

## STEP THERAPY POLICY

- POLICY:** Calcium Channel Blockers – Verapamil Products Step Therapy Policy
- Calan® (verapamil immediate-release tablets – Pharmacia, generics)
  - Calan® SR (verapamil sustained-release caplets – Pharmacia, generics)
  - Isoptin SR® (verapamil sustained-release tablets – generics only)
  - Verelan® (verapamil extended-release capsules – Schwarz Pharma, generics)
  - Verelan® PM (verapamil extended-release capsules, controlled onset – Kremers Urban Pharmaceuticals, generics)
  - Covera-HS® (verapamil extended-release tablets, controlled onset – Pfizer, generics only)

**REVIEW DATE:** 06/17/2020

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### 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.<sup>1-3</sup> 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.<sup>1-2</sup> 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).<sup>5-7</sup> 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 occurs 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.<sup>7-8</sup> 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.<sup>9</sup> The trial results did not provide evidence to support the concept of chronotherapeutics.<sup>9</sup> 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 extended-release controlled onset 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.<sup>10</sup>

### **POLICY STATEMENT**

A step therapy program has been developed to encourage the use of one generic Step 1 product prior to the use of a Step 2 product. If the step therapy rule is not met for a Step 2 agent at the point of service, coverage will be determined by the step therapy criteria below. All approvals are provided for 12 months in duration.

**Automation:** Patients with a history of one Step 1 drug within the 130-day look-back period are excluded from step therapy.

**Step 1** (generic verapamil product): verapamil immediate-release tablets, verapamil sustained-release tablets, verapamil extended-release capsules, verapamil extended-release PM capsules

**Step 2** (brand name verapamil product): Verelan PM, Calan, Calan SR, Verelan

### **CRITERIA**

1. If the patient has tried one generic verapamil product (Step 1), than approve a brand name verapamil product (Step 2).

### **REFERENCES**

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2. Verelan<sup>®</sup> PM extended-release capsules controlled-onset [prescribing information]. Seymour, IN and Gainesville, GA: Kremers Urban Pharmaceuticals and Recro; November 2016.
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