LOUISIANA BLUE

GLP-1, GIP/GLP-1 Agonists for Diabetes

Policy # 00324
Original Effective Date: 11/16/2011
Current Effective Date: 01/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Wegovy™‡ (semaglutide) is addressed separately in medical policy 00886.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of the available data, the Company may consider glucagon-like-peptide-1 (GLP-1) receptor agonists and glucose-dependent insulinotropic polypeptide (GIP)/(GLP-1) receptor agonists that are FDA approved for the treatment of diabetes, including but not limited to Byetta®‡ (exenatide), Bydureon®‡ BCise (exenatide ER), Liraglutide injection (Victoza®‡, Authorized [branded] Generic), Trulicity™‡ (dulaglutide), Ozempic®‡ (semaglutide), Rybelsus®‡ (semaglutide), and Mounjaro™‡ (tirzepatide), to be eligible for coverage** when the patient selection criteria below are met for the requested drug:

Patient Selection Criteria

Coverage eligibility will be considered when selection criteria below are met for the requested drug:

- For Trulicity (dulaglutide), Ozempic (semaglutide), Rybelsus (semaglutide),or Mounjaro (tirzepatide) requests:
  - Patient has a diagnosis of type 2 diabetes mellitus; AND
  - Diagnosis has been confirmed by documentation of ONE of the following:
    - Hemoglobin A1c ≥ 6.5%; OR
    - Fasting plasma glucose (FPG) ≥ 126 mg/dL; OR
    - 2-hour plasma glucose (2-h PG) ≥ 200 mg/dL; AND
  - For Trulicity requests ONLY:
    - Patient is ≥ 10 years of age; OR
  - For Ozempic, Rybelsus, and Mounjaro requests ONLY:
    - Patient is ≥ 18 years of age; OR

- For Byetta (exenatide), Bydureon BCise (exenatide ER), or Liraglutide injection (Victoza, Authorized [branded] Generic) requests:
    - Patient has a diagnosis of type 2 diabetes mellitus; AND
    - Diagnosis has been confirmed by documentation of ONE of the following:
        - Hemoglobin A1c ≥ 6.5%; OR
        - Fasting plasma glucose (FPG) ≥ 126 mg/dL; OR
        - 2-hour plasma glucose (2-h PG) ≥ 200 mg/dL; AND
    - Patient has tried and failed (e.g., intolerance or inadequate response) at least TWO of the following products: Trulicity (dulaglutide injection), Ozempic (semaglutide injection), Rybelsus (semaglutide tablet), or Mounjaro (tirzepatide injection); AND (*Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met*)
    - For Byetta requests ONLY:
        - Patient is ≥ 18 years of age; OR
    - For Bydureon BCise and Liraglutide injection (Victoza, Authorized [branded] Generic) requests ONLY:
        - Patient is ≥ 10 years of age.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Byetta (exenatide), Bydureon BCise (exenatide ER), and Liraglutide injection (Victoza, Authorized [branded] Generic) WITHOUT having tried and failed at least TWO of the following products: Trulicity (dulaglutide), Ozempic (semaglutide), Rybelsus (semaglutide), or Mounjaro (tirzepatide) to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of GLP-1 and GIP/GLP-1 agonists that are FDA approved for the treatment of diabetes for any non-FDA approved indication for that specific drug to be **investigational.***

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Schematic

Preferred	Non-Preferred
Trulicity Ozempic Rybelsus Mounjaro	Byetta Bydureon BCise Victoza Liraglutide injection (Authorized [branded] Generic)

Background/Overview

The GLP-1 receptor agonists and the GLP-1/GIP agonist addressed in this policy are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. Byetta, Bydureon BCise, Victoza, Trulicity, and Ozempic are antihyperglycemic agents for subcutaneous injection. Rybelsus is the only GLP-1 agonist product that is currently in an oral dosage form. These products are incretin mimetic agents that bind and activate the human GLP-1 receptor. Activation of this receptor increases glucose-dependent insulin secretion by pancreatic beta-cells and suppresses glucagon secretion and slows gastric emptying. Byetta, Bydureon BCise, Victoza, Trulicity, Ozempic, and Rybelsus are FDA approved for adult patients with type 2 diabetes. Victoza, Trulicity, and Bydureon BCise are additionally indicated for type 2 diabetes in pediatric patients ≥ 10 years of age. Byetta is administered subcutaneously twice daily. Bydureon BCise, Trulicity, and Ozempic are administered subcutaneously once weekly, and Victoza is administered subcutaneously once daily. Rybelsus is taken orally once daily. Ozempic, Rybelsus, Trulicity, and Victoza also have labeled indications for cardiovascular risk reduction in adults with type 2 diabetes.

