Clinical Policy Title:	amlodipine/atorvastatin
Policy Number:	RxA.53
Drug(s) Applied:	Caduet®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All line of business

Background

Amlodipine/atorvastatin (Caduet®) is a combination of amlodipine, a calcium channel blocker, and atorvastatin, an HMG CoA-reductase inhibitor. It is indicated in patients for whom treatment with both amlodipine and atorvastatin is appropriate.

Amlodipine is indicated for the treatment of:

- Hypertension, to lower blood pressure
- Coronary Artery Disease (CAD)
  - Symptomatic treatment of chronic stable angina
  - Treatment of confirmed or suspected vasospastic angina (Prinzmetal's or Variant Angina)
  - Angiographically documented CAD
    - To reduce the risk for hospitalization for angina and coronary revascularization procedure in patients with recently documented CAD by angiography and without heart failure or an ejection fraction <40%

Atorvastatin is indicated as an adjunct therapy to diet for:

- Prevention of Cardiovascular Disease:
  - Reduce the risk of myocardial infarction (MI), stroke, and revascularization procedures and angina in adult patients without clinically evident coronary heart disease (CHD), but with multiple risk factors for coronary heart disease (such as age, smoking, hypertension, low high-density lipoprotein cholesterol (HDL-C), or a family history of early coronary heart disease)
  - Reduce the risk of MI and stroke in patients with type 2 diabetes, and without clinically evident CHD, but with multiple risk factors (such as retinopathy, albuminuria, smoking, or hypertension)
  - Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for congestive heart failure (CHF), and reduce the risk of angina in patients with clinically evident CHD

- Hyperlipidemia
  - Heterozygous Familial and Nonfamilial Hypercholesterolemia:
    - As an adjunct to diet to reduce elevated total-cholesterol ((total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (apo B), and triglyceride (TG) levels and to increase HDL-C in patients with primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Fredrickson types IIa and IIb)
  - Elevated Serum TG levels:
    - As an adjunct to diet for the treatment of patients with elevated serum TG levels (Fredrickson type IV)
  - Primary Dysbetalipoproteinemia:

- Treatment of patients with primary dysbetalipoproteinemia (Fredrickson type III) who do not respond adequately to diet
- Homozygous Familial Hypercholesterolemia:
  - Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable
- Pediatric Patients:
  - As an adjunct to diet to reduce total-C, LDL-C, and apo B levels in pediatric patients, 10 to 17 years of age, with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present:
    - LDL-C remains ≥ 190 mg/dL or
    - LDL-C remains ≥ 160 mg/dL and:
      - There is a positive family history of premature cardiovascular disease or
      - Two or more other cardiovascular disease (CVD) risk factors are present in the pediatric patients

Limitation(s) of use: Atorvastatin has not been studied in conditions where the major lipoprotein abnormality is elevation of chylomicrons (Fredrickson Types I and V dyslipidemias).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Caduet®	For patients whom treatment with both amlodipine and atorvastatin is appropriate	Initial Adults: 2.5/10 mg orally once daily Pediatric (age 10 to 17 years): 2.5/10 mg orally once daily	Adult: 10/80 mg per day Pediatric: 5/20 mg per day

Dosage Forms

- Tablets: 2.5/10 mg, 2.5/20 mg, 2.5/40 mg, 5/10 mg, 5/20 mg, 5/40mg, 5/80 mg, 10/10 mg, 10/20 mg, 10/40 mg, 10/80 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. All FDA-Approved Indications (must meet all):

1. Diagnosis of one of the following (a, b, c, or d):
   a. Hypertension;
   b. Chronic stable angina;
   c. Confirmed or suspected vasospastic angina (Prinzmetal's or Variant Angina);
   d. Coronary artery disease documented by angiography and without heart failure or an ejection fraction < 40%;
2. Diagnosis of hyperlipidemia or one of the diagnoses for which atorvastatin is FDA- approved;
3. Medical justification supporting inability to use the individual components concurrently: atorvastatin and amlodipine;
4. Failure to achieve National Cholesterol Education Program (NCEP) goals (see Appendix D) to at least one

generic formulary statin (e.g., lovastatin, pravastatin, simvastatin, atorvastatin), followed by Vytorin® or Crestor®, unless all are contraindicated, or clinically significant adverse effects are experienced;

5. Dose does not exceed 10/80 mg per day of Caduet®.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. **All FDA-Approved Indications** (must meet all):

1. Currently receiving medication that has been authorized by Rxadvance or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 80 mg per day of atorvastatin.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

apo B: apolipoprotein B
CAD: coronary artery disease
CHD: coronary heart disease
CHF: congestive heart failure
CVD: cardiovascular disease
FDA: Food and Drug Administration
HDL-C: high-density lipoprotein cholesterol
LDL: low-density lipoprotein cholesterol
MI: myocardial infarction
NCEP: National Cholesterol Education Program
TG: triglyceride

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
atorvastatin (Lipitor®)	10 to 80 mg orally once daily	80 mg/day
amlodipine (Norvasc®)	2.5 to 10 mg orally once daily	10 mg/day
lovastatin	10 to 80 mg orally once daily or twice	80 mg/day
pravastatin (Pravachol®)	10 to 80 mg orally once daily	80 mg/day

simvastatin (Zocor®)	5 to 40 mg orally once daily (Note: coverage of the 80 mg strength requires PA)	80 mg/day
ezetimibe/simvastatin (Vytorin®)	10/10 mg to 10/80 mg orally once daily (Note: coverage of the 10/80 mg strength requires PA)	10/80 mg/day
rosuvastatin (Crestor®)	5 to 40 mg/day orally once daily	40 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels
  - Pregnancy
  - Lactation

- Boxed Warning(s):
  - none reported

APPENDIX D: General Information

NCEP Goals

Risk Category	LDL Goal
CHD or CHD Risk Equivalents (10-year risk* >20%)	< 100 mg/dL
Multiple (2+) Risk Factors and 10-year risk* ≤ 20%	< 130 mg/dL
0 to 1 risk factor	< 160 mg/dL

**Refer to Framingham point scores for 10-year risk % (https://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf)*

References

1. Caduet Prescribing Information. New York, NY: Pfizer, Inc.; January 2021. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=531. Accessed February 01, 2021.
2. Lipitor Prescribing Information. New York, NY: Pfizer, Inc.; December 2020. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=587. Accessed February 01, 2021.
3. Norvasc Prescribing Information. New York, NY: Pfizer, Inc.; January 2019. Available at: http://labeling.pfizer.com/showlabeling.aspx?id=562. Accessed February 01, 2021.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.;2020. Available at: http://clinicalpharmacology-ip.com/.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
1. Updated Initial Approval Criteria #5: Added max dose of Caduet® (10/80 mg) 2. Updated references	04/24/2020	05/20/2020

Updated Criteria II, A, i to: Currently receiving medication that has been authorized by Rxadvance, or documentation supports that member is currently receiving Cabometyx or Cometriq for a covered indication and has received this medication for at least 30 days;	05/08/2020	05/20/2020
Policy was reviewed: 1. Clinical Policy Title Table was updated. 2. Line of Business Policy Applies to was update to all lines of business. 3. APPENDIX B: Therapeutic Alternatives verbiage was updated to “Below are suggested therapeutic alternatives based on clinical guidance...." 4. Initial and Continued Approval criteria: Commercial and Medicaid approval duration was updated from Length of benefit to 12 months. 5. References were updated.	02/01/2021	03/09/2021