aprocitentan (Tryvio™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO299

Description

Aprocitentan (Tryvio) is an orally administered endothelin receptor antagonist.

Length of Authorization

- Initial: Length of Benefit
- Renewal: Lenth of Benefit

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
aprocitentan (Tryvio)	Resistant hypertension	12.5 mg tablets	30 tablets/30 days*

**Quantity exceptions exceeding quantity limit are not allowed*

Initial Evaluation

I. **Aprocitentan (Tryvio)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a cardiologist or hypertension specialist; **AND**
   C. A diagnosis of **resistant hypertension** when the following are met:
      1. Provider attestation that the member's blood pressure remains above target goal despite appropriate adherence to standard of care therapies; **AND**
      2. Provider attestation that secondary causes of hypertension have been ruled out (i.e. pseudo-resistant hypertension, white coat hypertension); **AND**
      3. Treatment with at least one agent in all of the following groups has been ineffective or not tolerated, or all are contraindicated:
         i. Group 1: renin-angiotensin system (RAS) inhibitors (e.g., losartan, valsartan, lisinopril, enalapril)
         ii. Group 2: calcium channel blockers (CCB) (e.g., amlodipine, felodipine, nifedipine, verapamil, diltiazem)
         iii. Group 3: thiazide/thiazide-like diuretics (e.g., hydrochlorothiazide, chlorthalidone, indapamide); **AND**
         iv. Group 4: mineralocorticoid receptor antagonist (e.g., spironolactone, eplerenone); **AND**
      4. Treatment with an additional antihypertensive agent of a different mechanism of action (e.g., beta blockers [e.g., bisoprolol, atenolol, metoprolol], hydralazine, clonidine, etc.) has been ineffective, not tolerated, or all are contraindicated; **AND**
      5. Background blood pressure therapies will be continued along with aprocitentan (Tryvio), unless contraindicated or not tolerated.

II. Aprocitentan (Tryvio) is considered investigational when used for all other conditions, including but not limited to:
    A. Pulmonary hypertension

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms (e.g., reduced blood pressure) **AND**
IV. Background blood pressure therapies will be continued along with aprocitentan (Tryvio), unless contraindicated or not tolerated.

Supporting Evidence

I. Aprocitentan (Tryvio) was studied in a multicenter, blinded, randomized, parallel-group Phase 3 trial (PRECISION). The main portion of the trial included a 4-week, double-blind, randomized treatment of aprocitentan 12.5 mg, aprocitentan 25 mg, or placebo (part 1), followed by a single (patient)-blind, active treatment portion for 32 weeks where all participants received aprocitentan 25 mg (part 2), and concluded with a 12-week, double-blind, re-randomized withdrawal phase to either aprocitentan 25 mg or placebo (part 3).
II. The primary outcome was the change of sitting office systolic BP (SBP) from baseline to week 4 and the key secondary outcome was change of sitting office SBP from withdrawal baseline (week 36) to week 40. The primary outcome was met with a decrease in SBP by -15.3 mmHg and -11.5 mmHg for aprocitentan 12.5mg and placebo, respectively (difference of -3.8 mmHg [97.5% CI, -6.8 to -0.8; p=0.0042].
III. Although the change in SBP from baseline was found to be numerically larger and statistically significant, the difference in mean change of aprocitentan (Tryvio) compared to placebo is not considered to be clinically meaningful. Additionally, sustained reduction at the FDA approved dose (12.5mg) is questionable as readable data for this dose is limited to 4 weeks post-initiation, limiting the confidence in the clinical benefit in the FDA-approved population. Therefore, due to the lack of clinically meaningful benefit compared to placebo and limited data to support long-term efficacy of the FDA-approved dose in a chronic disease state, the overall quality of evidence is low.
IV. Edema or fluid retention was the most reported adverse event during the trial in the aprocitentan groups, with most cases considered mild to moderate in severity, and found to be dose dependent. The incidence rates were 9.1% vs. 2.1% for the 12.5mg and placebo,

respectively. This adverse event occurred most frequently in patients with CKD. One other side effect of note was anemia at 3.7% vs. 0% between the 12.5mg tablet and placebo, respectively. There was a total of 13 deaths reported, 11 of which were considered treatment emergent and ultimately were ruled as not being related to the study drug. Five deaths were CV-related and primarily occurred in the 25mg arm. There were no documented deaths in the 12.5mg group.

V. The 25mg is not FDA approved as it did not demonstrate a meaningful improvement in blood pressure reduction when compared to the 12.5 mg dose and there was an increase in ADEs especially edema and fluid retention. For this reason, quantity exceptions to allow for a quantity above 12.5 mg are not allowed.

VI. The 2017 High Blood Pressure Guidelines from American College of Cardiology /American Heart Association (ACC/AHA) define resistant hypertension as not achieving blood pressure (BP) control despite taking three or more agents with complementary mechanisms of action (MOAs) or achieving BP control but requiring at least four medications to do so. Their treatment recommendations for resistant hypertension include a triple-therapy regimen consisting of a thiazide diuretic, calcium channel blocker (CCB), and an angiotensin converting enzyme inhibitor (ACE-I) OR angiotensin receptor blocker (ARB). Guidelines recommend addition of spironolactone (or other agent with a complementary or a different mechanism if intolerable) if BP goal is not achieved despite proper adherence on triple-therapy regimen.

VII. The European Society for Hypertension (ESH) 2023 guidelines defines resistant hypertension as failure to lower BP to <140/90 mmHg despite appropriate lifestyle measures and maximized dose with at least three or more medications. Their recommendations for resistant hypertension treatment includes maximizing a triple-therapy regimen that should include an ACE-I OR ARB, a CCB, and a thiazide diuretic. If not controlled, then other agents with other MOAs can be included, preferring spironolactone (if not contraindicated). Other agents that could be added instead are beta-blockers, alpha blockers, or centrally acting agents.

References

1. Tryvio. Package Insert. Idorsia Pharma; March 2024.
2. Food and Drug Administration. NDA Approval letter, March 2024. Accessed March 2024. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2024/217686Orig1s000ltr.pdf
3. Schlaich MP, Bellet M, Weber MA, et al. Dual endothelin antagonist aprocitentan for resistant hypertension (PRECISION): a multicentre, blinded, randomised, parallel-group, phase 3 trial [published correction appears in Lancet. 2023 Jan 28;401(10373):268]. *Lancet*. 2022;400(10367):1927-1937. doi:10.1016/S0140-6736(22)02034-7
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 [published correction appears in Hypertension. 2018 Jun;71(6):e140-e144]. *Hypertension*. 2018;71(6):e13-e115. doi:10.1161/HYP.0000000000000065
5. Mancia G, Kreutz R, Brunstrom M, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). Journal of Hypertension 41(12):p 1874-2071, December 2023. | DOI: 10.1097/HJH.0000000000003480

Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2024