Clinical Policy: Aprocitentan (Tryvio)

Reference Number: CP.PHAR.676
Effective Date: 06.01.24
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Aprocitentan (Tryvio™) is an endothelin receptor antagonist.

FDA Approved Indication(s)

Tryvio is indicated for the treatment of hypertension in combination with other antihypertensive drugs, to lower blood pressure in adult patients who are not adequately controlled on other drugs. Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions.

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 Tryvio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hypertension (must meet all)**:**

1. Diagnosis of hypertension;
2. Age ≥ 18 years;
3. Documentation of recent (within the last 30 days) blood pressure ≥ 140/90 mmHg, and both of the following (a and b):
   a. Tryvio is prescribed concurrently with an antihypertensive regimen containing THREE or more drug classes, unless clinically significant adverse effects are experienced or all are contraindicated (*see Appendix B for examples*);
   b. Member has been adherent for at least the last 4 weeks at up to maximally tolerated doses of an antihypertensive drug regimen containing at least three different antihypertensive drug classes;
4. Tryvio is not prescribed concurrently with endothelin receptor antagonists (e.g., ambrisentan [Letairis®], bosentan [Tracleer®], Opsumit®, Filspari®);
5. Dose does not exceed 12.5 mg (1 tablet) per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Hypertension (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. Tryvio is not prescribed concurrently with endothelin receptor antagonists (e.g., ambrisentan [Letaris], bosentan [Tracleer], Opsumit, Filspari);
4. If request is for a dose increase, new dose does not exceed 12.5 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and 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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
REM: restricted distribution program

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Thiazide or thiazide-type diuretics (e.g., chlorthalidone, hydrochlorothiazide (HCTZ), metolazone)	Varies	Varies
Angiotensin-converting enzyme (ACE) inhibitors (e.g., benazepril, captopril, enalapril, lisinopril, quinapril)	Varies	Varies
Angiotensin-receptor blockers (ARB) (e.g., candesartan, irbesartan, losartan, olmesartan, telmisartan, valsartan)	Varies	Varies
Calcium-channel blockers (e.g., amlodipine, nicardipine, diltiazem, verapamil)	Varies	Varies
Loop diuretics (e.g., bumetanide, furosemide, torsemide)	Varies	Varies
Potassium sparing diuretics (e.g., amiloride, triamterene)	Varies	Varies
Aldosterone antagonists (e.g., spironolactone, eplerenone)	Varies	Varies
Beta blockers (e.g., atenolol, bisoprolol, metoprolol, propranolol, carvedilol)	Varies	Varies
Direct renin inhibitor (e.g., aliskiren)	Varies	Varies
Alpha-1 blockers (e.g., doxazosin, prazosin, terazosin)	Varies	Varies
Centrally acting drugs (e.g., clonidine, methyldopa, guanfacine)	Varies	Varies
Direct vasodilators (e.g., hydralazine, minoxidil)	Varies	Varies

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): pregnancy; hypersensitivity
- Boxed warning(s): embryo-fetal toxicity; Tryvio is only available through a restricted distribution (REMS)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hypertension	12.5 mg PO QD	12.5 mg/day

VI. Product Availability

Tablet: 12.5 mg

VII. References

1. Tryvio Prescribing Information. Radnor, PA: Idorsia Pharmaceuticals US Inc. April 2024. Available at: https://www.tryvio.com. Accessed February 14, 2025.
2. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; 2025. URL: www.clinicalkeys.com/pharmacology.
3. Danaietash P, Verweij P, Wang JG, et al; PRECISION investigators. Identifying and treating resistant hypertension in PRECISION: A randomized long-term clinical trial with aprocitentan. *J Clin Hypertens* (Greenwich). 2022 Jul;24(7):804-813. doi: 10.1111/jch.14517.
4. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline 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. *Hypertension*. 2018 Jun;71(6):1269-1324. doi: 10.1161/HYP.0000000000000066. Epub 2017 Nov 13. Erratum in: Hypertension. 2018 Jun;71(6):e136-e139. Erratum in: Hypertension. 2018 Sep;72(3):e33.
5. Carey RM, Calhoun DA, Bakris GL, et al; Resistant hypertension: Detection, evaluation, and management: A scientific statement from the American Heart Association. *Hypertension*. 2018 Nov;72(5):e53-e90. doi: 10.1161/HYP.0000000000000084.
6. Arguedas JA, Leiva V, Wright JM. Blood pressure targets in adults with hypertension. *Cochrane Database Syst Rev*. 2020 Dec 17;12(12):CD004349. doi: 10.1002/14651858.CD004349.pub3.
7. Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension.* 2020 Jun;75(6):1334-1357. doi: 10.1161/HYPERTENSIONAHA.120.15026.
8. McEvoy JW, McCarthy CP, Bruno RM, et al; ESC Scientific Document Group. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J.* 2024 Oct 7;45(38):3912-4018. doi: 10.1093/eurheartj/ehae178. Erratum in: *Eur Heart J.* 2025 Feb 11:ehaf031. doi: 10.1093/eurheartj/ehaf031.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.09.24	05.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2025 annual review: no significant changes; references reviewed and updated.	02.14.25	05.25

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.

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.