

## Pharmacy Fact Sheet: Diabetes

February 2017

### Key points

- Several new agents with novel mechanisms of actions have been approved recently offering **many options for patients with diabetes**. The intent of this Fact Sheet is to familiarize providers with some of the new agents, and the cost impact to patients and LCPN.
- Pharmacy PMPM (per member per month) trend for LCPN has increased by 8.6% through Q3. 2016 while overall TME (total medical expenses) trend for LCPN increased by 5.6%. Pharmacy spend is currently about 20% of all LCPN TME expenses. [For more information on the cost impact of prescribing on the LCPN, please [refer to the Pharmacy Fact Sheet The Cost of Prescribing: How Prescription Medication Expenses Impact the Clinician & Health System \(LCPN\)](#)]
- **Diabetes therapy is one of the top classes** of pharmacy spend, **increasing 37.3% YTD Q3.2016** compared to same time period in 2015. Drivers of this increase include **rising costs and utilization of new insulins** and **branded agents** in the GLP-1 Receptor Agonist, DPP-4 inhibitor, and SGLT2 inhibitor classes.
- Important considerations when intensifying treatment with some of the newer agents after initial treatment with metformin:
  - What “bang do you get for your buck”? Consider the **average cost of script vs. potential A1C reduction**.
  - What are the **pros and cons of each agent?** Combining agents?
  - How does the cost of each agent and number of agents affect **patient affordability?**
- Refer to the chart on the back to get an overview of agents in each class and some of their considerations. →

### Case Study: Failure of Metformin Monotherapy – A 68-year-old male with Type 2 DM, HTN, dyslipidemia

- Hypertension and lipids are well-controlled (ACE-inhibitor, thiazide diuretic and low-dose statin)
- Body Mass Index (BMI) is down to 28 kg/m<sup>2</sup> from 35 kg/m<sup>2</sup> over the last 2 years after focused efforts on diet and exercise
- Tolerated optimal metformin monotherapy (2000 mg/day) for the last 2 years.
- **He now presents at the clinic with an HbA1c of 7.8%.**

During consultation, the patient **mentions that he has seen advertisements** for canagliflozin (Invokana) and questioned if it is right for him.

After reviewing the available therapeutic choices and using a shared decision-making model, a **dipeptidyl peptidase-4 (DPP-4) inhibitor is selected as add-on therapy** based upon simplicity of use, tolerability, and the patient's wish to avoid anything that might cause weight gain. Because he is an uncircumcised male, he decided against canagliflozin once informed of the potential side effect of a genital mycotic infection.

### Discussion: A common challenge in primary care = how to manage a decline in glycemic control on monotherapy

Before intensifying regimen with add-on therapy, **ensure current treatments are being used optimally** (review dosing, adherence, lifestyle)

- In this case, the patient has already done very well in terms of weight reduction and maintenance.
- At this point, add-on therapy may be needed to improve glycemic control. Where the patient was only modestly above his ADA-recommended HbA1c goal of 7.0%, aggressive therapy—which may be associated with adverse effects—was not warranted.
- Although not obese, this patient was concerned about body weight, treatments associated with weight gain—eg, sulfonylureas (SUs) and insulin—may not be suitable.

Patients in the US may be exposed to **direct-to-consumer advertising**, and it is common for patients to express opinions about named drugs. In these situations, it is important to **listen carefully** to the patient's thoughts. Allowing the patient a **role in the decision-making process** may help **obviate some of the patient-related barriers** to optimal glycemic control, and it **improves the chances of good adherence and disease understanding**. When the treatment requested by the patient is not ideal, time spent on patient education is critical. The reasons why the suggested therapy is not preferred should be outlined and the patient should be involved as much as possible in the choice of an alternative therapy.

- In this case, the patient and doctor opted for a DPP-4 inhibitor as add-on treatment. **Other reasonable options** might include a 3-month trial of **lifestyle modification**, a glucagon-like peptide-1 receptor agonist (**GLP-1RA**), or a sodium-glucose cotransporter-2 (**SGLT-2**) inhibitor.
  - **GLP-1RAs were not the best choice** as the patient was disinclined to use an injectable agent
  - Although **SGLT-2 inhibitors would be reasonable** (and was specifically requested by the patient), being **uncircumcised**, he may be at **increased risk for a genital mycotic infection** seen with this class of agents. Such infections are less common in men than in women, but being uncircumcised increases his risk.
  - **Alpha-glucosidase inhibitor has low GI tolerability**, hence the shared decision to use a DPP-4 inhibitor.

