Effective Date **10/1/2023**
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Coverage Policy Number **IP0484**

Amlodipine Oral Solution

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Related Coverage Resources

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.

Overview

This policy supports medical necessity review for the following amlodipine products:

- **Katerzia**™ (amlodipine oral suspension)
- **Norliqva**® (amlodipine oral solution)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Coverage criteria are listed for products **in below table:**

Non-Covered Product	Criteria
Katerzia (amlodipine) oral suspension	**EFFECTIVE 1/1/2024** Documentation of **BOTH** of the following: 1. Inability to swallow amlodipine tablets 2. Failure or intolerance to Norliqva [may require prior authorization]

Non-Covered Product	Criteria
Norliqva (amlodipine) oral solution	Documented inability to swallow amlodipine tablets

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of amlodipine oral solution (Norliqva) and amlodipine oral suspension (Katerzia) is considered medically necessary when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial and reauthorization approval duration: 12 months

Background

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] Some of the DHB 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 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 coronary artery disease (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 (ACC), 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 2012, the Clinical Guidelines Committee of the American College of Physicians published guidelines for the management of stable ischemic heart disease.[18] Long-acting nitrates or CCBs should be prescribed for relief of symptoms when beta-blockers are contraindicated or cause unacceptable adverse effects in patients with ischemic heart disease. Long-acting nitrates or CCBs in combination with beta-blockers should be given for the relief of symptoms when initial treatment with beta-blockers is not successful in patients with stable ischemic heart disease. A particular CCB is not specified.

Heart Failure
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 (ACCF)/American Heart Association (AHA)/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]

References

1. Norvasc tablets [prescribing information]. New York, NY: Pfizer; January 2019.
2. Felodipine extended-release tablets [prescribing information]. Morgantown, WV: Mylan; February 2013.
3. Isradipine capsules [prescribing information]. Parsippany, NJ: Actavis; June 2017.
4. DynaCirc CR controlled-release tablets [prescribing information]. Research Triangle Park, NC; GlaxoSmithKline; November 2009.
5. Nicardipine capsules [prescribing information]. Morgantown, WV: Mylan; September 2016.
6. Prestalia tablets [prescribing information]. Durham, NC: Adhera; August 2019.
7. Adalat capsules [prescribing information]. West Haven, CT: Bayer; June 2000.
8. Procardia capsules [prescribing information]. New York, NY: Pfizer; December 2014.
9. Adalat CC extended-release tablets [prescribing information]. Wayne, NJ: Bayer; February 2011.

10. Procardia XL extended-release tablets [prescribing information]. New York, NY: Pfizer; May 2021.
11. Nisoldipine extended-release tablets 20 mg, 30 mg and 40 mg [prescribing information]. Morgantown, WV: Mylan; January 2010.
12. Sular extended-release tablets 8.5 mg, 17 mg, 25.5 mg, and 34 mg [prescribing information]. Florham Park, NJ: Shinogi; December 2019.
13. Nimotop capsules [prescribing information]. Wayne, NJ: Bayer; February 2008.
14. Nymalize oral solution [prescribing information]. Atlanta, GA: Arbor; April 2020.
15. Epstein BJ, Vogel K, Palmer BF. Dihydropyridine calcium channel antagonists in the management of hypertension. *Drugs*. 2007; 67(9):1309-1327.
16. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults. Report from the panel members appointed to the eighth joint national committee (JNC 8). *JAMA*. 2014; 311(5):507-520.
17. Flynn JT, Kaelber DC, Baker-Smith CM, et al, for the subcommittee on screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017; 140(3):e20171904.
18. Qaseem A, Fihn SD, Dallas P, et al, for the Clinical Guidelines Committee of the American College of Physicians. Management of stable ischemic heart disease: summary of a clinical practice guideline from the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association of Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. *Ann Intern Med*. 2012; 157:735-743.
19. Packer M, O'Connor CM, Ghali J, et al. for the Prospective Randomized Amlodipine Survival Evaluation (PRAISE) study group. Effect of amlodipine on morbidity and mortality in severe chronic heart failure. *N Engl J Med*. 1996; 335:1107-1114.
20. Cohn J, Ziesche S, Smith R, and the V-HeFT Study Group. Effect of the calcium antagonist felodipine as supplementary vasodilator therapy in patients with chronic heart failure treated with enalapril: VeHeFT III. *Circulation*. 1997; 96:856-863.
21. Littler WA, Sheridan DJ. Placebo-controlled trial of felodipine in patients with mild to moderate heart failure. UK Study Group. *Br Heart J*. 1995; 73(5):428-433.
22. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022; 145(18):e895-e1032.
23. 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 Associatoin Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71(19):e127-e248. Available at: http://www.onlinejacc.org/content/71/19/e127?_ga=2.84766993.903959650.1528823172-806969345.1528823172. Accessed on June 29, 2022.
24. Conjupri tablets [prescribing information]. CSPC Ouyi; December 2019.
25. Katerzia oral suspension [prescribing information]. Wilmington, MA: Azurity; May 2020.
26. Norliqva oral solution [prescribing information]. Farmville, NC: CMP; February 2022.
27. Levamlodipine tablets [prescribing information]. Ridgeland, MS: Xspire/CSPC Ouyi; November 2021.