BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR AGONISTS: BYDUREON BCISE® (exenatide) BYETTA® (exenatide) Liraglutide OZEMPIC® (semaglutide) RYBELSUS® (semaglutide) TRULICITY® (dulaglutide) VICTOZA® (liraglutide) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** A glucagon-like peptide (GLP-1) receptor agonist and/or a generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual's age is consistent within the FDA approved product labeling

2. Individual has a confirmed diagnosis of type 2 diabetes determined by **ONE** of the following:
    a. A1C of 6.5% or greater
    b. Fasting plasma glucose (FPG) of at least 126mg/dl or greater
    c. 2-hour plasma glucose (PG) of 200mg/dl or greater during oral glucose tolerance test (OGTT)
    d. Random plasma glucose (PG) of 200 mg or greater

3. Requested medication will be used as an adjunct to diet and exercise to improve glycemic control

4. Medication is **NOT** solely being used for weight loss

5. There are **NO** FDA-label contraindications such as:
    a. Personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
    b. **Additional criteria for Bydureon BCise and Byetta:** History of drug-induced immune-mediated thrombocytopenia from exenatide products

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

Initial approval duration: 12 months
- Individual may be referred to case management for diabetes related ancillary services

➢ **Criteria for continuation of coverage (renewal request):** A glucagon-like peptide (GLP-1) receptor agonist and/or a generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual has a confirmed diagnosis of type 2 diabetes mellitus and requested medication will be used as an adjunct to diet and exercise to improve glycemic control

2. Individual's condition has responded while on therapy with response defined as a decrease in A1c from baseline

3. Individual has been adherent with the medication

4. Medication is **NOT** solely being used for weight loss

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has not developed any significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Pancreatitis
        ii. Severe hypersensitivity reaction (e.g., anaphylaxis and angioedema)
        iii. Acute kidney injury
        iv. Severe gastrointestinal disease (e.g., gastroparesis)
        v. Drug induced immune-mediated thrombocytopenia
        vi. Acute gallbladder disease (e.g., cholelithiasis, cholecystitis)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Glucagon-like peptide-1 (GLP-1) receptor agonists activate the GLP-1 receptor and increase intracellular cyclic AMP (cAMP) leading to insulin release in a glucose-dependent manner. They also decrease glucagon secretion and slow gastric emptying. They do not usually cause hypoglycemia in the absence of therapies that otherwise cause hypoglycemia. An additional benefit in many individuals with type 2 diabetes is weight-loss.

Bydureon BCise (exenatide) is an extended-release formulation of exenatide that is indicated 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. It is not recommended as first-line therapy for patients inadequately controlled on diet and exercise.

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Byetta (exenatide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Ozempic (semaglutide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus and to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease.

Rybelsus (semaglutide oral tablet) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. It is not recommended as first-line therapy for patients inadequately controlled on diet and exercise.

Trulicity is indicated 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 and to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors. Trulicity is not recommended in patients with severe gastrointestinal disease, including severe gastroparesis.

Victoza (liraglutide) indicated 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 and to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations for use: All the above agents are not for treatment of type 1 diabetes mellitus. All of the above agents, except Victoza (liraglutide), have not been studied in patients with a history of pancreatitis and other antidiabetic therapies should be considered in these patients.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Criteria for the diagnosis of diabetes in nonpregnant individuals

Meets ONE of the following:	Additional Information
1. A1c ≥ 6.5%*	The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay
2. FPG ≥ 126mg/dl*	Fasting is defined as no caloric intake for at least 8 hours

3. 2-hour PG ≥ 200mg/dl during OGTT*	The test should be performed as described by the WHO, using glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water
4. In an individual with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dl	Random is any time of the day without regard to time since previous meal

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test, NGSP, National Glycohemoglobin Standardization Program; WHO, World Health Organization; *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

