Effective Date: 04/01/2022
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Policy Number: C21858-A

Antidiabetic Agents, IL Medicaid Only

PRODUCTS AFFECTED

SINGLE AGENTS:
ALOGLIPTIN, NESINA (alogliptin), ONGLYZA (saxagliptin), SAXAGLIPTIN, BYDUREON BCISE (exenatide), BYETTA (exenatide), OZEMPIC (semaglutide), RYBELSUS (semaglutide), MOUNJARO (tirzepatide), SYMLINPEN (pramlintide), GLUCOTROL XL (glipizide), GLYNASE (glyburide), METFORMIN 625MG TABLET, RIOMET (metformin), RIOMET ER (metformin), GLUMETZA (metformin), METFORMIN ER MODIFIED RELEASE, METFORMIN ER OSMOTIC, REPAGLINIDE, BAQSIMI (glucagon), GVOKE HYPOPEN (glucagon), GVOKE KIT (glucagon), GLUCAGON EMERGENCY KIT, GLUCAGEN HYPOKIT, KORLYM (mifepristone), CYCLOSET (bromocriptine), ACTOS (pioglitazone), STEGLATRO (ertugliflozin)

COMBINATION AGENTS:
XULTOPHY (insulin degludec/liraglutide), SOLIQUA (insulin glargine/lixisenatide), ALOGLIPTIN/METFORMIN, KAZANO (alogliptin/metformin), JENTADUETO (linagliptin/metformin), JENTADUETO XR (linagliptin/metformin), KOMBIGLYZE XR (metformin/saxagliptin), SAXAGLIPTIN/METFORMIN, JANUMET (metformin/sitagliptin), JANUMET XR (metformin/sitagliptin), ALOGLIPTIN/PIOGLITAZONE, OSENI (alogliptin/pioglitazone), REPAGLINIDE/METFORMIN, INVOKAMET (canagliflozin/metformin), INVOKAMET XR (canagliflozin/metformin), XIGDUO XR (dapagliflozin/metformin), SYNJARDY (empagliflozin/metformin), SYNJARDY XR (empagliflozin/metformin), SEGLUROMET (ertugliflozin/metformin), QTERN (dapagliflozin/saxagliptin), GLYXAMBI (empagliflozin/linagliptin), STEGLUJAN (ertugliflozin/sitagliptin), TRIJARDY XR (empagliflozin/linagliptin/metformin), DUETACT (pioglitazone/glimepiride), PIOGLITAZONE/GLIMEPIRIDE, ACTOPLUS MET (pioglitazone/metformin), PIOGLITAZONE/METFORMIN

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Type 1 diabetes mellitus, Type 2 diabetes mellitus, Heart failure

REQUIRED MEDICAL INFORMATION:

A. DIABETES WITH HYPOGLYCEMIA:
   1. Prescriber attests (or the clinical reviewer has found) that the requested drug has been prescribed for the management of diabetes with hypoglycemia.
      AND
   2. Prescriber attests to (or the clinical reviewer has found) the member is not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review.
      AND
   3. FOR NON-FORMULARY/NON-PREFERRED AGENTS: Member has had an inadequate response, intolerance, or contraindication to an ALL FORMULARY/ PREFERRED agents within the same class.

B. TYPE 2 DIABETES:
   1. Prescriber attests (or the clinical reviewer has found) that the requested drug has been prescribed for the management of type 2 diabetes.
      AND
   2. Prescriber attests to (or the clinical reviewer has found) the member is not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review.
      AND
   3. FOR RYBELSUS (PREFERRED WITH PA): Prescriber attestation that the member has needle phobia and that the member does not need the cardiovascular protection offered by other agents in the class OR the member has had an inadequate response or had an intolerance to ALL preferred GLP-1 agents. [Inadequate response is defined as not achieving expected A1C lowering while adherent to therapy]
      OR
   4. FOR NON-PREFERRED SINGLE AGENT METFORMIN PRODUCTS: Documentation of a trial and inadequate response to all preferred metformin products. [Inadequate response is defined as not achieving expected A1C lowering while adherent to therapy]
      OR
   5. FOR NON-FORMULARY/NON-PREFERRED SINGLE AGENTS: Member has had an inadequate response, intolerance, or contraindication to an ALL FORMULARY/ PREFERRED agents within the same class. [Inadequate response is defined as not achieving expected A1C lowering while adherent to therapy]
      OR
   6. FOR NON-FORMULARY/NON-PREFERRED COMBINATION PRODUCTS: Documentation that member has had an inadequate response to formulary preferred single agents in the matching classes (SGLT2/GLP1/DPP4) within the combination product. [Inadequate response is defined as not achieving expected A1C lowering while adherent to therapy]
      OR
   7. FOR NON-PREFERRED BRAND NAME REQUESTS: Documentation that member has tried and failed the generic equivalent, if available, on the preferred drug list.

