There are many medications to treat diabetes, and the list continues to grow. Specifically, there are 13 classes of diabetes medications and several drugs within each class. See Table 1 for the full list. With several new medications approved and others on the horizon, it can be very hard to keep up! This article will describe updates in diabetes therapies over the past year and what may be coming in the pipeline.

**BCG Vaccine for Type 1 Diabetes**

There has been a lot of hype about the BCG vaccine that is used to prevent tuberculosis. A prospective, randomized, controlled trial by Kühtreiber and colleagues printed in *NPJ Vaccines* and presented at ADA2018 demonstrated a statistically significant A1C reduction after 5 years and 8 years with 2 doses of the BCG vaccine given 4 weeks apart. Headlines were coming out saying “BCG vaccine can reverse type 1 diabetes to almost undetectable levels.” What these headlines failed to mention is that all patients were still injecting insulin at the end of the study and there were 9 patients retained at the 5-year point and only 3 patients at the 8-year mark. The ADA and JDRF came out with a joint statement saying these results must be interpreted with caution. Bottom line—please don’t recommend this vaccine to your patients to “cure” their diabetes.

### Table 1. Drug Classes for Diabetes

- Biguanide
- Sulfonylureas
- Meglitinides
- Thiazolidinediones (TZDs)
- Dipeptidylpeptidase-4 (DPP-4) inhibitors
- Glucagon-like-peptide-1 (GLP-1) receptor agonists
- Sodium glucose cotransporter-2 (SGLT-2) inhibitors
- Bile acid sequestrants
- Dopamine-2-agonist
- Amylin mimetic
- Alpha-glucosidase inhibitors
- Insulin
- Glucagon
Faster Acting Insulin Aspart
The existing rapid acting insulins have not been able to match physiologic insulin produced by a person without diabetes. Faster acting insulin aspart (Fiasp) was FDA approved in September 2017 and is formulated with niacinamide, which enhances absorption, and L-arginine, which acts as a stabilizer. It is available in a 10 mL vial and FlexTouch pen. It can be injected at the start of a meal and up to 20 minutes after. When injected at the start of the meal, it reduces post-prandial glucose excursions more effectively than insulin aspart (Novolog). It was also studied in insulin pumps where it was slightly more effective at reducing post-prandial hyperglycemia compared to Novolog (although not statistically significant). However, there was an increase in infusion site reactions (3% in the Novolog group vs 7% in the Fiasp group). Currently, it is not FDA approved for use in insulin pumps in the United States, although it is in Europe.

New Glucagon Formulations
There is lots of excitement around glucagon, the life-saving medication for people with diabetes experiencing severe hypoglycemia. The current formulation requires reconstitution and can be difficult to administer in an emergency situation. There are 2 new formulations that were submitted to the FDA during the summer of 2018. The first is a 3 mg nasal glucagon made by Lilly. This is a nasal powder that delivers its contents into a person’s nose by pushing the bottom of a dispenser. There is no need to inhale, and studies in patients with nasal congestion demonstrated consistent dosing. The second glucagon formulation is a pen made by Xeris Pharmaceuticals. This would come in a 0.5 mg or 1.0 mg 1-time use pen and would be the first liquid glucagon that has long-term stability at room temperature so there is no reconstitution required. The pen device is very easy to use, functioning similarly to an epi-pen. We should know the FDA’s decision by summer 2019. Other studies are under way with liquid glucagon for dual-hormone insulin pumps.

Semaglutide (Ozempic)
The FDA approved this once-weekly GLP-1 agonist in December 2017, making it the sixth one in this class. However, this “late comer” already stands out from the others in its class based on its average A1C reduction of 1.5% and average weight loss along the magnitude of 4 kg to 6 kg, in addition to a once-daily oral formulation in the pipeline! The SUSTAIN-6 trial also demonstrated a reduction in cardiovascular events versus placebo.
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(although not FDA approved for this indication), with a slight increase in retinopathy complications. Semaglutide comes in 2 different pens: 1 pen is for administering 0.25 mg and 0.5 mg doses, while the other is used to administer the 1 mg dose. The packaging includes NovoFine Plus 32 G × 4 mm pen needles already, so a separate prescription for needles is not necessary. The once-daily oral formulation of semaglutide so far sounds promising, with the PIONEER 1 study showing A1C reductions (all doses) and weight loss (14 mg dose only) with semaglutide versus placebo.

SGLT2 Inhibitors
Another agent approved in December 2017 was ertugliflozin (Steglatro), a ‘me too’ agent offering similar A1C reduction, weight loss, and blood pressure lowering as other SGLT2 inhibitors already on the market. Its cardiovascular outcomes trial (VERTIS-CV) is ongoing, with an estimated completion date of September 2019. This has been priced lower than other SGLT2 inhibitors and is starting to become preferred on some formularies.

A more exciting development in this class of medications is sotagliflozin (Zynquista), a dual SGLT1/SGLT2 inhibitor currently under review by the FDA as an adjunct to insulin therapy in type 1 diabetes. This medication not only inhibits reuptake of glucose in the kidneys (SGLT2) but also in the small intestine (SGLT1), which is hypothesized to help decrease post-prandial glucose levels and suppress post-prandial glucagon release through a negative feedback mechanism. The main trial investigating its safety and efficacy (inTandem3) had a 3-pronged primary outcome (A1C < 7%, no severe hypoglycemia, and no DKA), achieved by significantly more people in the sotagliflozin arm than placebo (28.6% vs 15.2%). However, this is balanced by an increased frequency of various adverse events, including DKA (3.0% vs 0.6%), genital mycotic infections (6.4% vs 2.1%), volume depletion (1.9% vs 0.3%), and diarrhea (4.1% vs 2.3%). It is also important to note that DKA was more common in patients on insulin pumps (4.4% vs 0.7%) than patients on subcutaneous insulin injections (2.1% vs 0.5%). The FDA accepted the new drug application for sotagliflozin in May 2018, so continue to watch for updates in the next few months!

New Devices
Exenatide ER (Bydureon) was the first once-weekly GLP-1 receptor agonist, available in 2010. The first kit required reconstitution and wasn’t very easy to use. In 2014, a pen device became available, but it has a large needle that must be attached prior to use. A pen formulation called Bydureon
BCise is a simpler, 1-time use, disposable pen, using autoinjector technology where the needle is never seen. It only requires shaking for 15 seconds compared to the other pen device that requires 80 taps. Unfortunately, the needle is still the same size. Bydureon is known to cause subcutaneous nodules in some people. These are not harmful and go away when the drug is discontinued.

Insulin glargine U300 (Toujeo), a long-acting insulin, now has a Max Solostar that goes up to 160 units per injection. The increments go by 2, so just be sure to dose by even numbers. Insulin lispro (Humalog), a meal-time insulin, now has a Junior Kwikpen. This is the first low-dose disposable pen that can be dosed in half-unit increments. The max dose is 30 units. Prior to this, the pen was not disposable and required special cartridges.

Summary
There are many new drugs and devices available and on the horizon for diabetes treatment.
Areas for particular growth are GLP-1 receptor agonists, SGLT-2 inhibitors, and new glucagon formulations.

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REFERENCES

