



CA-ADAP Formulary Review: Oral and Non-Insulin Diabetes Treatment

JULY 2022

CARRIE HOLDEN, PHARM.D.,

MagellanRx
MANAGEMENTSM

CA-ADAP Formulary Review: AGENDA

1 Disease State Overview in PLWH

2 Medications currently on formulary & their utilization

3 Recommendations



Therapeutic Class Review

DIABETES TREATMENT
(ORAL AND NON-INSULIN OPTIONS)

Diabetes in People Living with HIV (PLWH)



- 37.3 million people in the U.S have diabetes (11.3% of the population)
 - In California, 10.5%+ of the population is estimated to have Diabetes
- Leading cause of major health complications:
 - End-Stage Renal Disease (ESRD) and lower extremity amputations
 - Ischemic heart disease
 - Stroke
 - Peripheral vascular disease
 - Vision loss
- PLWH are at an increased risk for developing Type 2 Diabetes:
 - Due to aging (≥ 45 years of age)
 - Chronic Inflammation
 - HIV medications (older agents)
 - NRTIs: zidovudine, stavudine and didanosine
 - PIs: indinavir, lopinavir
- Non-Pharmacological Treatment is Key:
 - Maintain a healthy weight
 - Dietary modification
 - Physical Activity

1. CDC. [Diabetes: National Diabetes Statistics Report.](#)
2. AIDSinfo. <https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-diabetes>
3. [https://www.niddk.nih.gov/health-information/diabetes/overview.](https://www.niddk.nih.gov/health-information/diabetes/overview)

Therapeutic Class Review: Diabetes Treatment



- **Biguanides**: decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity (by increasing peripheral glucose uptake and utilization).
 - **Metformin**: indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients ≥ 10 years of age and older with type 2 diabetes mellitus (T2DM).
 - **Place in therapy**: The preferred initial treatment for type 2 Diabetes by the American Diabetes Association (ADA), American Academy of Clinical Endocrinologists/American College of Endocrinology (AACE)/(ACE), Endocrine Society, and the American College of Physicians (ACP) diabetes treatment guidelines.
 - Reduce A1C by 1-2% as monotherapy or reduction in fasting plasma glucose (FPG) by 60-70 mg/dL
 - Favorable effects of patient cholesterol levels (reduction of triglycerides, LDL-C, and increase in HDL-C)
 - Weight neutral or weight loss

Agent	Generic	CA ADAP FORMULARY	AZ	CT	FL	NY	TX	WA	Comments
Metformin	Y	Y	Y	Y	Y	Y	Y	Y	<ul style="list-style-type: none"> • Oral therapies • Often co-formulated with other oral agents

Therapeutic Class Review: Diabetes Treatment - Sulfonylureas



- **Sulfonylureas:** Stimulate insulin release from the pancreatic beta cells; reduce glucose output from the liver; increase insulin sensitivity at peripheral target sites.
 - **Place in therapy:** indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM. Used as initial therapy in patients who have contraindications to Metformin and those with severe hyperglycemia (fasting plasma glucose >250 mg/dL [13.9 mmol/L], random glucose consistently >300 mg/dL or A1C >9.5, but without ketonuria or unintentional weight loss.
 - Can be used as monotherapy or as add-on therapy
 - Reduce A1C by 1-2% as monotherapy
 - Generally well tolerated, but hypoglycemia is the most common side effect
 - Recommended, patients start with a shorter acting sulfonylurea for initial therapy (i.e. Glipizide, Glimepiride)

Agent	Generic	CA ADAP FORMULARY	CA ADAP						Comments
			AZ	CT	FL	NY	TX	WA	
Glipizide	Y	Y	Y	Y	Y	Y	-	Y	
Glipizide/ Metformin	Y	-	-	-	-	Y	-	Y	• Combo of largest utilized oral DM agents
Glimepiride	Y	-	-	-	Y	Y	-	Y	• Less risk for hypoglycemia and weight gain • Consider adding
Glyburide	Y	-	Y	Y	Y	Y	-	Y	
Glyburide/ Metformin	Y	Y	-	-	Y	-	-	Y	

