



STEP THERAPY POLICY

- POLICY:** Calcium Channel Blockers – Dihydropyridine Products Step Therapy Policy
- nicardipine immediate-release capsules (generic only)
 - Conjupri® (levamlodipine tablets – CSPC Ouyi)
 - isradipine immediate-release capsules (generic only)
 - Katerzia™ (amlodipine oral suspension – Azurity)
 - Norvasc® (amlodipine tablets – Viatris, generic)
 - Levamlodipine tablets – Xspire/CSPC Ouyi (authorized generic)
 - Norliqva® (amlodipine oral solution – CMP)
 - felodipine extended-release tablets (generic only)
 - Prestalia® (perindopril arginine and amlodipine tablets – Adhera)
 - Procardia XL® (nifedipine extended-release tablets – Pfizer, generic)
 - Procardia® (nifedipine immediate-release capsules – Pfizer, generic)
 - Sular® (nisoldipine extended-release tablets – Shionogi, generic)

REVIEW DATE: 06/18/2025

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

All of the dihydropyridine (DHP) calcium channel blockers (CCBs), with the exception of immediate-release (IR) nifedipine and nimodipine, are indicated for the **treatment of hypertension in adults**.^{1-14,9} Some of the DHP CCBs have unique indications:

- Agents that are indicated for the **management of chronic stable angina** include amlodipine, nicardipine IR, nifedipine IR, and nifedipine extended-release (ER) [Procardia XL formulation].
- Agents that are indicated for the **treatment of vasospastic angina** include amlodipine, nifedipine IR, and nifedipine ER (Procardia XL formulation).
- **Amlodipine** possess a unique indication in **patients with recently documented coronary artery disease (CAD) by angiography and without heart failure (HF) or an ejection fraction < 40% to reduce the risk of hospitalization due to angina** and to **reduce the risk of a coronary revascularization procedure**. Amlodipine is indicated for use in adults and pediatric patients ≥ 6 years of age.
- **Conjupri** is indicated for the **treatment of hypertension** in adults and pediatric patients ≥ 6 years of age to lower blood pressure.²⁴ An authorized generic is available.²⁷
- **Katerzia** may be used alone or in combination with other antihypertensive or antianginal medications for the **treatment of hypertension** in adults and children ≥ 6 years of age and **CAD** (chronic stable angina, vasospastic angina, and angiographically documented CAD in patients without heart failure or an ejection fraction < 40%).²⁵
- **Norliqva** may be used alone or in combination with other antihypertensive or antianginal medications for the **treatment of hypertension** in adults and children ≥ 6 years of age and **CAD** [chronic stable angina, vasospastic angina, and angiographically documented CAD in patients without heart failure or an ejection fraction < 40%].²⁶

Prestalia contains amlodipine and perindopril, an angiotensin converting enzyme (ACE) inhibitor.⁶

The DHP CCB nimodipine is not discussed in this document since it is only indicated to improve neurological deficits associated with subarachnoid hemorrhage and is given every 4 hours for a 21-day period.^{13,14}

Many of the available DHP CCBs can be dosed once daily (QD), which may be important in the treatment of hypertension to ensure adequate blood pressure control over a 24-hour period and in the treatment of angina to avoid fluctuations in blood pressure and heart rate. The only DHP CCBs that are not dosed QD are isradipine IR, dosed twice daily (BID), and nicardipine IR and nifedipine IR, both of which are dosed three to four times daily (TID to QID).

Hypertension

The DHP CCBs indicated in the treatment of hypertension have been found to be effective. These agents are useful for many reasons, such that the blood pressure response is less contingent on patient factors such as race and age, the agents are metabolically neutral and do not disturb glucose homeostasis, and some agents

have conferred cardiovascular benefit.¹⁵ In 2017, the **American College of Cardiology**, along with other nationally-recognized groups, published extensive guidelines regarding the management of high blood pressure in adults. CCBs are recommended among the choice of first-line agents as antihypertensive medications. Refer to the full guidelines for additional details.²³ The Eighth Report of the **Joint National Committee** (JNC 8) 2014 evidence-based guideline for the management of high blood pressure in adults recommends CCBs as one of the initial choices of therapy in various scenarios.¹⁶ Currently, the only DHP CCB indicated for the treatment of hypertension in children is amlodipine (patients aged 6 to 17 years).¹ In 2017, the **American Academy of Pediatrics** published a clinical practice guideline regarding the management of high blood pressure in children and adolescents.¹⁷ Long-acting CCBs are among the first-line choices for patients initiating antihypertensive therapy.

Angina

In 2023, the **American Heart Association** and the **American College of Cardiology**, along with other national organizations, published guidelines regarding the management of patients with chronic coronary disease.¹⁸ Either a calcium channel blocker or beta blocker is recommended as first-line antianginal therapy. In adults with chronic coronary disease and hypertension (systolic blood pressure \geq 130 and/or diastolic blood pressure BP \geq 80 mm Hg), in addition to nonpharmacological strategies, guideline-directed medication therapy with angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), or beta blockers are recommended as first-line therapy for compelling indications (e.g., recent MI or angina), with additional antihypertensive medications (e.g., dihydropyridine calcium channel blockers [CCB], long-acting thiazide diuretics, and/or mineralocorticoid receptor antagonists) added as needed to optimize blood pressure control. In patients with chronic coronary disease and angina, antianginal therapy with either a beta blocker, CCB, or long-acting nitrate is recommended for relief of angina or equivalent symptoms. In such patients who remain symptomatic after initial treatment, addition of a second antianginal agent from a different therapeutic class (beta blockers, CCBs, long-acting nitrates) is recommended for relief of angina or equivalent symptoms.