In June of 2024, an authorized generic of Victoza was launched, carrying the same indications as the brand product. Victoza became the first GLP-1 receptor agonist to have a generic formulation on the market.

Mounjaro is a subcutaneous injection indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. It selectively binds and activates both the GIP and GLP-1 receptors. It works in a glucose dependent manner by enhancing first- and second-phase insulin secretion and reducing glucagon levels. In addition to suppressing glucagon secretion, increasing glucose-dependent insulin secretion, and delaying gastric emptying, the drug also works to increase insulin sensitivity. Mounjaro is administered subcutaneously once weekly.

The active ingredient in the non-preferred products have not demonstrated superiority in head to head studies comparing preferred products with the non-preferred products.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Byetta, Rybelsus, and Mounjaro are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Bydureon BCISE 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.

Victoza and branded Liraglutide injection are 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.

Ozempic 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 (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Trulicity is 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 and to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

As monotherapy, Byetta 5 mcg or 10 mcg twice daily in adjunct to diet and exercise reduced glycosylated hemoglobin (HbA1c) 0.5 to 0.7% (placebo corrected); a placebo corrected weight loss of 2.7 kg to 2.9 kg was noted at the end of the 24 week trial. In general, Byetta appears to lower HbA1c by 0.5% to 1%. In addition to HbA1c reduction, Byetta reduces food intake, and on average produces a 2 kg to 3 kg weight loss over a 6-month period in diabetic patients. Byetta 10 mcg twice daily as an adjunct to metformin, a sulfonylurea, or both in patients with type 2 diabetes decreased body weight by 1.6 kg to 2.8 kg after 30 weeks. In an interim analysis involving a 52 week open-label uncontrolled extension study, which followed the 30 week double-blind period, the average weight loss in type 2 diabetics (n = 314) after a total of 82 weeks of Byetta therapy was 4.4 kg. A similar analysis of an interim report noted weight loss in type 2 diabetics (n = 92) after 82 weeks of Byetta treatment was 5.3 kg. In a multicenter, open-label, randomized, controlled trial in patients with type 2 diabetes (n = 551), at 26 weeks, treatment with Byetta led to a 2.3 kg reduction in body weight compared with a 1.8 kg increase for patients treated with insulin glargine (Lantus®)‡. Addition of Byetta to a thiazolidinedione ([TZD] with or without metformin) resulted in a 1.51 kg mean reduction in bodyweight after 16 weeks. Reductions in bodyweight in type 2 diabetic patients treated with Byetta have been sustained for up to two years.

As monotherapy in a 52 week trial, Victoza 1.2 mg and 1.8 mg in adjunct to diet and exercise resulted in mean HbA1c reduction of 0.8% to 1.1% and a 2.1 kg to 2.5 kg weight reduction. Victoza was studied in combination with one or two other oral anti-diabetic agents in four 26 week studies. When added to metformin, Victoza 1.8 mg and 1.2 mg resulted in a mean placebo corrected HbA1c and weight reduction of 1.1% and 1.1 kg to 1.3 kg, respectively. As add-on to sulfonylurea (glimepiride), Victoza 1.2 mg and 1.8 mg treatment resulted in a placebo corrected mean HbA1c reduction of 1.3% to 1.4%. As part of a triple therapy combination with metformin and glimepiride, Victoza 1.8 mg reduced HbA1c (placebo corrected mean) by 1.1% and resulted in a mean weight reduction of 1.4 kg (placebo corrected). When added to metformin and rosiglitazone mean placebo corrected reduction in HbA1c and weight with Victoza (1.8 mg and 1.2 mg) were 0.9% (both doses) and 2.6 kg and 1.6 kg, respectively. In a head-to-head trial with Byetta, weight was significantly reduced in both Byetta (10 mcg twice daily) and Victoza (1.8 mg daily) and was non-significant between groups (-2.87 kg vs. -3.24 kg, respectively).

