# Aprocitentan (TRYVIO)
# Criteria for Use
# May 2025

**VA Pharmacy Benefits Management Services and National Formulary Committee**

*The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.*

The Product Information should be consulted for detailed prescribing information.

See the VA National Formulary Committee Monograph on this drug at the *PBM INTRAnet* site for further information.

## Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive aprocitentan.

- ☐ Resistant or pseudoresistant hypertension due to nonadherence, suboptimal antihypertensive therapy, or secondary causes including primary aldosteronism^1
- ☐ Recent cerebrovascular or cardiovascular event (e.g., transient ischemic attack, stroke, myocardial infarction in the past 6 months)
- ☐ Clinically significant unstable cardiac disease (e.g., uncontrolled symptomatic arrythmias, current decompensated heart failure (HF), baseline class III or IV HF, or class II HF with relevant mitral valve insufficiency or aortic stenosis)^2
- ☐ Severe renal impairment with eGFR less than 15 ml/min or on dialysis^3
- ☐ ALT (alanine transferase) or AST (aspartate transferase) elevations of greater than 3 times the upper limit of normal, or moderate to severe hepatic impairment (Child-Pugh class B and C)
- ☐ Baseline severe anemia (e.g., hemoglobin less than 10 g/dL)
- ☐ Treatment with another endothelin receptor antagonist (ERA)
- ☐ Known pregnancy
- ☐ Lactating

## Inclusion Criteria

All of the following criteria must be met.

- ☐ Provider is a VA or VA Community Care cardiology or nephrology specialist or other locally designated provider
- ☐ Resistant hypertension defined as inadequate control of blood pressure with documented adherence and the use of maximally tolerated doses of triple therapy and spironolactone (if appropriate)^4
- ☐ Medication profile reviewed to eliminate or minimize the concurrent use of drugs that elevate blood pressure (e.g., NSAIDs)
- ☐ Lifestyle modifications on how to reduce blood pressure have been discussed with patient and documented (e.g., diet, alcohol consumption, exercise)
- ☐ Baseline evaluation of labs including serum transaminases, bilirubin, hemoglobin, and NT-proBNP (or BNP)

### Additional Inclusion Criteria

- ☐ For females who can become pregnant: Pregnancy must be excluded prior to receiving aprocitentan.
- ☐ For females who can become pregnant: Counseling provided on potential risks vs benefits of treatment and the use of effective contraception during therapy and for one month after stopping treatment.
- ☐ For males of reproductive potential: Counseling provided on the potential risk of aprocitentan to adversely affect spermatogenesis and impair fertility.

1. Work up of secondary causes of resistant hypertension should include plasma renin activity and serum aldosterone to calculate aldosterone/renin ratio.

2. Aprocitentan is associated with risk of fluid retention, edema, and worsening of heart failure, especially in patients with cardiovascular risk factors.
3. Patients with stage 3 and 4 chronic kidney disease stage were enrolled in the clinical trial; however, patients with renal artery stenosis may be predisposed to fluid retention/pulmonary edema. Because of the risk of fluid retention with aprocitentan, alternate therapies should be considered in patients with renal artery stenosis.
4. Triple therapy should include a diuretic (thiazide-type diuretic), calcium channel blocker, and angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker (beta-blocker may also be used for patients with another compelling indication). Spironolactone (or eplerenone if spironolactone is not tolerated) should be considered as a fourth line agent in patients when appropriate (e.g., in patients without contraindications, prior intolerance, severe renal impairment, high potassium, etc.).

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