C. REDUCE RISK OF HOSPITALIZATION FOR HEART FAILURE (XIDGDUO XR ONLY):
   1. (a) Documentation member has a diagnosis of heart failure consistent with individual product FDA label
      OR

(b) Documentation member has: (i) a diagnosis of Type 2 diabetes AND (ii) at high risk for cardiovascular events [(a) established cardiovascular disease OR (b) age >55 years in men/>60 years in women AND ONE of the following: dyslipidemia, hypertension or current tobacco use]
AND

2. Prescriber attests that member is concurrently receiving guideline-directed medical therapy (Heidenreich et al., 2022 AHA/ACC/HFSA guideline for the management of heart failure: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines 2022)
AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Xigduo XR (dapagliflozin and metformin) include: severe renal impairment (eGFR below 30 mL/min/1.73m2), end stage renal disease or dialysis, history of serious hypersensitivity to dapagliflozin or hypersensitivity to metformin, and metabolic acidosis, including diabetic ketoacidosis.]

CONTINUATION OF THERAPY:

A. DIABETES WITH HYPOGLYCEMIA:
Prescriber attests to (or clinical reviewer has found) no evidence of intolerable adverse effects or drug toxicity.

B. TYPE 2 DIABETES:
1. Prescriber attests to (or clinical reviewer has found) adherence to therapy at least 85% of the time OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation.
AND
2. Prescriber attests to (or clinical reviewer has found) no evidence of intolerable adverse effects or drug toxicity.
AND
3. Prescriber attests to (or clinical reviewer has found) positive clinical response as demonstrated by improvement in member's glycemic targets (e.g., hemoglobin A1C or other glycemic measurement).

C. REDUCE RISK OF HOSPITALIZATION FOR HEART FAILURE (XIGDUO XR ONLY):
1. Prescriber attests to (or clinical reviewer has found) adherence to therapy at least 85% of the time OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation.
AND
2. Prescriber attests to (or clinical reviewer has found) no evidence of intolerable adverse effects or drug toxicity.
AND
3. Prescriber attests to (or clinical reviewer has found) positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms.

DURATION OF APPROVAL:
Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
None.

AGE RESTRICTIONS:
Bydureon/Bydureon BCise/Synjardy: 10 years and older
All Other Agents: 18 years or older

QUANTITY: See Illinois Medicaid Drug Formulary or use maximum quantity per FDA label

PLACE OF ADMINISTRATION:
The recommendation is that oral and injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral, Subcutaneous

DRUG CLASS:
Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors & SLGT 2/DPP-4 Inhibitor Combinations Incretin Mimetic Agents, (GLP-1) Receptor Agonists and Combinations Dipeptidyl Peptidase-4 Inhibitors (DPP4) and Combinations, Incretin Mimetic Agents (GIP & GLP-1 Receptor Agonists)

FDA-APPROVED USES:
Gvoke, Baqsimi, Glucagon:

- For the treatment of severe hypoglycemia in patients with diabetes mellitus
- *Limitations of use: Glucagon is contraindicated in patients with pheochromocytoma because glucagon may stimulate the release of catecholamines from the tumor.*

Jentadueto (linagliptin/metformin), Jentadueto XR (linagliptin/metformin extended- release):

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- *Limitations of use: Not for treatment of type 1 diabetes. Has not been studied in patients with a history of pancreatitis.*

Nesina (alogliptin), Kazano (alogliptin/metformin), Oseni (alogliptin/pioglitazone), Onglyza (saxagliptin), Janumet (sitagliptin/metformin), Janumet XR (sitagliptin/metformin extended- release):