A randomized, open-label 24-week comparative trial was conducted with Bydureon and Byetta for safety and efficacy in 252 patients with type 2 diabetes. These patients had inadequate glycemic control with diet and exercise alone or with oral antidiabetic therapy, including metformin, a sulfonylurea, a TZD, or combination of two of those therapies. Patients were treated with diet and exercise alone (19%), a single oral antidiabetic agent (47%), or combination therapy of oral antidiabetic agents (35%). The mean baseline HbA1c was 8.4%. Patients were randomly assigned to receive Bydureon 2 mg once every seven days (weekly) or Byetta (10 mcg twice daily), in addition to existing oral antidiabetic agents. Patients assigned to Byetta initiated treatment with 5 mcg twice-daily then increased the dose to 10 mcg twice daily after 4 weeks. The primary endpoint was change in HbA1c from baseline to week 24 (or the last value at time of early discontinuation). Change in body weight was a secondary endpoint. Treatment with Bydureon was superior to Byetta for mean HbA1c reduction over 24 weeks.

Trulicity was studied in various trials as monotherapy as well as in addition to oral therapies and in addition to insulin. As monotherapy, Trulicity lowered the HbA1c from 0.7-0.8% vs. metformin's lowering of 0.6%. Trulicity as monotherapy also lowered the fasting plasma glucose by 26 to 29 mg/dL vs. a lowering of 24 mg/dL with metformin. In the combo therapy trials, the HbA1c lowering ranged from 0.8 to 1.6% depending on the treatment that Trulicity was combined with.

Ozempic has been studied as monotherapy and in combination with metformin, metformin and sulfonylureas, metformin and/or thiazolidinedione, and basal insulin in patients with type 2 diabetes mellitus. The efficacy of Ozempic was compared with placebo, sitagliptin, Bydureon, and insulin glargine. Most trials evaluated the use of Ozempic 0.5 mg, and 1 mg, with the exception of the trial comparing Ozempic and Bydureon where only the 1 mg dose was studied. In patients with type 2 diabetes mellitus, Ozempic produced clinically relevant reduction from baseline in HbA1c compared with placebo. The various HbA1c lowering ranged from 1.1-1.6% depending on the clinical comparison.

Rybelsus' study program included 10 randomized, placebo-controlled or active-comparator trials. Studies included comparisons between Rybelsus and placebo, other oral anti-diabetic agents (Jardiance®, Januvia®), other GLP-1 agonist products (Victoza, Ozempic), along with additions to metformin and sulfonylurea. The various HbA1c lowering ranged from 0.6-1.9% depending on the clinical comparison.

The effectiveness of Mounjaro as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus was established in five trials. In these trials, Mounjaro was studied as monotherapy; as an add-on to metformin, sulfonylureas, and/or sodium-glucose co-transporter 2 inhibitors (SGLT2 inhibitors); and in combination with basal insulin with or without metformin. In these trials, Mounjaro was compared with placebo, semaglutide 1 mg, insulin degludec, and/or insulin glargine. Monotherapy with Mounjaro once weekly for 40 weeks resulted in a statistically significant reduction in HbA1c compared with placebo that ranged from a 1.7-1.8% decrease. Depending on the clinical comparisons of Mounjaro in combination with other agents, the HbA1c lowering ranged from 1.9-2.4%.

Based on a review of the available data and in the absence of any of the caveats mentioned, there is no advantage of using the non-preferred agents mentioned in this policy over the preferred agents mentioned in this policy.

This policy is also intended to ensure that the GLP-1 and GIP/GLP-1 agonist products approved for the treatment of type 2 diabetes are used for the indication of type 2 diabetes only.

