



## STEP THERAPY POLICY

- POLICY:** Vitamin B12 (Cyanocobalamin) Products Step Therapy Policy
- Cyanocobalamin injection (generic only – Various)
  - Nascobal® (cyanocobalamin nasal spray – Par)

**REVIEW DATE:** 04/26/2023

### **INSTRUCTIONS FOR USE**

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

### **CIGNA NATIONAL FORMULARY COVERAGE:**

#### **OVERVIEW**

Nascobal, a vitamin B12 nasal spray, is indicated for the following:

- **Pernicious anemia**, vitamin B12 maintenance therapy in adults who are in remission following intramuscular vitamin B12 therapy and who have no nervous system involvement.
- **Vitamin B12 deficiency, treatment**, in adults with dietary, drug-induced, or malabsorption-related vitamin B12 deficiency not due to pernicious anemia.
- **Vitamin B12 deficiency, prevention**, in adults with vitamin B12 requirements in excess of normal.

Nascobal is supplied in a nasal spray containing 500 mcg cyanocobalamin per actuation.<sup>1</sup> Additionally, cyanocobalamin is available as an intramuscular injection (1,000 mcg per mL), which is indicated for **vitamin B12 deficiencies** due to malabsorption, which may be associated with the following conditions: pernicious anemia; gastrointestinal pathology, dysfunction, or surgery (including gluten enteropathy or sprue, small bowel bacteria overgrowth, or total or partial gastrectomy); fish tapeworm infestation; malignancy of the pancreas or bowel, or folic acid deficiency.<sup>2</sup> Over-the-counter vitamin B12 oral supplements are also

available, although these are poorly absorbed when intrinsic factor is absent (i.e., pernicious anemia).<sup>3</sup>

### **Disease Overview**

Vitamin B12, a water-soluble vitamin, is necessary for proper red blood cell formation, neurological function, and DNA synthesis.<sup>3</sup> Vitamin B12, bound to protein in food, is released by hydrochloric acid and gastric protease in the stomach. Vitamin B12 then complexes with intrinsic factor and is absorbed in the distal ileum. Thus, patients with deficiencies in stomach acid, intrinsic factor, or gastrointestinal absorption are at risk for development of vitamin B12 deficiency. Oral vitamin B12 supplements are provided in the free (not protein bound) form, therefore individuals with hydrochloric acid deficiency are typically able to meet their vitamin B12 needs with oral vitamin supplementation or fortified foods. Likewise, oral vitamin B12 supplementation has demonstrated efficacy in correcting deficiency related to gastrointestinal malabsorption, including gastric bypass and Crohn's disease.<sup>4-6</sup> Conversely, in pernicious anemia (characterized by the absence of intrinsic factor), only 1% of oral vitamin B12 is absorbed.<sup>3</sup> Thus, patients with pernicious anemia are typically treated with injectable vitamin B12.

### **POLICY STATEMENT**

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

**Vitamin B12 (Cyanocobalamin) product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.**

**Step 1:** cyanocobalamin injection

**Step 2:** Nascobal

### **CRITERIA**

**1.** If the patient has tried one Step 1 Product, approve a Step 2 Product.

### **REFERENCES**

1. Nascobal® nasal spray [prescribing information]. Chestnut Ridge, NY: Par; November 2018.
2. Cyanocobalamin injection [prescribing information]. Shirley, NY: American Regent; October 2018.
3. Vitamin B12 Fact Sheet for Health Professionals. National Institutes of Health Office of Dietary Supplements. Updated March 9, 2022. Available at: <https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/>. Accessed on April 4, 2023.

4. Andrès E, Zulfiqar AA, Serraj K, et al. Systematic review and pragmatic clinical approach to oral and nasal vitamin B12 (cobalamin) treatment in patients with vitamin B12 deficiency related to gastrointestinal disorders. *J Clin Med.* 2018; 7(10):304.
5. Gomollón F, Gargallo CJ, Muñoz JF, et al. Oral Cyanocobalamin is Effective in the Treatment of Vitamin B12 Deficiency in Crohn's Disease. *Nutrients.* 2017; 9(3):308.
6. Schijns W, Homan J, van der Meer L, et al. Efficacy of oral compared with intramuscular vitamin B-12 supplementation after Roux-en-Y gastric bypass: a randomized controlled trial. *Am J Clin Nutr.* 2018; 108(1):6-12.

## HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	04/27/2022
Annual Revision	No criteria changes.	04/26/2023

"Cigna Companies" refers to operating subsidiaries of Cigna Corporation. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of Cigna Health Corporation. © 2023 Cigna