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- *Limitations of use: Should not be used in patients with type 1 diabetes.*
- *Additional limitation for Onglyza (saxagliptin): Not used for treatment of diabetic ketoacidosis. Additional limitation for Janumet (sitagliptin/metformin), Janumet XR (sitagliptin/metformin extended-release): Has not been studied in patient with a history of pancreatitis.*

Kombiglyze (saxagliptin/metformin):

- Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.
- *Limitations of use: Not use for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.*

Adlyxin (lixisenatide), Xultophy (insulin degludec and liraglutide), Soliqua (insulin glargine and lixisenatide)

- Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- *Limitations of use (Adlyxin): Has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. Not for treatment of type 1 diabetes. Has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.*
- *Limitations of use (Xultophy): Not recommended as first-line therapy for patients inadequately*

controlled on diet and exercise. Not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist. Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. Has not been studied in combination with prandial insulin.

- *Limitations of use (Soliqua): Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. Not recommended for use in combination with any other product containing a GLP-1 receptor agonist. Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis. Not recommended for use in patients with gastroparesis. Has not been studied in combination with prandial insulin.*

Bydureon (exenatide):

- As an adjunct to diet and exercise to improve glycemic control in adults (immediate release and extended release) and pediatric patients aged 10 years and older (extended release only) with type 2 diabetes mellitus.
- *Limitations of use: Not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise. Not indicated to treat type 1 diabetes mellitus. Bydureon Bcise is an extended-release formulation of exenatide and should not be used with other exenatide-containing products. Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.*

Byetta (exenatide)

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- *Limitations of use: Should not be used for the treatment of type 1 diabetes. Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.*

Ozempic (semaglutide), Rybelsus (semaglutide):

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (both); to reduce the risk of major cardiovascular events (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (Ozempic only).
- *Limitations of use: Has not been studied in patients with a history of pancreatitis. Consider another antidiabetic therapy. Not for treatment of type 1 diabetes mellitus.*

Mounjaro (tirzepatide)

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- *Limitations of use: Has not been studied in patients with a history of pancreatitis. Is not indicated for use in patients with type 1 diabetes mellitus.*

Xigduo XR (dapagliflozin and metformin):

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes
- to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors
- to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (NYHA class II-IV) with reduced ejection fraction
- to reduce the risk of sustained eGFR decline, end stage kidney disease, cardiovascular death and hospitalization for heart failure in adults with chronic kidney disease at risk of progression
- *Limitations of use: Not for treatment of type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients. Because of the metformin component, the use of Xigduo XR is limited to adults with type 2 diabetes mellitus for all indications. Not recommended for the treatment of chronic kidney disease in patients with polycystic kidney disease or patients requiring or with a recent history of immunosuppressive therapy for the treatment of kidney*

disease. Xigduo XR is not expected to be effective in these populations.

Qtern (dapagliflozin/saxagliptin):
- Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- *Limitations of use: Not for treatment of type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.*

Invokana (canagliflozin):
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease
- To reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria
- *Limitations of use: Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients. Not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 m2.*

Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin extended-release):
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- Canagliflozin is indicated to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease
- Canagliflozin is indicated to reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria
- *Limitations of use: Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.*

Synjardy (empagliflozin/metformin), Synjardy XR (empagliflozin/metformin extended-release):
- As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus
- Empagliflozin when used as a component of Synjardy and Synjardy XR is indicated in adults with type 2 diabetes mellitus to reduce the risk of cardiovascular death in adults with established cardiovascular disease and cardiovascular death and hospitalization for heart failure in adults with heart failure
- *Limitations of use: Not recommended for use in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients. Because of the metformin component, Synjardy and Synjardy XR are not recommended for use in patients with heart failure without type 2 diabetes mellitus.*

Glyxambi (empagliflozin/linagliptin), Trijardy XR (empagliflozin, linagliptin, and metformin hydrochloride extended-release tablets):
- indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.
- *Limitations of Use: Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients. Has not been studied in patients with a history of pancreatitis. Additional limitation of use for Glyxambi: Not recommended for use to iprove glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 m2.*

Steglatro (ertugliflozin), Segluromet (ertugliflozin/metformin), Steglujan (ertugliflozin/sitagliptin):

- indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- *Limitations of Use (Steglatro): Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.*
- *Limitations of use (Segluromet): Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. It may increase the risk of diabetic ketoacidosis in these patients.*
- *Limitations of Use (Steglujan): Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. It may increase the risk of diabetic ketoacidosis in these patients. Has not been studied in patient with a history of pancreatitis.*

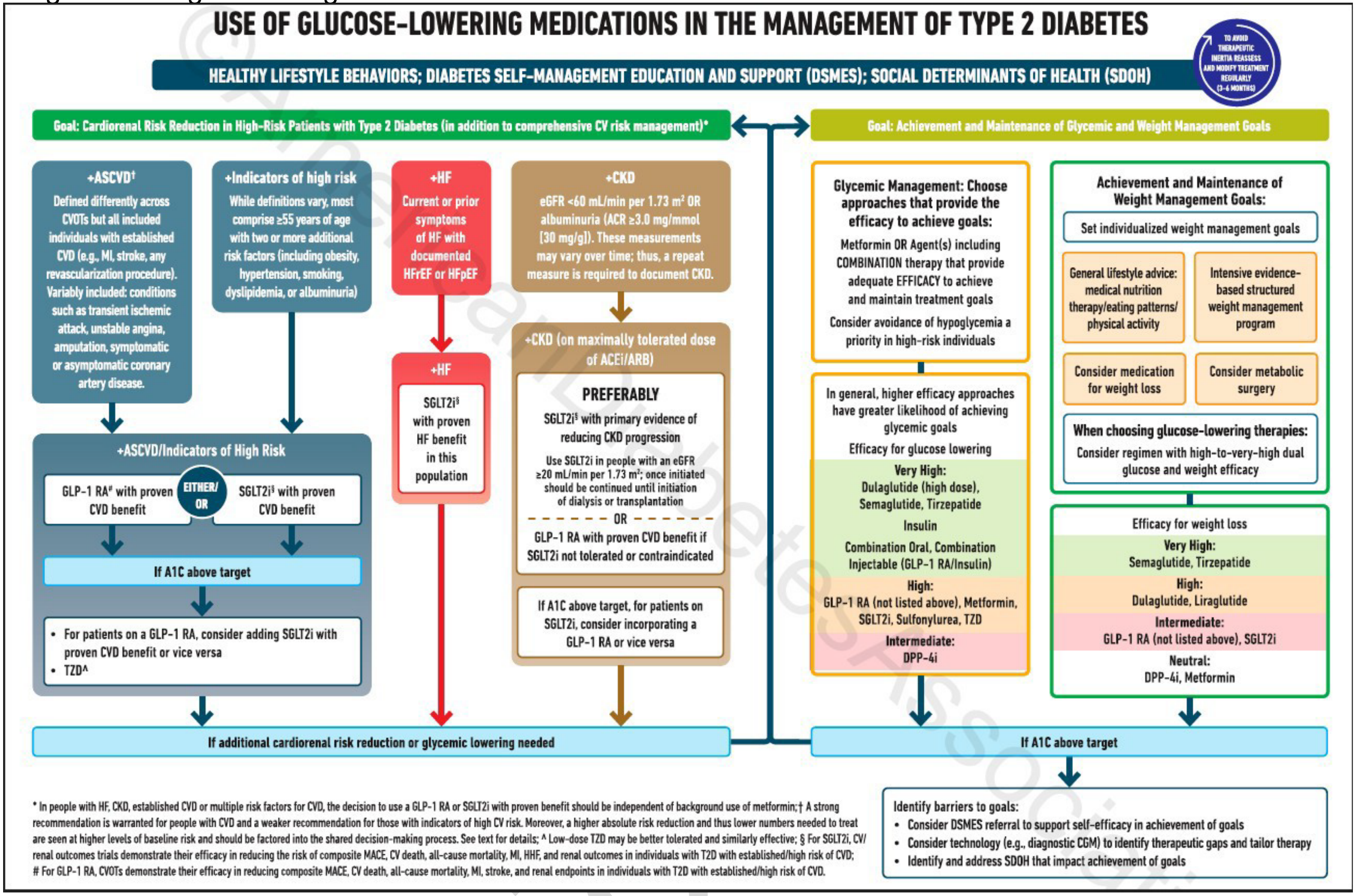
COMPENDIAL APPROVED OFF-LABELED USES:
N/A