References

1. Express Scripts Prior Authorization policy on Glucagon-Like Peptide (GLP-1) Agonists (Byetta [exenatide injection Amylin] and Victoza [liraglutide injection- NovoNordisk]). May 2014.
2. Byetta injection [package insert]. San Diego, CA: Amylin Pharmaceuticals, Inc.; Updated November 2024.
3. Victoza [package insert]. Princeton, NJ: Novo Nordisk, Inc.; Updated November 2024.
4. Bydureon for injectable suspension [package insert]. San Diego, CA: Amylin Pharmaceuticals; Updated November 2024.
5. Moretto TJ, Milton DR, Ridge TD, et al. Efficacy and tolerability of exenatide monotherapy over 24 weeks in antidiabetic drug-naive patients with type 2 diabetes: a randomized, double-blind, placebo-controlled, parallel-group study. Clin Ther. 2008;30(8):1448-60.
6. Nathan DM. Buse JB, Davidson MB, Ferrannini E et al. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. A consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2009;32(1):193-203.
7. DeFronzo RA, Ratner RE, Han J, Kim DD, Fineman MS, Baron AD. Effects of exenatide (Exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. Diabetes Care. 2005;28(5):1092-1100.

8. Buse JB, Henry RR, Han J, et al. Effects of exenatide (Exendin-4) on glycemic control over 30 weeks in sulfonylurea-treated patients with type 2 diabetes. Diabetes Care. 2004;27(11):2628-2635.
9. Kendall DM, Riddle MC, Rosenstock J, et al. Effects of exenatide (Exendin-4) on glycemic control over 30 weeks in patients with type 2 diabetes treated with metformin and a sulfonylurea. Diabetes Care. 2005;28(5):1083-1091.
10. Blonde L, Klein EJ, Han J, et al. Interim analysis of the effects of exenatide treatment on A1C, weight an cardiovascular risk factors over 82 weeks in 314 overweight patients with type 2 diabetes. Diabetes Obes Metab. 2006;8:436-447.
11. Ratner RE, Maggs D, Nielsen LL, et al. Long-term effects of exenatide therapy over 82 weeks on glycaemic control and weight in over-weight metformin-treated patients with type 2 diabetes mellitus. Diabetes Obes Metab. 2006;8:419-428.
12. Heine RJ, Van Gaal LF, Johns D, et al. Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes. A randomized trial. Ann Intern Med. 2005;143:559-569.
13. Cretkovic RS, Plosker GL. Exenatide: a review of its use in patients with type 2 diabetes mellitus (as an adjunct to metformin and/or a sulfonylurea). Drugs. 2007;67(6):935-954.
14. Garber A, Henry R, Ratner R, et al; for the LEAD-3 (Mono) study group. Liraglutide versus glimepiride monotherapy for type 2 diabetes (LEAD-3 mono): a randomized, 52-week, phase III, double-blind, parallel-treatment trial. Lancet. 2009;373:473-481.
15. Nauck M, Frid A, Hermansen K, et al; for the LEAD-2 study group. Efficacy and safety comparison of liraglutide, glimepiride, and placebo, all in combination with metformin, in type 2 diabetes. Diabetes Care. 2009;32:84-90.
16. Marre M, Shaw J, Brandle M, et al; on behalf of the LEAD-1 SU study group. Liraglutide, a once-daily human GLP-1 analogue, added to a sulphonylurea over 26 weeks produces greater improvements in glycaemic and weight control compared with adding rosiglitazone or placebo in subjects with type 2 diabetes (LEAD-1 SU). Diabet Med. 2009;26:268-278.
17. Russel-Jones D, Vaag A, Schmitz O, et al; on behalf of the Liraglutide Effect and Action in Diabetes 5 (LEAD-5) met + SU study group. Diabetologia. 2009;52:2046-2055.
18. Zinman B, Gerich J, Buse JB, et al. Efficacy and safety of the human glucagon-like peptide-1 analog liraglutide in combination with metformin and thiazolidinediones in patients with type 2 diabetes (LEAD-4 Met + TZD). Diabetes Care. 2009:32(7):1224-1230.
19. Buse JB, Rosenstock J, Sesti G, et al; for the LEAD-6 study group. Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomized, parallel-group, multinational, open-label trial (LEAD-6). Lancet. 2009;374:39-47.
20. Rodbard, HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: An algorithm for glycemic control. Endocr Pract. 2009;15(6):541-559.
21. Astrup A, Rossner S, Van Gaal L et al. Effects of liraglutide in the treatment of obesity: a randomized, double-blind, placebo controlled study. Lancet. 2009;1606-1616.
22. Rosenstock J, Kladd LJ, Northrup J, et al. Effects of exenatide and lifestyle modification on body weight and glucose tolerance in obese subjects with and without pre-diabetes. Diabetes Care. 2010;33(6):1173-1175.