<b>Diabetes Therapy</b>	<b>Total Avg Cost / Rx</b>	<b>Patient Monthly Copays*</b>	<b>Pros &amp; Cons</b>	<b>Weight Impact</b>	<b>A1C Reduction</b>
<b>Insulin Response Enhancers:</b> metformin (ER), pioglitazone	~ \$25	> \$3	Metformin: monotherapy associated with lower risk for cardiovascular mortality than sulfonylurea monotherapy. Metformin better than TZD, sulfonylureas or DPP-4 Inhibitor for weight. Increased GI side effects. TZD: Increased risk of edema, heart failure, fractures and weight gain.	Neutral / Loss	1.0 - 1.5%
metformin 500 mg XR/1000mg XR (generic of Glumentza, Fortamet)	> \$400	\$65 - \$125			
<b>Insulin-Release Stimulant Type: sulfonylureas</b> glimepiride, glipizide, glyburide	\$5 - \$15	>\$5	Increased risk of hypoglycemia Associated with worse weight outcomes Glyburide higher incidence of hypoglycemia & mortality than glipizide & glimepiride	Gain	1.0 - 1.5%
<b>Dipeptidyl Peptidase-4 (DPP-4) Inhibitors:</b> Sitagliptin (Januvia), Saxagliptin (Onglyza), Linagliptin (Trajenta), alogliptin	> \$300	\$45 - \$80	Saxagliptin & alogliptin may increase risk of heart failure particularly in patients who already have heart or kidney disease. Alogliptin & linagliptin containing products may be associated with cases of bullous pemphigoid Associated with joint pain	Neutral	0.5 to 1%
<b>Sodium Glucose Cotransporter-2 (SGLT2) Inhibitors:</b> Canagliflozin (Invokana), Dapagliflozin (Farxiga), Empagliflozin (Jardiance)	> \$300	\$20 - \$100	Increased risk of genital mycotic infections, dehydration, bone mineral loss/ fractures. Excessive urination Contraindicated in severe renal impairment / dialysis; risk of ketoacidosis	Neutral	0.5 to 1%
<b>Glucagon-like, peptide-1 (GLP-1) agonist or incretin mimetic:</b> Albiglutide (Tanzeum), Dulaglutide (Trulicity), Exenatide (Byetta), Exenatide extended-release (Bydureon), Liraglutide (Victoza)	> \$500	\$40 - \$100	Increased GI side effects Possible risk of acute pancreatitis	Loss	1.0 to 1.5%
<b>Insulins:</b> Insulin Aspart (Novolog), Insulin glulisine (Apidra), Insulin lispro (Humalog), Insulin glargine (Lantus, Toujeo), Insulin detemir (Levemir), Insulin degludec (Tresiba), Insulin aspart/degluc (Ryzodeg 70/30)	> \$400	\$20 - \$40	Increased risk of hypoglycemia Most A1C reduction Insulin glargine (Basaglar) is not a biosimilar or interchangeable biologic (classified as a "follow-on" insulin glargine. Cannot be substituted for Lantus without prescriber permission. ReliOn insulins may be beneficial when Medicare patients reach donut hole or for cash paying patients. <b>See Clinical Resource on initiation, adjustment and switching at this link</b>	Gain	1.5 to 3.5%
Insulin glargine (Basaglar)	~ \$300				
<b>OTC Insulins:</b> ReliOn/NPH (ReliOn) 100u/ml, ReliOn/R 100u/ml, ReliOn/Novolin 70/30 10ml - Walmart only	~ \$25/ vial	Cost of vials			

\* Commercial Plan Copays; For Medicare Part D patients, consider cost contribution to donut hole; when \$3800 in annual cost is reached, patient copay may be 40% of monthly cost of script (e.g. Lantus ~ \$160 per month out of pocket)

Green = least expensive, better A1C reduction, weight loss Red = more expensive, lower A1C reduction, weight gain

References:

- Express Scripts 2015 Drug Trend Report – March 2016
- 2017 ADA Standards of Medical Care in Diabetes [http://care.diabetesjournals.org/content/40/Supplement\\_1/Pharmacologic approaches section: http://diabetesed.net/wp-content/uploads/2017/01/Pharmacologic-approaches-for-Glycemic-Treatment-ADA-2107.pdf](http://care.diabetesjournals.org/content/40/Supplement_1/Pharmacologic%20approaches%20section)
- 2017 Oral Pharmacologic Treatment of Type 2 DM: ACP Clinical Practice Guideline <http://annals.org/aim/article/2595888/oral-pharmacologic-treatment-type-2-diabetes-mellitus-clinical-practice-guideline>
- Case Study: <http://www.consultant360.com/articles/case-studies-patients-type-2-diabetes-mellitus-exercises-problem-solving>
- Clinical Resource, Initiation and Adjustment of Insulin Regimens for Type 2 Diabetes. Pharmacist's Letter/Prescriber's Letter. March 2017.

<p><b>Want to learn more?</b></p> <p><b>Contact your Accountable Care Unit Pharmacist →</b></p> <p><b>Author</b> Carol Freedman, RPh, MAS, BCGP <a href="mailto:cfreed@nhs-healthlink.org">cfreed@nhs-healthlink.org</a></p> <p><b>LCPN</b> Pam Sherry, PharmD, BCACP Director, Network Pharmacy Management <a href="mailto:Pamela.S.Sherry@lahey.org">Pamela.S.Sherry@lahey.org</a></p>	<p><b>Lahey</b> Andrew Levitsky, PharmD, MEd, BCPS <a href="mailto:Andrew.M.Levitsky@lahey.org">Andrew.M.Levitsky@lahey.org</a></p> <p>Kenneth Noyes, PharmD, BCPS <a href="mailto:Kenneth.Noyes@lahey.org">Kenneth.Noyes@lahey.org</a></p>
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