Glucagon-like Peptide-1(GLP-1) receptor agonist
Policy Number: C5015-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
4/1/2014	3/11/2020	3/11/2021
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J3490	RxPA	Q2 2020 20200422C5015-A

PRODUCTS AFFECTED:
Adlyxin (lixisenatide), Bydureon (exanatide), Byetta (exenatide), Ozempic (semaglutide), Rybelsus (semaglutide), Trulicity (dulaglutide), Victoza (liraglutide)

DRUG CLASS:
Incretin Mimetic Agents, (GLP-1 Receptor Agonists)

ROUTE OF ADMINISTRATION:
Subcutaneous

PLACE OF SERVICE:
Retail Pharmacy

AVAILABLE DOSAGE FORMS:
Adlyxin 10mcg & 20mcg Pre-Filled Pen Starter Pack; Adlyxin 20mcg Pre-Filled Pen Maintenance Pack; Bydureon BCSISE: 2mg in 0.85mL single dose auto injector Bydureon: Single-dose 2mg vial or pen Byetta: 250mcg/mL: 5mcg per dose, 60 doses, 1.2mL prefilled pen OR 10mcg per dose, 60 doses, 2.4mL prefilled pen Ozempic: Pen, 2mg/1.5mL: 0.25mg or 0.mg per injection OR 1mg per injection; Rybelsus 3mg, 7mg, 14mg tabs; Trulicity: 0.75mg/0.5mL OR 1.5 mg/0.5 mL solution in a single-dose pen Victoza: 18gm/3ml 2 pen box or 3 pen box

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

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 Glucagon-like Peptide-1(GLP-1) receptor agonist [if presenting without significant symptoms member may be an appropriate candidate for dual or triple therapy that could include a Glucagon-like Peptide-1(GLP-1) receptor agonist 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 GLP1 agonist. failure is defined as not achieving expected A1C lowering while adherent to therapy)

DURATION OF APPROVAL:
Initial Authorization: 6 months, Continuation of Therapy: 12 months

QUANTITY:
Bydureon: 4 pens per 28 days, Byetta: 1 pen per month (30 days), Ozempic: 3 mL per 28 days, Rybelsus: 14 mg per day (1 tablet per day); Trulicity: 2mL per 28 days, Victoza: 9mL per 30 days

PRESCRIBER REQUIREMENTS:
No requirements

AGE RESTRICTIONS:
18 years of age and older

CONTINUATION OF THERAPY:
A. TYPE 2 DIABETES MELLITUS:
1. Patient continues to meet initial criteria
   AND
2. Documentation or refill history showing member compliance to therapy
   AND
3. If 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:
All other uses are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. For use in type 1 diabetes or diabetic ketoacidosis. Concurrent use with another GLP-1 agonist medicine. History of pancreatitis, severe renal impairment (creatinine clearance less than 30mL per minute), end stage renal disease, personal or family history of medullary thyroid carcinoma (MTC), Multiple Endocrine Neoplasia syndrome type 2 (MEN2) neoplasia syndrome type 2 (all GLP-1 receptor agonists other than Byetta, Adlyxin, and Soliqua)

- Trulicity is not for patients with pre-existing severe gastrointestinal disease.
- Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.
- Bydureon and Bydureon BCise are extended-release formulations of exenatide. Do not

coadminister with other exenatide containing products.

OTHER SPECIAL CONSIDERATIONS:

If A1C is over 10%, insulin should be started. Response to maximized insulin therapy should be assessed before starting an addition agent such as GLP-1 agonist. Saxenda indicated for chronic weight management (weight loss) and is considered benefit exclusion under most plans.

BACKGROUND:

The intent of the GLP-1 (glucagon-like peptide-1) Agonists criteria is to ensure appropriate selection of patients based on product labeling, and/or clinical guidelines, and/or clinical studies. Appropriate patients for exenatide or liraglutide therapy are those who are concurrently receiving or have tried metformin, a sulfonylurea, an oral combination product containing metformin or a sulfonylurea, or insulin.

The criteria and step edit allows continuation of therapy when patients have been receiving albiglutide, dulaglutide, exenatide or liraglutide. Patients without prerequisite agents in claims history or those who are unable to take a prerequisite agent due to documented intolerance, FDA labeled contraindication, or hypersensitivity will be reviewed when patient-specific documentation has been provided.

Boxed warning(s): thyroid C-cell tumors (all GLP-1 receptor agonists other than Byetta, Adlyxin, and Soliqua).

