Sodium-Glucose Co-Transporter-2 (SGLT2) Inhibitors and Combinations
Policy Number: C17804-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
6/1/2014	06/18/2020	06/18/2021
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
	Rx PA	Q3 2020 20200722C17804-A

PRODUCTS AFFECTED:
GLYXAMBI (empagliflozin / linagliptin), INVOKAMET XR (canagliflozin /metformin HCL extended-release), SYNJARDY (empagliflozin / metformin HCl), XIGDUO XR (dapagliflozin / metformin HCl), JARDIANCE (empagliflozin), FARXIGA (dapagliflozin), INVOKANA (canagliflozin) QTERN (dapagliflozin/saxagliptin), STEGLATRO (ertugliflozin) STEGLUJUAN (ertugliflozin/sitagliptin), INVOKAMET (canagliflozin/metformin), SEGLUROMET (ertugliflozin/metformin)

DRUG CLASS:
Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors & SLGT 2/DPP-4 Inhibitor Combinations)

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Retail Pharmacy

AVAILABLE DOSAGE FORMS:
Farxiga TABS 10MG, Farxiga TABS 5MG, Glyxambi TABS 10- 5MG, Glyxambi TABS 25-5MG, Invokana TABS 100MG, Invokana TABS 300MG, Jardiance TABS 10MG, Jardiance TABS 25MG, Qtern TABS 10-5MG, Steglatro TABS 15MG, Steglatro TABS 5MG, Steglujan TABS 15-100MG, Steglujan TABS 5-100MG Invokamet TABS 150-1000MG, 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, Segluromet TABS 2.5-1000MG, Segluromet TABS 2.5-500MG, Segluromet TABS 7.5-1000MG, Segluromet TABS 7.5-500MG, 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, 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

FDA-APPROVED USES:
Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus in multiple clinical settings

Farxiga (dapaglifozin): to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure with reduced rejection fraction (NYHA class II-IV)

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Type 2 diabetes mellitus

REQUIRED MEDICAL INFORMATION:
A. TYPE 2 DIABETES MELLITUS:
1. Documentation of diagnosis of type 2 diabetes mellitus
   AND
2. (a) If baseline Hemoglobin A1C < 9.0%: Documentation of an inadequate treatment response, contraindication or intolerance to TWO unique generic formulary agents. Inadequate response is defined as not achieving adequate glycemic control after 3 continuous months of receiving maximal daily doses despite current treatment.
   OR
   (b) If baseline A1C is > 9.0% and member is symptomatic (presenting with polyuria, polydipsia, or polyphagia), documentation that insulin use was initiated prior to the addition of a Sodium-Glucose Co-Transporter-2 (SGLT2) Inhibitors [if presenting without significant symptoms member may be an appropriate candidate for dual or triple therapy that could include a Sodium-Glucose Co-Transporter-2 (SGLT2) Inhibitors per (AACE/ACE 2020)]
   OR
   (c) Documentation patient has established atherosclerotic cardiovascular disease (ASCVD) or high risk (See Appendix), Stage 3 kidney disease, or heart failure with reduced ejection fraction
   AND
3. FOR NON-FORMULARY/NON-PREFERRED AGENTS: Member has had an inadequate response, intolerance, or contraindication to an ALL FORMULARY/PREFERRED SGLT2 inhibitor.(failure is defined as not achieving expected A1C lowering while adherent to therapy)
   AND
4. Member has an eGFR greater than or equal to ONE of the following: (a) Member on Farxiga, Xigduo XR, Qtern, Steglatro, Steglujan, and Segluromet: ≥ 60 mL/min/1.73m² (b) Member on Jardiance, Glyxambi, Synjardy or Synjardy XR: ≥ 45 mL/min/1.73m² (c) Member on Invokana 100mg: ≥ 45 mL/min/1.73m² (d) Member on Invokana > 100mg: ≥ 60 mL/min/1.73m² (e) Member on Invokamet or Invokamet XR 50mg: ≥ 45 mL/min/1.73m² (f) Patients on Invokamet or Invokamet XR > 50mg: ≥ 60 mL/min/1.73m²

B. REDUCE RISK OF HOSPITILZATION FOR HEART FAILURE/- FARXIGA ONLY:
1. (a) Documentation member has a diagnosis of heart failure (NYHA class II-IV) with reduced ejection fraction (40% or less)
   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 background standard of care for comorbidities
   AND
3. Prescriber attests that member does NOT have severe (eGFR <30 mL/min/1.73 m^2 by CKD-EPI), unstable or rapidly progressing renal disease

