

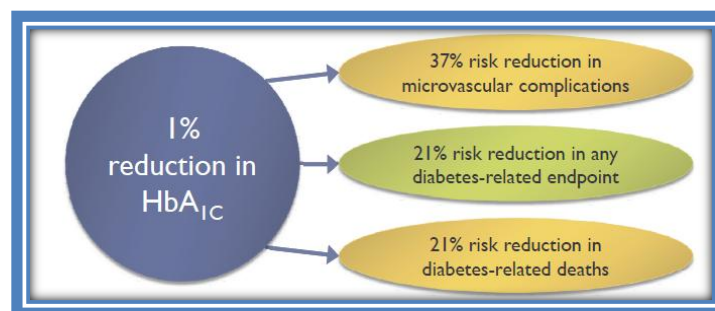
## *New Diabetes Medications: What are they; How do they work; & Where do they fit into treatment?*

Newer anti-diabetic agents have emerged for the treatment of diabetes. They are commonly referred to by their mechanisms of action, such as glucagon-like peptide-1 (GLP-1) agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors, **BUT** the mainstay of **initial** management of diabetes is still with **metformin, sulfonylureas and insulin.**

Drug Class	Medications	A1C ↓	MOA	Route	Dosing Frequency	Common Side Effects	Additional Comments
GLP-1 agonists	Byetta® (Exenatide) <sup>1</sup>	0.5-1%	Stimulate GLP-1 receptors which ↑ production of insulin, inhibits postprandial glucagon release, slows gastric emptying	SC	Twice Daily	Headache, nausea, diarrhea, weight loss	Contraindicated in CrCl <30mL/min
	Bydureon® (Exenatide) <sup>2</sup>				Once Weekly		Approved Jan. 2012, Contraindicated in CrCl <30mL/min, Boxed warning: associated with thyroid cell cancer
	Victoza® (Liraglutide) <sup>3</sup>				Once Daily		Approved 2010 Boxed warning: associated with thyroid cell cancer
DPP-4 inhibitors	Januvia® (sitagliptin) <sup>4</sup>	0.5-1%	Inhibits degradation of endogenous incretins which ↑ insulin secretion, ↓ glucagon secretion	PO	Once Daily	Acute upper respiratory tract infections, weight neutral	Dose adjust when CrCl <50mL/min
	Onglyza® (saxagliptin) <sup>5</sup>						Dose adjust when CrCl <50mL/min
	Tradjenta® (linagliptin) <sup>6</sup>						Approved May 2011

### Where do GLP-1 agonists and DPP-4 inhibitors fit into treatment?

- In the initial management of diabetes metformin, sulfonylureas, and insulin are more efficacious than DPP-4 inhibitors and GLP-1 agonists in lowering HbA1C.
- Average expected ↓ in HbA1C: <sup>6</sup>
  - **Metformin & Sulfonylureas: 1-2%**
  - **Insulin: >1.5%**
  - **GLP-1 agonists & DPP-4 inhibitors: 0.5-1%**
- Achieving a 1% reduction in HbA1C can have a significant impact on the reduction of microvascular and macrovascular events as was shown in the United Kingdom Prospective Diabetes Study (UKPDS 35). Therefore, beginning an agent that has the largest expected decrease in HbA1C should be the focus of initial medication selection for diabetes. <sup>7</sup>



- Remember, **metformin** and **sulfonylureas** should be considered for the initial pharmacological management of type 2 diabetes, while GLP-1 agonists & DPP-4 inhibitors may fit into treatment later on.

REFERENCES: 1) Byetta® [package insert]. Amylin Pharmaceuticals, Inc.; 2010. 2) Victoza® [package insert]. Novo Nordisk A/S; 2011. 3) Januvia® [package insert]. Merck & Co, Inc.; 2010. 4) Onglyza® [package insert]. Bristol-Myers Squibb Company; 2011. 5) Tradjenta® [package insert]. Boehringer Ingelheim; 2011. 6) Nathan DM, et al. Diabetes Care. 2009;32(1):193-203. 7) Stratton IM, et al. BMJ. Aug 12 2000;321(7258):405-412.