REMS: FDA has determined that a REMS is necessary to ensure that the benefits of Victoza (liraglutide) outweigh the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis http://www.victozapro.com/rems-program.aspx

APPENDIX:

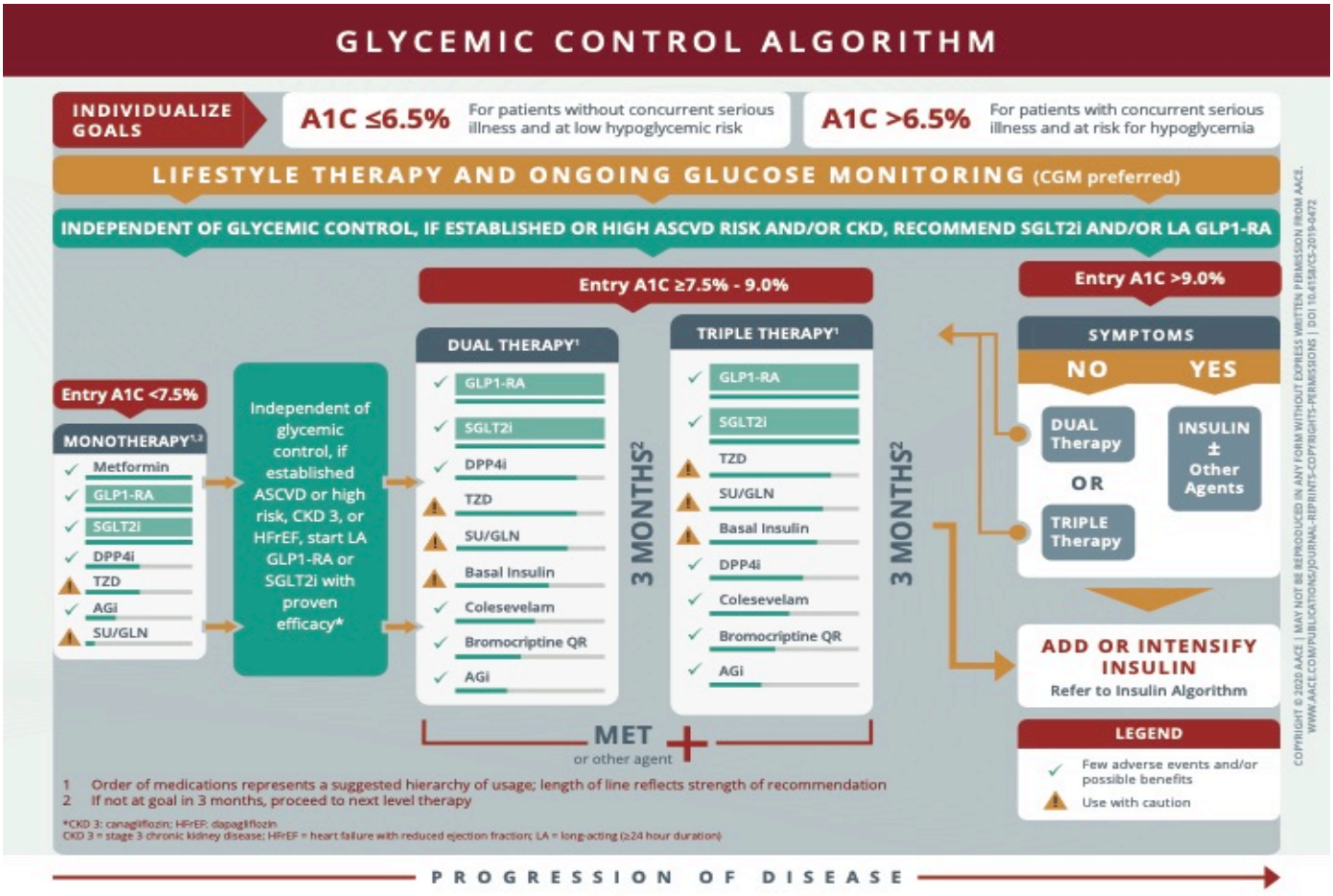

Table 1
AACE Lipid Targets for Patients With T2D or T2D Risk Factors (125)

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.

REFERENCES:

1. Adlyxin (lixisenatide) [prescribing information]. Bridgewater, NJ: Sanofi-Aventis US LLC; January 2019.
2. Bydureon (exenatide) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals; February 2019.
3. Bydureon BCise [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2018.
4. Byetta (exenatide) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; December 2018
5. Ozempic (semaglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc; January 2020
6. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes

(DiabetesCare 2018; 41: S73-S85).
7. Rybelsus (semaglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc; January 2020.
8. Trulicity (dulaglutide) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; September 2019.
9. Victoza (liraglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc; June 2019.
10. American Association of Clinical Endocrinologists and American College of Endocrinologists (AACE/ACE) Comprehensive Type 2 Diabetes Management Algorithm 2020. Available at: https://www.aace.com/pdfs/diabetes/algorithm-exec-summary.pdf OR AACE 2020 Feb PDF Accessed Feb 2020.