DURATION OF APPROVAL:
Initial Authorization: 6 months, Continuation of Therapy: 9 months

QUANTITY:
No requirement

PRESCRIBER REQUIREMENTS:
No requirement

AGE RESTRICTIONS:
18 years of age and older

CONTINUATION OF THERAPY:
A. TYPE 2 DIABETES MELLITUS:
1. Member continues to meet initial criteria
   AND
2. Documentation or refill history showing member compliance to therapy
   AND
3. If member has been on therapy at least 3 months: Documentation showing hemoglobin A1c is <7.0% or has improved from baseline while compliant to therapy.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
Glyxambi (empagliflozin/linagliptin) with an eGFR less than 45 mL/min/1.73 m2; Qtern (dapagliflozin/saxagliptin) or Steglujan (ertugliflozin/sitagliptin) with an eGFR less than 60 mL/min/1.73 m2; OR requesting for treatment of type 1 diabetes mellitus

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:
2018 American Diabetes Association: Standards of Medical Care in Diabetes Pharmacologic Therapy for Type 2 Diabetes Metformin, if not contraindicated and if tolerated, is the preferred initial pharmacologic agent for the treatment of type 2 diabetes. Long-term use of metformin may be associated with biochemical vitamin B12 deficiency, and periodic measurement of vitamin B12 levels should be considered in metformin treated patients, especially in those with anemia or peripheral neuropathy. Consider initiating insulin therapy (with or without additional agents) in patients with newly diagnosed type 2 diabetes who are symptomatic and/or have A1C ≥10% and/or blood glucose levels ≥ 300mg/dL. Consider initialing dual therapy in patients with newly diagnosed type 2 diabetes who have A1C ≥9% In patients without atherosclerotic cardiovascular disease, if monotherapy or dual therapy does not achieve or maintain the A1C goal over 3 months, add an additional antihyperglycemic agent based on drug-specific and patient factors. A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include efficacy, hypoglycemia risk, history of atherosclerotic cardiovascular disease, impact on weight, potential side effects, cost and patient preferences. In patients with type 2 diabetes and established atherosclerotic cardiovascular disease, antihyperglycemic therapy should begin with lifestyle management and metformin and subsequently incorporate an agent proven to reduce major adverse cardiovascular events and cardiovascular mortality (currently empagliflozin and liraglutide), after considering drug-specific and patient factors. (Level A level of evidence) Continuous re-evaluation of the medication regimen and adjustment as needed to incorporate patient factors and regimen complexity is recommended. In patients with type 2 diabetes and established atherosclerotic cardiovascular disease, after lifestyle management and metformin, the antihyperglycemic agent canagliflozin may be considered to reduce major adverse cardiovascular events, based on drug- specific and patient factors. (Level C level of evidence) For patients with type 2 diabetes who are not achieving glycemia goals, drug intensification, including consideration of insulin therapy, should not be delayed. Metformin should be continued when used in combination with other agents, including insulin, if not contraindicated and if tolerated.

APPENDIX:

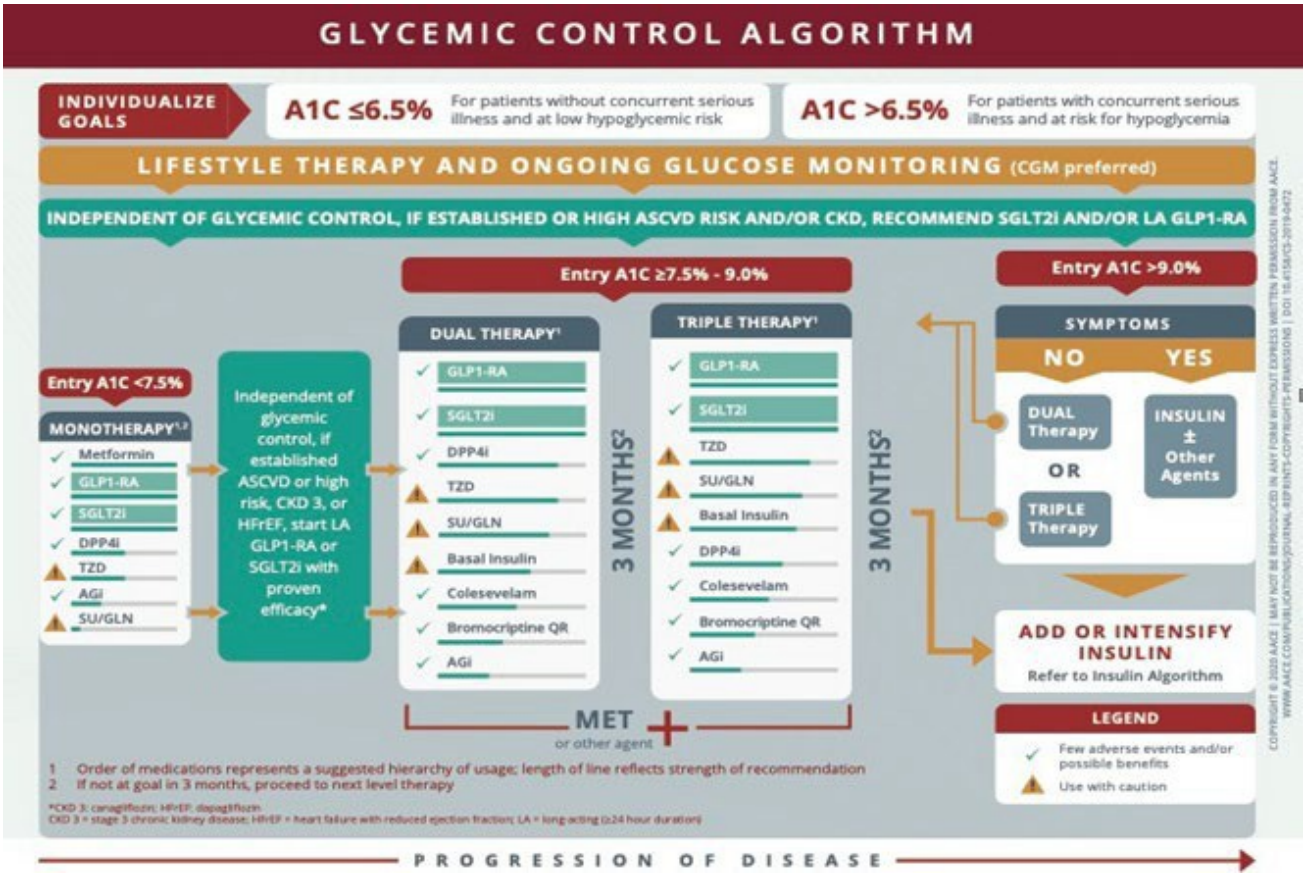

Table 1
AACE Lipid Targets for Patients With T2D or T2D Risk Factors (125)

Risk category	Risk factors[a]/10-year risk[b]	Treatment goals		
		LDL-C (mg/dL)	Non–HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	– Progressive ASCVD including unstable angina in patients after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in patients with DM, CKD 3/4, or HeFH – History of premature ASCVD (<55 male, <65 female)	<55	<80	<70
Very high risk	– Established or recent hospitalization for ACS, coronary, carotid, or peripheral vascular disease – Diabetes or CKD 3/4 with one or more risk factor(s) – HeFH	<70	<100	<80
High risk	≥2 risk factors and 10-year risk >10% or CHD risk equivalent[c], including diabetes or CKD 3/4 with no other risk factors	<100	<130	<90
Moderate risk	≥2 risk factors and 10-year risk <10%	<130	<160	NR
Low risk	≤1 risk factor	<160	<190	NR

Abbreviations: AACE = American Association of Clinical Endocrinologists; ACS = acute coronary syndrome; Apo = apolipoprotein; ASCVD = atherosclerotic cardiovascular disease; CHD = coronary heart disease; CKD = chronic kidney disease; DM = diabetes mellitus; HeFH = heterozygous familial hypercholesterolemia; HDL-C = high-density-lipoprotein cholesterol; LDL-C = low-density-lipoprotein cholesterol; NR = not recommended; T2D = type 2 diabetes.
[a]Major independent risk factors are high LDL-C, polycystic ovary syndrome, cigarette smoking, hypertension (blood pressure ≥140/90 mm Hg or on antihypertensive medication), low HDL-C (<40 mg/dL), family history of coronary artery disease (in males, first-degree relative younger than 55 years; in females, first-degree relative younger than 65 years), chronic renal disease (CKD) stage 3/4, evidence of coronary artery calcification and age (males ≥45 years; females ≥55 years). Subtract one risk factor if the person has high HDL-C.
[b]Framingham risk scoring is applied to determine 10-year risk.
[c]Coronary artery disease risk equivalents include diabetes and clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease).

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.

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3. Farxiga (dapagliflozin) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019.
4. Steglatro (ertugliflozin) [prescribing information]. Whitehouse Station, NJ: Merck Sharp& Dohme; November 2019.

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