Diabetes Medications

CLASS	Generic Name	Brand Name
Biguanide	Metformin	Glucophage, Glucophage XR, Glumetza, Fortamet, Riomet
Sulfonylurea	Glimepiride	Amaryl
	Glipizide, Glipizide XL	Glucotrol XL
	Glyburide	
DPP-4 Inhibitor	Sitagliptin	Januvia
	Saxagliptin	Onglyza
	Linagliptin	Tradjenta
	Alogliptin	Nesina
SGLT2 Inhibitor	Canagliflozin	Invokana
	Dapagliflozin	Farxiga
	Empagliflozin	Jardiance
	Ertugliflozin	Steglatro
GLP-1 Receptor Agonist (Incretin Mimetic)	Exenatide	Byetta, Bydureon BCise
	Liraglutide	Victoza
	Dulaglutide	Trulicity
	Lixisenatide	Adlyxin
	Semaglutide	Ozempic, Rybelsus
GIP/GLP-1 Receptor Agonist	Tirzepatide	Mounjaro
Thiazolidinedione (Insulin Sensitizing Agent)	Pioglitazone	Actos
Amylin Analog	Pramlintide	Symlin
Alpha-glucosidase inhibitor	Acarbose	
	Miglitol	
Meglitinide Analog	Nateglinide	
	Repaglinide	
Insulin	Glargine	Lantus, Basaglar, Toujeo, Semglee
	Detemir	Levemir
	Degludec	Tresiba
	NPH	Novolin N, Humulin N

	Lispro	Humalog, Admelog, Lyumjev
	Aspart	Novolog, Fiasp
	Glulisine	Apidra
	Regular	Humulin, Novolin
	Insulin inhalation powder	Afrezza
Combination Products		
DPP-4 Inhibitor/biguanide	Sitagliptin/metformin	Janumet, Janumet XR
	Linagliptin/metformin	Jentadueto, Jentadueto XR
	Alogliptin/metformin	Kazano
	Saxagliptin/metformin	Kombiglyze XR
DPP-4 Inhibitor/thiazolidinedione	Alogliptin/pioglitazone	Oseni
Insulin/GLP-1 Receptor Agonist	Glargine/lixisenatide	Soliqua
	Degludec/liraglutide	Xultophy
SGLT2 inhibitor/DPP-4 inhibitor	Empagliflozin/linagliptin	Glyxambi
	Dapagliflozin/saxagliptin	Qtern
	Ertugliflozin/sitagliptin	Steglujan
SGLT2 inhibitor/biguanide	Canagliflozin/metformin	Invokamet, Invokamet ER
	Ertugliflozin/metformin	Segluromet
	Empagliflozin/metformin	Synjardy, Synjardy XR
	Dapagliflozin/metformin	Xigduo XR
Sulfonylurea/biguanide	Glipizide/metformin	
	Glyburide/metformin	
Sulfonylurea/thiazolidinedione	Pioglitazone/glimepiride	Duetact
SGLT2 inhibitor/DPP-4 inhibitor/biguanide	Empagliflozin/linagliptin/metformin	Trijardy XR

Resources:

Bydureon BCise (exenatide) extended-release subcutaneous injection prescribing information, revised by AstraZeneca Pharmaceuticals LP 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 11, 2024.

Byetta (exenatide) subcutaneous injection prescribing information, revised by AstraZeneca Pharmaceuticals LP 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 11, 2024.

Trulicity (dulaglutide) subcutaneous injection prescribing information, revised by Eli Lilly and Company 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 11, 2024.

Liraglutide subcutaneous injection prescribing information, revised by Teva Pharmaceuticals USA, Inc 01-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 11, 2024.

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Victoza (liraglutide) subcutaneous injection prescribing information, revised by Novo Nordisk 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 11, 2024.

Ozempic (semaglutide) subcutaneous injection prescribing information, revised by Novo Nordisk 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 11, 2024.

Rybelsus (semaglutide) tablet prescribing information, revised by Novo Nordisk 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 11, 2024.

Dungan K, DeSantis A. Glucagon-like peptide 1-based therapies for the treatment of type 2 diabetes mellitus. In: UpToDate, Nathan DM, Rubinow K (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through November 2024. Last updated on December 04, 2024. Accessed December 11, 2024.

American Diabetes Association Professional Practice Committee. American Diabetes Association Standards of care in diabetes – 2024. Diabetes Care. 2024 January;47(Suppl 1): S1-328. Accessed January 22, 2024. Re-evaluated December 11, 2024.

Davies MJ, Aroda VR, Collins BS, et al.: Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2022;45(11):2753–2786. Accessed January 13, 2024. Re-evaluated December 11, 2024.

ElSayed NA, Aleppo G, Aroda VR, et al.: American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of Care in Diabetes—2023. Diabetes Care 2023;46(Suppl. 1): S140–S157. Accessed January 13, 2024. Re-evaluated December 11, 2024.