APPENDIX

APPENDIX:
Appendix 1:
Reference: Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes 2023. Diabetes Care 2023;46 (Suppl. 1): S140-S157

When A1C is ≥ 1.5% above the glycemic target, many individuals will require dual combination therapy or a more potent glucose-lowering agent to achieve and maintain their target A1C level. Insulin has the advantage of being effective where other agents are not and should be considered as part of any combination regimen when hyperglycemia is severe, especially if catabolic features (weight loss, hypertriglyceridemia, ketosis) are present. It is common practice to initiate insulin therapy for people who present with blood glucose levels > 300 mg/dL or in the individual has symptoms of hyperglycemia (i.e., polyuria or polydipsia) or evidence of catabolism (weight loss). As glucose toxicity resolves, simplifying the regimen and/or changing to noninsulin agents is often possible. However, there is evidence that people with uncontrolled hyperglycemia associated with type 2 diabetes can also be effectively treated with a sulfonylurea.
Combination therapy: Traditional recommendations have been to use stepwise addition of medications to metformin to maintain A1C at target. However, there are data to support initial combination therapy with dipeptidyl peptidase 4 (DPP-4) inhibitor and metformin. The VERIFY (Vildagliptin Efficacy in combination with metformin for early treatment of type 2 diabetes) trial demonstrated that initial combination therapy is superior to sequential addition of medications for extending primary and secondary failure. In the VERIFY trial, participants receiving the initial combination of metformin and the DPP-4 inhibitor vildagliptin had a slower decline of glycemic control compared with metformin alone and with vildagliptin added sequentially to metformin. These results have not been generalized to oral agents other than vildagliptin, but they suggest that more intensive early treatment has some benefits and should be considered through a shared decision-making process, as appropriate. Initial combination therapy should be considered in people presenting with A1C levels 1.5-2.0% above target.

Appendix 2:
Reference: Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes 2023 Diabetes Care 2023;46 (Suppl. 1): S140-S157


USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES
HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)
TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)
Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes (in addition to comprehensive CV risk management)*
+ASCVD†
Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.
+Indicators of high risk
While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)
+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF
+CKD
eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.
+ASCVD/Indicators of High Risk
GLP-1 RA# with proven CVD benefit
EITHER/OR
SGLT2i§ with proven CVD benefit
If A1C above target
• For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
• TZD^
+HF
SGLT2i§ with proven HF benefit in this population
+CKD (on maximally tolerated dose of ACEi/ARB)
PREFERABLY
SGLT2i§ with primary evidence of reducing CKD progression
Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation
OR
GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated
If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa
If additional cardiorenal risk reduction or glycemic lowering needed
Goal: Achievement and Maintenance of Glycemic and Weight Management Goals
Glycemic Management: Choose approaches that provide the efficacy to achieve goals:
Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals
Consider avoidance of hypoglycemia a priority in high-risk individuals
In general, higher efficacy approaches have greater likelihood of achieving glycemic goals
Efficacy for glucose lowering
Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide
Insulin
Combination Oral, Combination Injectable (GLP-1 RA/Insulin)
High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD
Intermediate:
DPP-4i
Achievement and Maintenance of Weight Management Goals:
Set individualized weight management goals
General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity
Intensive evidence-based structured weight management program
Consider medication for weight loss
Consider metabolic surgery
When choosing glucose-lowering therapies:
Consider regimen with high-to-very-high dual glucose and weight efficacy
Efficacy for weight loss
Very High:
Semaglutide, Tirzepatide
High:
Dulaglutide, Liraglutide
Intermediate:
GLP-1 RA (not listed above), SGLT2i
Neutral:
DPP-4i, Metformin
If A1C above target
Identify barriers to goals:
• Consider DSMES referral to support self-efficacy in achievement of goals
• Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
• Identify and address SDOH that impact achievement of goals
* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD;
# For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Per American Diabetes Association (ADA) 2021 guidelines, metformin is the preferred initial pharmacologic agent for the treatment of type 2 diabetes. Once initiated, metformin should be continued as long as it is tolerated and not contraindicated; other agents, including insulin, should be added to metformin. Early combination therapy can be considered in some patients at treatment initiation to extend the time to treatment failure. The early introduction of insulin should be considered if there is evidence of ongoing catabolism (weight loss), if symptoms of hyperglycemia are present, or when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (>300mg/dL [16.7mmol/L]) are very high. A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include effect on cardiovascular and renal comorbidities, efficacy, hypoglycemia risk, impact on weight, cost, risk for side effects, and patient preferences. Among patients with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high risk, established kidney disease, or heart failure, a sodium–glucose cotransporter 2 inhibitor or glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular disease benefit is recommended as part of the glucose-lowering regimen independent of A1C and in consideration of patient-specific factors. In patients with type 2 diabetes, a glucagon-like peptide 1 receptor agonist is preferred to insulin when possible. Recommendation for treatment intensification for patients not meeting treatment goals should not be delayed. The medication regimen and medication-taking behavior should be reevaluated at regular intervals (every 3–6 months) and adjusted as needed to incorporate specific factors that impact choice of treatment Clinicians should be aware of the potential for over basalization with insulin therapy. Clinical signals that may prompt evaluation of over basalization include basal dose more than 0.5 IU/kg, high bedtime-morning or post-preprandial glucose differential, hypoglycemia (aware or unaware), and high variability. Indication of over basalization should prompt reevaluation to further individualize therapy.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of listed agents and combinations are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to GLP-1 agonists or combinations include: Hypersensitivity to requested product, or any component of the formulation; history of or family history of medullary thyroid carcinoma (MTC); patients with multiple endocrine neoplasia syndrome type 2 (MEN2). Contraindications to alogliptin, saxagliptin, linagliptin, sitagliptins include: Hypersensitivity (e.g., anaphylaxis, angioedema, exfoliative skin conditions) to the request product or any component of the formulation. Contraindications to SGLT2 inhibitors include severe renal impairment, ESRD or dialysis, history of serious hypersensitivity to drug or components of the formulations.