Therapeutic Class Review: Diabetes Treatment - TZDs



- **Thiazolidinediones (TZDs)**: improves target cell response to insulin by binding and activating peroxisome proliferator-activated receptor gamma (PPAR- γ) in the skeletal muscle, adipose tissue, and liver. Its mechanism of action is dependent on presence of insulin for activity.
 - **Place in therapy**: used as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.
 - Can be used as monotherapy or as add-on therapy
 - Reduces A1C by 0.5-1.4% as monotherapy
 - Can increase HDL-C and reduce triglycerides, blood pressure, inflammatory markers, hepatic steatosis, and carotid/coronary artery thickening
 - Can cause weight gain, fluid retention, heart failure, and an increased risk for bone fractures
 - Black Box warnings: Congestive heart failure (Actos and Avandia), risk for Myocardial Infarction (Avandia)

Agent	Generic	CA ADAP FORMULARY	AZ	CT	FL	NY	TX	WA	Comments
Pioglitazone	Y	Y	-	Y	-	Y	-	Y	
Pioglitazone/ Metformin	Y	-	-	-	-	Y	-	Y	
Rosiglitazone	-	Y	-	-	-	Y	-	Y	• Removed from formulary

Therapeutic Class Review: Diabetes Treatment – SGLT2 Inhibitors



- **SGLT2 Inhibitors:** reduce reabsorption of filtered glucose and lower the renal threshold for glucose, thereby increasing urinary glucose excretion and improving blood glucose control.
 - **Place in therapy:** as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.
 - Reduces the risk of cardiovascular death in adult patients with T2DM and established cardiovascular disease
 - Empagliflozin (Jardiance)-class A recommendation by the ADA guidelines for use in patients with T2DM and known atherosclerotic cardiovascular disease (ASCVD).
 - Can be used as monotherapy or add-on therapy
 - Reduces A1C by 0.5-0.7% as monotherapy
 - Generally well tolerated, no risk for hypoglycemia, moderate weight loss

Agent	Generic	CA ADAP FORMULARY	AZ	CT	FL	NY	TX	WA	Comments
Empagliflozin (Jardiance)	-	-	Y	-	Y	Y	-	-	• Recommend adding
Canagliflozin (Invokana)	-	-	-	-	Y	Y	-	-	
Dapagliflozin (Farxiga)	-	-	-	-	Y	Y	-	-	
Ertugliflozin (Steglatro)	-	-	-	-	-	-	-	-	

Therapeutic Class Review: Diabetes Treatment – DPP-4 Enzyme Inhibitors



- **Dipeptidyl Peptidase-4 (DPP-4) Enzyme Inhibitors:** inhibits DPP4 resulting in prolonged active incretin levels (GLP-1 and GIP) to regulate glucose homeostasis by increasing insulin synthesis and release from the pancreatic beta cells and decrease glucagon secretion by the pancreatic alpha cells.
 - **Place in therapy:** as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.
 - Can be used as monotherapy or add-on therapy
 - Reduces A1C by 0.5-1% as monotherapy
 - Generally well tolerated, no risk for weight gain or hypoglycemia

Agent	Generic	CA ADAP FORMULARY	AZ	CT	FL	NY	TX	WA	Comments
Sitagliptin (Januvia)	-	-	Y	-	Y	Y	-	Y	• Consider adding
Linagliptin (Tradjenta)	-	-	-	-	-	Y	-	Y	
Saxagliptin (Onglyza)	-	-	-	-	-	Y	-	Y	
Alogliptin (Nesina)	Y	-	-	-	-	Y	-	Y	