23. Raman VS, Mason KJ, Rodriguez LM, et al. The role of adjunctive exenatide in pediatric type 1 diabetes. Diabetes Care. 2010;22(6):1294-1296.
24. Kielgast U, Krarup T, Holst JJ and Madsbad S. Four weeks of treatment with liraglutide reduces insulin dose without loss of glycemic control in type 1 diabetic patients with and without residual β-cell function. Diabetes Care. 2011;34:1463-1468.
25. Varanasi A, Bellini N, Rawal D, et al. Liraglutide as additional treatment for type 1 diabetes. Eur J Endocrinol. 2011;165:77-84.
26. Trulicity [package insert]. Eli Lilly and Company. Indianapolis, IN. Updated November 2024.
27. Ozempic [package insert]. Novo Nordisk. Plainsboro, New Jersey. Updated November 2024.
28. Rybelsus [package insert]. Novo Nordisk. Plainsboro, New Jersey. Updated November 2024.
29. Mounjaro [package insert]. Eli Lilly and Company. Indianapolis, Indiana. Updated November 2024.
30. Liraglutide injection [package insert]. Teva Pharmaceuticals. Parsippany, New Jersey. January 2024.

Policy History

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11/03/2011	Medical Policy Committee review
11/16/2011	Medical Policy Implementation Committee approval. New policy.
11/01/2012	Medical Policy Committee review
11/28/2012	Medical Policy Implementation Committee approval. Added Bydureon (exenatide ER) to the title and coverage statement.
11/07/2013	Medical Policy Committee review
11/20/2013	Medical Policy Implementation Committee approval. Revision to coverage language without changing the intent of the policy. Coverage eligibility unchanged.
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval. Changed title. Added Tanzeum to the policy. Updated background information and rationale to reflect new product and title change.
04/02/2015	Medical Policy Committee review
04/20/2015	Medical Policy Implementation Committee approval. Changed title. Added Trulicity to policy. Updated background and rationale.
04/07/2016	Medical Policy Committee review
04/20/2016	Medical Policy Implementation Committee approval. No change to coverage.
10/06/2016	Medical Policy Committee review
10/19/2016	Medical Policy Implementation Committee approval. Chose preferred products in this class (Byetta, Bydureon, Victoza, and Trulicity).
03/02/2017	Medical Policy Committee review
03/15/2017	Medical Policy Implementation Committee approval. Clarified to use two preferred products.
03/01/2018	Medical Policy Committee review
03/21/2018	Medical Policy Implementation Committee approval. No change to coverage.

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07/05/2018	Medical Policy Committee review
07/11/2018	Medical Policy Implementation Committee approval. Added Ozempic and Bydureon BCise to the policy.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. Moved Byetta and Bydureon/Bydureon BCise to non-preferred
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. No change to coverage.
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. Added a new drug, Rybelsus, as a preferred option. Removed Tanzeum from the policy as it has been discontinued.
09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. No change to coverage.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. Moved Byetta and Bydureon/Bydureon BCise from non-preferred to preferred. Updated the patient selection criteria and background information. Removed the original Bydureon formulation from the policy due to discontinuation as the Bydureon BCise auto-injector is the only formulation now available.
08/04/2022	Medical Policy Committee review
08/10/2022	Medical Policy Implementation Committee approval. Changed title of policy from GLP-1 Agonists for Diabetes to GLP-1, GIP/GLP-1 Agonists for Diabetes. Added new drug, Mounjaro, to policy as a preferred product.
08/03/2023	Medical Policy Committee review
08/09/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/01/2024	Medical Policy Committee review
08/14/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Removed Adlyxin from the policy due to discontinuation. Moved Byetta, Bydureon BCise, and Victoza from preferred to non-preferred. Added authorized Liraglutide generic to the policy as non-preferred with associated criteria. Updated background information.

Next Scheduled Review Date: 12/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.