



Drug Coverage Policy

Effective Date02/01/2025

Coverage Policy Number.....IP0713

Policy Title.....Tryvio

Cardiology – Tryvio

- Tryvio™ (aprocitentan tablets - Idorsia)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

OVERVIEW

Tryvio, an endothelin receptor antagonist, is indicated for the treatment of hypertension in combination with other antihypertensive medications, to lower blood pressure in adults who are not adequately controlled on other drugs.¹ Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions.

Guidelines

Guidelines have not addressed Tryvio. Guidelines are available for the management of hypertension in adults. There are many medications available for the management of hypertension.² These include thiazide-like diuretics (e.g., chlorthalidone, hydrochlorothiazide, metolazone), potassium-sparing diuretics (e.g., amiloride, triamterene), mineralocorticoid receptor antagonists (e.g., spironolactone, eplerenone), angiotensin converting enzyme (ACE) inhibitors (e.g., enalapril, lisinopril, ramipril, trandolapril), angiotensin receptor blockers (ARBs) [e.g., candesartan, irbesartan, valsartan], a direct renin inhibitor (i.e., aliskiren), dihydropyridine CCBs (e.g., felodipine, amlodipine), non-dihydropyridine CCBs (e.g., diltiazem, verapamil), beta blockers (e.g., atenolol, bisoprolol, metoprolol, acebutolol), alpha-adrenergic blockers (e.g., doxazosin, prazosin, terazosin), central alpha-adrenergic agonists (e.g., clonidine, guanfacine, methyldopa), and direct vasodilators (e.g., hydralazine, minoxidil).

- **American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines for High Blood Pressure:** The ACC/AHA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults (2017) cites normal blood pressure (systolic blood pressure [SBP]/diastolic blood pressure [DBP]) as < 120/80 mmHg; a SBP of 120 to 129 mmHg and a DBP < 80 mmHg is considered elevated.³ Stage 1 hypertension is denoted at SBPs of 130 to 139 mmHg and DBPs as 80 to 89 mmHg; Stage 2 hypertension is defined as a SBP/DBP ≥ 140/90 mmHg.³ The guidelines are extensive. In general, for initiation of antihypertensive drug therapy (SBP/DBP ≥ 130/80 mmHg), first-line medications are thiazide diuretics, CCBs, and ACE inhibitors or ARBs. Beta blockers are also recommended in certain clinical scenarios in patients with hypertension (e.g., patients with stable ischemic heart disease or heart failure). For resistant hypertension, consider spironolactone, if appropriate. The addition of other agents with different mechanisms of action may also be useful (e.g., hydralazine, minoxidil, doxazosin, clonidine).
- **AHA Statement on Resistant Hypertension:** In 2018, the AHA published a Scientific Statement on resistant hypertension.⁴ Resistant hypertension is defined as above goal elevated blood pressure in a patient despite the concurrent use of three antihypertensive drug classes, commonly including a long-acting CCB, a blocker of the renin-angiotensin system (ACE inhibitor or an ARB), and a diuretic. The antihypertensive drugs should be given at maximum or maximally tolerated daily doses. Resistant hypertension also includes patients whose blood pressure achieves target values with use of four or more antihypertensive medications. Management of resistant hypertension includes use of long-acting thiazide-like diuretics (chlorthalidone or indapamide), the addition of a mineralocorticoid receptor antagonist (spironolactone or eplerenone), and, if blood pressure remains elevated, the addition in a stepwise manner of antihypertensive medications with complementary mechanisms of action to lower blood pressure.

Medical Necessity Criteria

Tryvio is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Hypertension.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A)** Patient is ≥ 18 years of age; AND
- B)** Patient has tried, or is currently receiving, at least three other antihypertensive agents for the treatment of hypertension from at least three of the following pharmacological classes (i, ii, iii, iv, v, vi, vii, viii, ix, and x).

Note: A combination product from two or more different classes would count as an alternative from each class.

- i.** Angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB);
Note: Examples of ACE inhibitors include benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, ramipril, and trandolapril. Examples of ARBs include azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, and valsartan;
- ii.** Non-dihydropyridine calcium channel blocker;
Note: Examples include diltiazem and verapamil.
- iii.** Dihydropyridine calcium channel blocker;
Note: Examples include amlodipine, felodipine, isradipine, nifedipine, and nisoldipine.
- iv.** Diuretic;
Note: Examples of thiazide diuretics include chlorthalidone, chlorothiazide, hydrochlorothiazide, indapamide, and metolazone. Examples of potassium-sparing diuretics are amiloride and triamterene.
- v.** Mineralocorticoid receptor antagonist;
Note: Examples include eplerenone and spironolactone.
- vi.** Beta blocker;
Note: Examples of beta blockers include acebutolol, atenolol, betaxolol, bisoprolol, carvedilol, metoprolol, nadolol, nebivolol, pindolol, propranolol, and timolol.
- vii.** Alpha-adrenergic blocker;
Note: Examples of alpha-adrenergic blockers are doxazosin, prazosin, and terazosin.
- viii.** Central alpha-adrenergic agonist;
Note: Examples of central alpha-adrenergic agonists are clonidine, guanfacine, and methyl dopa.
- ix.** Direct vasodilator;
Note: Examples of direct vasodilators are hydralazine and minoxidil.
- x.** Direct renin inhibitor;
Note: An example of a direct renin inhibitor is aliskiren.

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.

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

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

References

1. Tryvio™ tablets [prescribing information]. Radnor, PA: Idorsia; March 2024.
2. The Medical Letter. Drugs for hypertension. *Med Lett Drugs Ther.* 2024;66(1703):81-88.

3. 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. *Circulation*. 2018;138:e484-e594.
4. Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: detection, evaluation, and management: a scientific statement from the American Heart Association. *Hypertension*. 2018;72(5):e53-e90.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	02/01/2025

The policy effective date is in force until updated or retired.

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