, including the pancreas, liver, gastrointestinal tract, muscle, adipose tissue (fat), and brain," says Susan Cornell, Pharm.D., CDE, assistant professor of pharmacy practice at Midwestern University Chicago College of Pharmacy in Downers Grove, Illinois.



In your pharmacy

New

Cycloset, the first in a new class of drugs, is a pill containing quick-release bromocriptine mesylate. Approved by the U.S. Food and Drug Administration in 2009, it's just making its way onto drugstore shelves. The pill, taken once a day within two hours of waking, restores the brain-based hormone dopamine to normal activity by resetting your circadian rhythm. This action lowers blood glucose. It was the first blood glucose-lowering drug to clear the FDA hurdle requiring more studies to ensure heart safety.

U-500 insulin, which has been available for years, is getting second looks. It's five times more

concentrated than the common U-100 type. Experts are experimenting with U-500 for people who need large amounts of insulin by injections or a pump, such as those who are overweight and/or have significant insulin resistance. Red flags, according to Laura Shane-McWhorter, Pharm.D., CDE, professor of pharmacotherapy at University of Utah College of Pharmacy in Salt Lake City, are its longer action time and concentration, both of which can cause dosing confusion. She advocates a treatment plan that details ways to respond if too much U-500 insulin is given mistakenly.

Improved

Incretin mimetic liraglutide (Victoza) adds one more drug to this class of injectables, also known as GLP-1 analogs. They stimulate insulin output, decrease glucagon output, and lower after-meal glucose rise. By doing so, these drugs decrease appetite and food intake. To date they have the best track record of any blood glucose-lowering drug in helping people with type 2 trim pounds. Victoza's virtue? It's taken once a day. (Byetta, taken twice a day, has been available for several years.) You're likely to see more drugs in this class and approval from the FDA for their use with basal insulin. (New uses for already-approved drugs require additional studies and approval.)

DPP-4 inhibitor saxaglipton (Onglyza) is the second entry in this class; sitagliptin (Januvia) was first. You'll recognize this class of pills by the common "gliptin" suffix. These drugs work on the gut by slowing the breakdown of the DPP-4 enzyme, which in turn slows the rate at which food speeds through the gastrointestinal tract. The actions of DPP-4 inhibitors are similar to incretin mimetics but don't have quite the oomph in blood glucose-lowering power and weight loss.

Also new is Kombiglyze, the first DPP-4 inhibitor combination drug. It contains saxagliptin and extended-release metformin.

On the horizon

New

Sodium-glucose transporter 2 (SGLT-2) inhibitors would be the first drug class to target blood glucose-lowering action on the kidneys. Several are nearing the FDA finish line, and others are in companies' pipelines. Their common suffix is "gliflozin," with full names such as dapagliflozin and canagliflozin. SGLT-2 inhibitors block a transporter protein that returns glucose to the bloodstream after it's filtered through the kidneys. Blocking this protein causes more glucose to be flushed out in the urine. On their own the medicines don't cause low blood sugar (hypoglycemia) or weight gain. The SGLT-2 inhibitors are likely candidates for combo drugs and also may be useful in treating type 1 diabetes, Close says.

Improved

DPP-4 inhibitors alogliptin and **linagliptin** may be approved before the year's end. Linagliptin is the first DPP-4 inhibitor with a twist—it's cleared from the body mainly through the liver, not through the

kidneys. This is a plus because about 40 percent of PWDs, especially people with high blood pressure and 10 years or more of diabetes, are estimated to have chronic kidney disease.

Extended-release exenatide (Bydureon), an incretin mimetic, was poised for approval at the end of 2010, but the FDA requested more information and an additional study related to its safety for the heart. The exciting plus of Bydureon: just one weekly injection.

Fast-acting insulins fill a need in both type 1 and type 2 diabetes because the available rapid-acting insulins aren't fast enough to control postmeal blood glucose rise. To this end, MannKind has been trying to get inhalable Afrezza on the market. The FDA, however, has again requested additional studies of this nasal insulin delivered through a fits-in-your-hand inhaler device. It's designed to be taken before meals to lower blood glucose immediately after eating—a fast start and quick finish hold the promise of reducing hypoglycemia. Afrezza, if approved, would be paired with an injectable long-acting insulin or other long-acting medicine. Another fast-acting insulin sent back to the drawing board by the FDA is Linjeta (formerly called VIAject).

Long-acting basal insulin, the insulin that regulates blood glucose between meals and overnight, is the focus of new formulations at the three major worldwide insulin manufacturers. Novo Nordisk may be closest to the finish line with Degludec, as well as a concentrated U-200 formulation for people taking more than 80 units a day. Sanofi-aventis is working on technology to reduce injection frequency, and Lilly is working on two basal insulins.

Your prescription

At diagnosis PWDs type 2 have, at best, just half of their dwindling insulin-making pancreatic beta cells left, says Richard Bergenstal, M.D., executive director of the International Diabetes Center at Park Nicollet in Minneapolis. Aggressively preserving your remaining beta cells is key for glucose control. (Currently, we don't have a way to halt the autoimmune attack on beta cells and preserve them in type 1 diabetes.) Here's how to take control:

- **Talk to your provider about the best starting drug for you.** Most guidelines suggest starting with a low dose of metformin, which decreases insulin resistance and improves fasting blood glucose.
- **Ask about next steps.** If you don't hit your glucose and A1C targets in 2–3 months, your provider should progress your amount and/or type of medicine.
- **Do your best to follow a healthful eating plan and to be physically active.** Glucose-lowering medicines work best meshed with a healthful lifestyle. You may be able to take lower doses of fewer meds over the years. Plus, you'll feel better, Cornell says.

Hope Warshaw, R.D., CDE, coauthor of *Real Life Guide to Diabetes* (American Diabetes Association, 2010) is a *Diabetic Living* contributing editor.