



Dr. Johnson is a family practice doctor in Grand Forks with a special interest in diabetes -- and a special knack for writing. As a member of the Dakota Diabetes Coalition, he has generously made himself available to answer questions through our listserv. If you have comments, or questions for Dr. Johnson to address in future columns, please contact gailhand@qwest.net

Visit the Coalition's website!
<http://www.ndhealth.gov/diabetescoalition/>

Incretins and Diabetes

Type 2 meds for those with insulin production

Q. What are the Incretin-Based medications? How do they work to control diabetes?

A. Incretin-based therapies are relatively new agents on the market for diabetes treatment. Currently, there are two medications available in different, but related classes. Exenatide (Byetta) was the first on the market, followed by Vildagliptin (Januvia). The primary mechanism of action of these medications is based on the Incretin system, which are hormones secreted by the gut, primarily Glucagon-like Peptide 1 (GLP-1). GLP-1 helps stabilize blood sugars by the following actions:

- 1) Stimulation of insulin production by the pancreas
- 2) Decreasing glucagon release; one role of glucagon is to increase blood sugar by mobilization of glucose from the liver and muscle
- 3) Increasing a sense of satiety, or feeling full after eating
- 4) Decreasing the rate of stomach emptying

Byetta is available only by injection in a pen device, usually given twice daily. It is an analogue of GLP-1, and mimics the action of this gut hormone as noted above. It has a longer duration of action compared to naturally occurring GLP-1 in the body. An additional benefit to using this medication is that many patients will be able to lose weight while using it, usually about 5-10% of body weight.

Its primary side effect is nausea, but most patients find this to be a short-lived or minor problem. Currently, Byetta is FDA indicated for type 2 diabetes to be used in combination with metformin, and/or sulfonyureas, and/or TZD's (Actos or Avandia). At

present, it does not have a 'stand-alone' indication or with insulin. Byetta will not produce hypoglycemia (low blood sugar) unless combined with a sulfonylurea.

Januvia is an oral agent (pill) in the DPP-IV inhibitor family. It acts by inhibiting the breakdown of GLP-1, naturally produced by the gut. Blood sugar control is produced in the same general way as Byetta, but patients usually do not have the weight loss seen with Byetta. The drug is considered to be weight neutral. Again, mild nausea can occur, but it rarely leads to patient discontinuation of the drug.

Januvia is indicated in type 2 diabetes, and can be used with metformin. It currently does not have an indication with other diabetes agents, including insulin. Januvia has the benefit of no known drug interactions. It appears to have 'durability' in diabetes treatment similar to TZD's. There is some interest in this drug for the geriatric population, as hypoglycemia generally does not occur. Other agents such as metformin, sulfonylureas, and TZD's can be problematic in this population. Again, Januvia's action, as with Byetta, works in conjunction with insulin.

Since both of these agents only offer real benefit in patients with adequate insulin production, those patients with long-standing diabetes will not likely respond with improved blood sugars. Most persons with long-standing type 2 diabetes will need insulin replacement to achieve blood glucose targets.

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[Incretins and Diabetes, Dr. Johnson's Column #10, Nov. 30, 2007](#)

Make sure you are up to date -- and following guidelines. The ADA Standards of Care for diabetes are updated each January and can be found at this site:

http://care.diabetesjournals.org/cgi/reprint/30/suppl_1/S4
