



STEP THERAPY POLICY

- POLICY:** Calcium Channel Blockers – Verapamil Products Step Therapy Policy
- Calan® (verapamil immediate-release tablets – Pfizer, generic)
 - Calan® SR (verapamil sustained-release caplets – Pfizer, generic)
 - Verelan® (verapamil extended-release capsules – Schwarz, generic)
 - Verelan® PM (verapamil extended-release capsules, controlled onset – Schwarz/Elan, generic)
 - verapamil extended-release tablets, controlled onset (brand Covera-HS® is no longer available)
 - verapamil sustained-release tablets – generic only (brand Isoptin SR® is no longer available)

REVIEW DATE: 06/28/2023

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

All of the available verapamil formulations are indicated for the treatment of **hypertension**. Covera-HS is also indicated for the treatment of angina. Verapamil immediate-release is also indicated for the treatment of angina and specific cardiac arrhythmias.¹⁻³ Verapamil has also been used for off label conditions, such as adjunctive treatment of hypertrophic cardiomyopathy and prophylaxis of migraine and cluster headaches. Both immediate-release and once-daily verapamil formulations are available generically.

Covera-HS and Verelan PM are extended-release controlled onset (COER) formulations designed to release verapamil 4 to 5 hours after ingestion and should be administered once daily at bedtime. Both COER formulations result in a maximum plasma concentration of verapamil in the morning hours, approximately 11 hours

after ingestion.^{1,2} It has been hypothesized that the COER verapamil formulations may be more safe and effective in patients with hypertension than other verapamil formulations because their concentrations during a 24-hour period are synchronized with biological rhythm (chronotherapy).⁵⁻⁷ In theory, these formulations may have an advantage over other sustained-/extended-release verapamil formulations as they would attenuate the increase in blood pressure, heart rate, cardiac ischemia, and catecholamines that naturally occur upon awakening and they would not cause hypotension during sleep. However, the role of verapamil as it relates to chronotherapy in the primary prevention of cardiovascular (CV) morbidity and mortality (e.g., myocardial infarction [MI], stroke) has not been demonstrated in controlled, comparative clinical trials.^{7,8} The Controlled Onset Verapamil InvestigatiN of Cardiovascular Endpoints (CONVINCE) trial, which was terminated two years early for commercial reasons, was conducted in part to determine if there is a difference in the incidence of fatal or nonfatal MI, fatal or nonfatal stroke, or CV-related death between extended-release controlled onset verapamil ± hydrochlorothiazide (HCTZ), HCTZ alone, atenolol alone, or HCTZ in combination with atenolol.⁹ The trial results did not provide evidence to support the concept of chronotherapeutics. Also, one small study comparing the effects of COER verapamil on the diurnal pattern of forearm vascular resistance in hypertensive and normotensive patients noted that COER verapamil minimized the diurnal pattern in forearm vascular resistance but it did not hinder the early morning rate of blood pressure rise, despite being at peak concentration.¹⁰

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.

Calcium Channel Blockers – Verapamil Products 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: verapamil extended-release capsules, verapamil extended-release PM capsules, verapamil immediate-release tablets, verapamil sustained-release tablets

Step 2: Calan, Calan SR, Verelan, Verelan PM

CRITERIA

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

REFERENCES

1. Covera-HS® extended-release tablets controlled-onset [prescribing information]. New York, NY: Pfizer; January 2022.
2. Verelan® PM extended-release capsules controlled-onset [prescribing information]. Smyrna, GA and Gainesville, GA: Schwarz and Elan; October 2019.
3. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2023. Available at: <http://fco.factsandcomparisons.com/lco/action/home>. Accessed on: June 24, 2023.
4. Anwar YA, White WB. Chronotherapeutics for cardiovascular disease. *Drugs*. 1998;55:631-643.
5. Smolensky MH, Portaluppi F. Chronopharmacology and chronotherapy of cardiovascular medications: relevance to prevention and treatment of coronary heart disease. *Am Heart J*. 1999;137:S14-S24.
6. Carter BL. Optimizing delivery systems to tailor pharmacotherapy to cardiovascular circadian events. *Am J Health-Syst Pharm*. 1998;55(Suppl 3):17-23.
7. Conlin PR, Williams GH. Use of calcium channel blockers in hypertension. *Adv Intern Med*. 1998;43:533-562.
8. Black HR, Elliott WJ, Neaton JD, et al. Rationale and design for the Controlled Onset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE) trial. *Control Clin Trials*. 1998;19(4):370-390.
9. Black HR, Elliott WJ, Grandits G, et al. Principal results of the Controlled Onset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE) trial. *JAMA*. 2003;289(16):2073-82.
10. Nguyen BN, Parker RB, Noujedehi M, Sullivan JM, Johnson JA. Effects of COER-verapamil on circadian pattern of forearm vascular resistance and blood pressure. *J Clin Pharmacol*. 2000;40(12 Pt 2):1480-1487.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/29/2022
Annual Revision	No criteria changes.	06/28/2023

"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