OTHER SPECIAL CONSIDERATIONS:

- Black box warning for risk of thyroid c-cell tumors: Bydureon BCise (exenatide), Xultophy (insulin degludec and liraglutide), Ozempic (semaglutide), Rybelsus (semaglutide), Mounjaro (tirzepatide)
- Black box warning for lactic acidosis: Synjardy (empagliflozin/metformin, Synjardy XR (empagliflozin/metformin ER), Segluromet (ertugliflozin/metformin), Janumet (sitagliptin/metformin), Janumet XR (sitagliptin/metformin extended- release), Jentadueto (linagliptin/metformin), Jentadueto XR (linagliptin/metformin extended-release), Kazano (alogliptin/metformin), Kombiglyze XR (saxagliptin/metformin extended-release), Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin extended-release).
- Black box warning for congestive heart failure: Oseni (alogliptin/pioglitazone).
- Weight loss is excluded from coverage per Social Security 1927(d)(2)(A)

AVAILABLE DOSAGE FORMS:

Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors & SGLT2/DPP-4 Inhibitor Combinations & SGLT2-Biguanide Combinations & SGLT2/DPP-4 Inhibitor/Biguanide Combination

Glyxambi TABS 10-5MG
Glyxambi TABS 25-5MG
Invokamet TABS 150-1000MG
Invokamet TABS 150-500MG
Invokamet TABS 50-1000MG
Invokamet TABS 50-500MG
Invokamet XR TB24 150-1000MG
Invokamet XR TB24 150-500MG
Invokamet XR TB24 50-1000MG
Invokamet XR TB24 50-500MG
Invokana TABS 100MG
Invokana TABS 300MG
Qtern TABS 10-5MG
Qtern TABS 5-5MG
Segluromet TABS 2.5-1000MG
Segluromet TABS 2.5-500MG
Segluromet TABS 7.5-1000MG
Segluromet TABS 7.5-500MG
Steglatro TABS 15MG
Steglatro TABS 5MG
Steglujan TABS 15-100MG
Steglujan TABS 5-100MG
Synjardy TABS 12.5-1000MG
Synjardy TABS 12.5-500MG
Synjardy TABS 5-1000MG
Synjardy TABS 5-500MG
Synjardy XR TB24 10-1000MG
Synjardy XR TB24 12.5-1000MG
Synjardy XR TB24 25-1000MG
Synjardy XR TB24 5-1000MG
Trijardy XR TB24 10-5-1000MG
Trijardy XR TB24 12.5-2.5-1000MG
Trijardy XR TB24 25-5-1000MG
Trijardy XR TB24 5-2.5-1000MG
Xigduo XR TB24 10-1000MG
Xigduo XR TB24 10-500MG
Xigduo XR TB24 2.5-1000MG
Xigduo XR TB24 5-1000MG
Xigduo XR TB24 5-500MG