Heart Failure (HF)

Most of the clinical data available on the use of DHP CCBs in patients with HF are with amlodipine, followed by felodipine, although neither product is indicated for HF.¹⁹⁻²¹ The amlodipine prescribing information notes that amlodipine has been compared with placebo in several studies of 8 to 12 weeks duration in patients with New York Heart Association (NYHA) Class II/III HF (n = 697) and no evidence of worsening HF was noted.¹ The Prospective Randomized Amlodipine Evaluation (PRAISE) study (n = 1,153) is also detailed which involved use of amlodipine (5 to 10 mg) in patients with Class III/IV HF who were receiving other medications for HF (diuretics, digoxin, ACE inhibitors).^{1,19} Amlodipine had no effect on the primary endpoint, which was the combined endpoint of all-cause mortality and cardiac morbidity. The primary endpoint occurred in 42% of patients given placebo vs. 39% in the amlodipine group after a median follow-up of 13.8 months.^{1,19} The PRAISE-2 trial is also mentioned in the amlodipine prescribing information which

randomized patients with NYHA Class III (80%) or IV (20%) HF who had no clinical symptoms or objective evidence of underlying ischemic disease to receive placebo or amlodipine, in addition to other HF therapies. After a mean follow-up of 33 months, there was no difference between amlodipine and placebo in the primary endpoint of all-cause mortality.¹ The 2022 **American College of Cardiology Foundation /American Heart Association /Heart Failure Society of America** guideline for the management of HF states that DHP CCBs are not recommended for patients with heart failure and a reduced ejection fraction; no distinct benefits are noted.²² DHP CCBs may be used for the treatment of hypertension in patients who have elevated blood pressure despite optimization of guideline-directed medication therapy. Among the DHP CCBs, amlodipine and felodipine are thought to have less myocardial depressant activity and may be more favorable agents.²²

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, for all agents except Prestalia. For Prestalia, this program requires the patient to try one Step 1 Product (a generic dihydropyridine-calcium channel blocker [DHP CCB] or a generic DHP CCB-combination product) and one angiotensin converting enzyme (ACE) inhibitor. 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.

Step 1: Afeditab CR, amlodipine, amlodipine/atorvastatin, amlodipine/benazepril, felodipine ER, isradipine IR, nicardipine IR, nifedipine ER, nifedipine IR, nifedipine XL, Nifediac CC, Nifedical XL, nisoldipine ER

Step 2: Conjugpri, Katerzia, Levamlodipine (authorized generic), Norliqva, Norvasc, Prestalia, Procardia, Procardia XL, Sular

Calcium Channel Blockers – Dihydropyridine Products Step Therapy Policy 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.

CRITERIA

1. For all agents except Prestalia, if the patient has tried one Step 1 Product, approve a Step 2 Product.

2. For Prestalia, if the patient has tried one Step 1 Product AND one angiotensin converting enzyme inhibitor, approve Prestalia.

Note: Examples of angiotensin converting enzyme inhibitors include perindopril, enalapril, lisinopril, benazepril.

3. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve Katerzia or Norliqva.

REFERENCES

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2. Felodipine extended-release tablets [prescribing information]. Morgantown, WV: Mylan; February 2013.
3. Isradipine capsules [prescribing information]. Parsippany, NJ: Actavis; November 2023.
4. Nicardipine capsules [prescribing information]. Morgantown, WV: Mylan; September 2016.
5. Prestalia® tablets [prescribing information]. Durham, NC: Adhera; August 2019.
6. Procardia® capsules [prescribing information]. New York, NY: Pfizer; December 2014.
7. The Medical Letter. Drugs for hypertension. *Med Lett Drugs Ther.* 2024;66(1703):81-88.
8. Procardia XL® extended-release tablets [prescribing information]. New York, NY: Pfizer; November 2023.
9. Nisoldipine extended-release tablets 20 mg, 30 mg and 40 mg [prescribing information]. Morgantown, WV: Mylan; September 2022.
10. Sular® extended-release tablets 8.5 mg, 17 mg, 25.5 mg, and 34 mg [prescribing information]. Florham Park, NJ: Shinogi; December 2019.
11. Nimotop® capsules [prescribing information]. Wayne, NJ: Bayer; February 2008.
12. Nymalize® oral solution [prescribing information]. Woborn, MA; Azurity; March 2023.
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21. Whelton PK, Carey RM, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/AphA/ASH/ASPC/NMA/PCNA guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2018;71(19):e127-e248.
22. Conjupri® tablets [prescribing information]. CSPC Ouyi; December 2019.
23. Katerzia™ oral suspension [prescribing information]. Woborn, Azurity; April 2023.
24. Norliqva® oral solution [prescribing information]. Farmville, NC: CMP; February 2022.
25. Levamlodipine tablets [prescribing information]. Ridgeland, MS: Xspire/CSPC Ouyi; November 2021.
26. The Medical Letter. Drugs for hypertension. *Med Lett Drugs Ther.* 2024;66(1703):81-88.

HISTORY

Type of Revision	Summary of Changes	Review Date
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Annual Revision	No criteria changes.	06/28/2023
Annual Revision	Adalat CC: Removed from Step 2 as it is no longer available.	06/26/2024
Annual Revision	No criteria changes.	06/18/2025

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