Therapeutic Class Review: Diabetes Treatment – GLP-1 Receptor Agonists



- **Glucagon-Like Peptide 1 (GLP-1) Receptor Agonists:** augments glucose dependent insulin secretion and slows gastric emptying.
 - **Place in therapy:** as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.
 - Can be used as monotherapy or add-on therapy
 - Reduces A1C by 0.5-1% as monotherapy
 - As a class, all but one agent (Rybelsus) is administered as a subcutaneous injection
 - ADA guidelines give preference to GLP-1 agonists over insulin in patients who require an injectable agent.
 - Generally well tolerated, with minimal risk for hypoglycemia
 - Can have weight loss benefit of 2-3 kgs
 - Can reduce ASCVD risk as a class (i.e. Dulaglutide-ADA Class A recommendation)

Agent	Generic	CA ADAP FORMULARY	AZ	CT	FL	NY	TX	WA	Comments
Dulaglutide (Trulicity)	-	-	Y	-	-	Y	-	-	• Consider adding one from class
Liraglutide (Victoza)	-	-	Y	-	-	Y	-	-	• Consider adding one from class
Exenatide (Byetta/Bydureon)	-	-	-	Y	-	Y	-	-	
Semaglutide (Ozempic)	-	-	-	-	-	-	-	-	
Semaglutide (Rybelsus)	-	-	-	-	-	-	-	-	• Oral formulation of Semaglutide

Therapeutic Class Review: Diabetes Treatment - Others



- **Alpha-Glucosidase Inhibitors:** competitive inhibitor of pancreatic α -Amylase and intestinal brush border α -glucosidases, resulting in delayed hydrolysis of ingested complex carbohydrates and disaccharides and absorption of glucose.

Agent	Generic	CA ADAP FORMULARY	AZ Formulary	CT Formulary	FL Formulary	NY Formulary	TX Formulary	WA Formulary	Comments
Acarbose	Y	-	-	-	-	Y	-	Y	

- **Meglitinides:** blocks ATP-dependent potassium channels, depolarizing the membrane and facilitating calcium entry through calcium channels. Increased intracellular calcium stimulates insulin release from the pancreatic beta cells.

Agent	Generic	CA ADAP FORMULARY	AZ Formulary	CT Formulary	FL Formulary	NY Formulary	TX Formulary	WA Formulary	Comments
Repaglinide (Prandin)	Y	-	-	-	-	Y	-	Y	

Formulary Management Recommendations: Diabetes Treatment



1 Sulfonylureas
(Glimepiride)

Recommend addition to the ADAP
formulary.

2 TZDs

No changes recommended.

3 SGLT2 Inhibitors
(Empagliflozin -*Jardiance*)

Recommend addition to the ADAP
formulary.

Formulary Management Recommendations cont'd



4

DPP-4 Inhibitors:
(Sitagliptin -*Januvia*)

Consider addition to the ADAP formulary.

5

GLP-1 Agonist:
(Dulaglutide -*Trulicity*,
Liraglutide -*Victoza*)

Consider addition to the ADAP
formulary.

References



1. Centers for Disease Control and Prevention. 2022. *National Diabetes Statistics Report*. [online] Available at: <https://www.cdc.gov/diabetes/data/statistics-report/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fdiabetes%2Fdata%2Fstatistics%2Fstatistics-report.html> [Accessed 4 April 2022].AIDSinfo.
2. Hivinfo.nih.gov. 2021. *HIV and Diabetes | NIH*. [online] Available at: <<https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-diabetes>> [Accessed 4 April 2022].
3. National Institute of Diabetes and Digestive and Kidney Diseases. n.d. *Diabetes Overview | NIDDK*. [online] Available at: <<https://www.niddk.nih.gov/health-information/diabetes/overview.>> [Accessed 5 April 2022].

Confidentiality statement



By receipt of this presentation, each recipient agrees that the information contained herein will be kept confidential and that the information will not be photocopied, reproduced, or distributed to or disclosed to others at any time without the prior written consent of Magellan Health, Inc.

The information contained in this presentation is intended for educational purposes only and is not intended to define a standard of care or exclusive course of treatment, nor be a substitute for treatment.

The information contained in this presentation is intended for educational purposes only and should not be considered legal advice. Recipients are encouraged to obtain legal guidance from their own legal advisors.