Clinical Policy: Ranolazine (Ranexa)

Reference Number: CP.PMN.34
Effective Date: 08.01.09
Last Review Date: 02.20
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ranolazine (Ranexa®) is an antianginal agent.

FDA Approved Indication(s)

Ranexa is indicated for the treatment of chronic angina.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Ranexa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Angina (must meet all)**:**

1. Diagnosis of chronic angina;
2. Prescribed by or in consultation with a cardiologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a, b, or c):
   a. Failure of concurrent use of a beta-blocker and long-acting nitrate at therapeutic doses for ≥ 30 days within the previous 6 months;
   b. Failure of concurrent use of a calcium channel blocker and long-acting nitrate at therapeutic doses for ≥ 30 days within the previous 6 months;
   c. Member experienced clinically significant adverse effects or has contraindications to both calcium channel blockers and beta blockers, or long-acting nitrates.
5. Does not exceed 2,000 mg (2 tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Chronic Angina (must meet all)**:**

1. Currently receiving medication via Centene benefit 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 2,000 mg (2 tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Beta-Blockers		
acebutolol (Sectral®)*	400 mg to 1,200 mg PO per day in 2 to 3 divided doses	800 mg/day
atenolol (Tenormin®)	50 mg to 100 mg PO QD	200 mg/day
betaxolol (Kerlone®)*	5 mg to 80 mg PO QD	80 mg/day
bisoprolol (Zebeta®)*	5 mg to 20 mg PO QD	20 mg/day
carvedilol (Coreg®)*	25 mg to 50 mg PO BID	100 mg/day
metoprolol (Lopressor®, Toprol XL®)	100 mg PO per day	400 mg/day
nadolol (Corgard®)	40 mg to 80 mg PO QD	240 mg/day
pindolol (Visken®)*	Initial: 2.5 mg to 5 mg PO QD Maintenance: 10 mg to 40 mg PO QD in divided doses	40 mg/day
propranolol (Inderal® LA, Innopran XL®)	80 mg to 320 mg per day	320 mg/day
sotalol (Betapace®, Betapace AF®)*	120 mg to 480 mg PO per day in divided doses	480 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
timolol*	10 mg to 60 mg PO per day in divided doses	60 mg/day
Long-Acting Nitrates		
isosorbide dinitrate (Isordil®, Dilatrate-SR®)	Immediate-release (IR): 5 mg to 80 mg PO per day in divided doses Sustained-release (SR): 40 mg to 160 mg PO per day	480 mg/day IR; 160 mg/day SR
isosorbide mononitrate (Monoket®, Imdur®)	IR: 20 mg BID Extended-release (ER): 30 mg to 240 mg PO QD	40 mg/day IR; 240 mg/day ER
nitroglycerin (Nitro-Time®, Nitro-Dur®)	Oral: 2.5 mg to 6.5 mg PO 3 to 4 times per day Transdermal: 1 patch (0.1 mg to 0.8 mg per hour) per day	26 mg/day oral; 1 patch per day
Calcium Channel Blockers		
amlodipine (Norvasc®)	5 mg to 10 mg PO QD	10 mg/day
diltiazem (Cardizem® CD, Cartia XT®, Tiazac®, Taztia XT®, Matzim® LA, Cardizem® LA)	Regular-release: 120 mg to 360 mg PO per day in divided doses ER capsules: 120 mg to 540 mg PO QD ER tablets: 180 mg to 360 mg PO QD	360 mg/day; 450 mg/day ER capsules; 420 mg/day ER tablets
felodipine (Plendil®)	2.5 mg to 5 mg PO BID	10 mg/day
isradipine	2.5 mg to 7.5 mg PO TID	22.5 mg/day
nicardipine (Cardene®)	20 mg to 40 mg PO TID	120 mg/day
nifedipine (Procardia®, Procardia XL®, Adalat® CC)	IR: 10 mg to 30 mg PO per day in divided doses ER: 30 mg to 60 mg PO QD	180 mg/day IR 120 mg/day ER
verapamil (Calan®, Calan® SR, Verelan®, Verelan® PM)	IR: 80 to 120 mg PO TID ER: 180 to 480 mg PO QD	480 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.
**Off-label use*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - In patients taking strong inhibitors of CYP2A
  - In patients taking inducers of CYP3A
  - In patients with liver cirrhosis
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic angina	500 mg to 1,000 mg PO BID	2,000 mg/day

VI. Product Availability

Extended-release tablets: 500 mg, 1,000 mg

VII. References

1. Ranexa Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; October 2019. Available at: https://www.ranexa.com/. Accessed November 4, 2019.
2. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation 2012; 126:e354.
3. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2014 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease. November 2014; 64(18):1929-49
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/.
5. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 1, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added language to criteria to include calcium channel blockers plus long acting nitrate therapy as an "OR" statement. References updated	08.12	08.12
References updated	08.14	08.14
Converted to new template Added appropriate age for use to approval criteria	08.15	08.15
Criteria: Updated to include intolerance to first line agents; Modified criteria to require ≥ 30 day trial of first line agents within the previous 6 months; added requirement that dosing frequency does not exceed BID in accordance with FDA dosing guidelines; modified specific max quantity limit to generalized FDA max recommended dose and health plan approved QL statement; Updated references to reflect current literature search	05.16	08.16
Converted to new integrated template. Initial: removed age requirement per new template and added prescriber specialty; modified trial and failure criteria to require use of beta-blocker and long-acting nitrate or calcium channel blocker	12.16	02.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
and long-acting nitrate at therapeutic doses; modified generalized FDA maximum recommended dose and health plan approved daily QL to specific max dose and QL statement; removed requirement related to twice daily dosing since criteria modified to include specific QL of 2 tablets/day. Re-auth: added positive response to therapy requirement; modified generalized FDA maximum recommended dose and health plan approved daily QL to specific max dose and QL statement; removed requirement related to twice daily dosing since criteria modified to include specific QL of 2 tablets/day. Updated references.		
1Q18 annual review: Policies combined for Medicaid and commercial; No significant clinical changes from previously approved corporate policy; Commercial: added the requirement of first line generic agent trial; Age added; References reviewed and updated.	12.12.17	02.18
1Q 2019 annual review: removed commercial line of business; no significant changes; references reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.04.19	02.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.