Incretin Mimetic Agents, GLP-1 Receptor Agonists, and GIP and GLP-1 Receptor Agonists, and combinations

Bydureon BCise AUIJ 2MG/0.85ML
Bydureon PEN 2MG
Byetta 10 MCG Pen SOPN 10MCG/0.04ML
Byetta 5 MCG Pen SOPN 5MCG/0.02ML
Mounjaro SOPN 10MG/0.5ML
Mounjaro SOPN 12.5MG/0.5ML
Mounjaro SOPN 15MG/0.5ML
Mounjaro SOPN 2.5MG/0.5ML
Mounjaro SOPN 5MG/0.5ML
Mounjaro SOPN 7.5MG/0.5ML
Ozempic (0.25 or 0.5 MG/DOSE) SOPN 2MG/1.5ML
Ozempic (0.25 or 0.5 MG/DOSE) SOPN 2MG/3ML
Ozempic (1 MG/DOSE) SOPN 2MG/1.5ML
Ozempic (1 MG/DOSE) SOPN 4MG/3ML
Ozempic (2 MG/DOSE) SOPN 8MG/3ML
Rybelsus TABS 14MG
Rybelsus TABS 3MG
Rybelsus TABS 7MG
Soliqua SOPN 100-33UNT-MCG/ML
Xultophy SOPN 100-3.6UNIT-MG/ML

Dipeptidyl Peptidase-4 Inhibitors (DPP4) and Combinations

Alogliptin Benzoate TABS 12.5MG
Alogliptin Benzoate TABS 25MG
Alogliptin Benzoate TABS 6.25MG
Alogliptin-metFORMIN HCl TABS 12.5-1000MG
Alogliptin-metFORMIN HCl TABS 12.5-500MG
Alogliptin-Pioglitazone TABS 12.5-15MG
Alogliptin-Pioglitazone TABS 12.5-30MG
Alogliptin-Pioglitazone TABS 12.5-45MG
Alogliptin-Pioglitazone TABS 25-15MG
Alogliptin-Pioglitazone TABS 25-30MG
Alogliptin-Pioglitazone TABS 25-45MG
Janumet TABS 50-1000MG
Janumet TABS 50-500MG
Janumet XR TB24 100-1000MG
Janumet XR TB24 50-1000MG
Janumet XR TB24 50-500MG
Jentadueto TABS 2.5-1000MG
Jentadueto TABS 2.5-500MG
Jentadueto TABS 2.5-850MG
Jentadueto XR TB24 2.5-1000MG
Jentadueto XR TB24 5-1000MG
Kazano TABS 12.5-1000MG

Kazano TABS 12.5-500MG
Kombiglyze XR TB24 2.5-1000MG
Kombiglyze XR TB24 5-1000MG
Kombiglyze XR TB24 5-500MG
Nesina TABS 12.5MG
Nesina TABS 25MG
Nesina TABS 6.25MG
Onglyza TABS 2.5MG
Onglyza TABS 5MG
Oseni TABS 12.5-15MG
Oseni TABS 12.5-30MG
Oseni TABS 12.5-45MG
Oseni TABS 25-15MG
Oseni TABS 25-30MG
Oseni TABS 25-45MG

Other Combinations

Actoplus Met TABS 15-500MG
Actoplus Met TABS 15-850MG
Pioglitazone HCl-Glimepiride TABS 30-2MG
Pioglitazone HCl-Glimepiride TABS 30-4MG
Pioglitazone HCl-metFORMIN HCl TABS 15-500MG
Pioglitazone HCl-metFORMIN HCl TABS 15-500MG

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SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW - Notable revisions: Products Affected Required Medical Information Drug Information Background and Other Considerations Available Dosage Forms References	01/2024
Annual updates. Removal of drugs due to stipulated language.	07/2023
New criteria creation	04/2022