STEP THERAPY POLICY

POLICY: Calcium Channel Blockers – Verapamil Products Step Therapy Policy

- Calan® SR (verapamil sustained-release caplets – Pfizer, generic)
- Verelan® PM (verapamil extended-release capsules, controlled onset – Lannett/Recro/Alkermes, 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: 06/26/2024

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 InvestigatioN 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.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: verapamil extended-release capsules, verapamil extended-release PM capsules, verapamil immediate-release tablets, verapamil sustained-release tablets

Step 2: Calan SR, Verelan, Verelan PM

CRITERIA

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

2. No other exceptions are recommended.

REFERENCES

1. Covera-HS® extended-release tablets controlled-onset [prescribing information]. New York, NY: Pfizer; November 2023.
2. Verelan® PM extended-release capsules controlled-onset [prescribing information]. Philidelphia, PA, and Gainesville, GA: Lannett/Recro/Alkermes; 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, 2024.
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.