TRYVIO™
(aprocitentan) 12.5mg tablets

TAKE THE PRESSURE DOWN

Help lower difficult-to-control hypertension by adding once-daily TRYVIO.[1]

TRYVIO—the **first and only** dual endothelin receptor antagonist for systemic hypertension—takes a unique pathway to lower blood pressure.[1-3]

INDICATION

TRYVIO is an endothelin receptor antagonist (ERA) 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.

IMPORTANT SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY

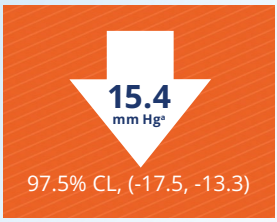
- **TRYVIO is contraindicated for use during pregnancy because it may cause fetal harm if used by pregnant patients. Therefore, in patients who can become pregnant, exclude pregnancy prior to initiation of TRYVIO.**
- **Advise use of effective contraception before the start of TRYVIO, during treatment, and for one month after stopping treatment.**
- **When pregnancy is detected, discontinue TRYVIO as soon as possible.**

PRECISION: Efficacy

TRYVIO significantly reduced systolic blood pressure by targeting the endothelin pathway[1]

In patients taking TRYVIO and at least 3 blood pressure medications (N=243), TRYVIO demonstrated statistically superior blood pressure reductions vs placebo.[1]

Primary endpoint: Change in sitting office SBP (SiSBP) from baseline to week 4[1]



Reduction in sitting trough SBP for the placebo with antihypertensive background therapy group (N=244) was 11.6 mm Hg, for a difference of 3.8 vs TRYVIO 12.5 mg (97.5% CL, [-6.8, -0.8]; *P*=0.0043).[1,b]

- The treatment effect for TRYVIO was consistent for systolic and diastolic blood pressure.[1]

The BP-lowering effect of TRYVIO appeared consistent among subgroups defined by age, sex, race, BMI, baseline eGFR, baseline UACR, and medical history of diabetes.[1]

[a]Calculated as least squares mean.[1]
[b]Statistically significant at the 2.5% level as prespecified in the testing strategy.[1]

BMI = body mass index; CL = confidence limits; eGFR = estimated glomerular filtration rate; SBP = systolic blood pressure; UACR = urine albumin-to-creatinine ratio.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

TRYVIO is contraindicated:

- in patients who are pregnant
- in patients who are hypersensitive to aprocitentan or any of its excipients

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

Based on data from animal reproduction studies with endothelin receptor antagonists (ERAs), TRYVIO may cause fetal harm when administered during pregnancy and is contraindicated for use in patients who are pregnant. The available human data for endothelin receptor antagonists do not establish the presence or absence of fetal harm related to the use of TRYVIO.

PRECISION: Safety profile

Demonstrated long-term safety profile (48 weeks)[1,2]

The safety of TRYVIO was evaluated in a placebo-controlled phase 3 clinical study in 724 adults who had uncontrolled BP (SBP ≥140 mm Hg) despite the use of at least 3 antihypertensive medications.

The most frequently reported adverse reactions were edema/fluid retention and anemia.[1]

Reported adverse reactions

Adverse reaction	TRYVIO 12.5 mg N=243	Placebo N=242
Edema/fluid retention	9.1%	2.1%
Anemia	3.7%	0

A decrease in hemoglobin to below 10.0 g/dL was observed in 3% of TRYVIO-treated patients compared to 0 patients taking placebo.[1]

- ✔ No patients discontinued TRYVIO 12.5 mg due to edema or fluid retention[4]
- ✔ No clinically relevant drug-drug interactions were reported[1,2]
- ✔ No evidence of increased incidence of hyperkalemia or hypotension was reported[1,2,4,5]

BP = blood pressure; SBP = systolic blood pressure.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Embryo-Fetal Toxicity (continued)

Counsel patients who can become pregnant about the potential risk to a fetus. Obtain a pregnancy test prior to initiation of treatment with TRYVIO. Advise patients who can become pregnant to use effective contraception during treatment, and for one month after the final dose of TRYVIO. When pregnancy is detected, discontinue TRYVIO as soon as possible.

Hepatotoxicity

Elevations of aminotransferases and hepatotoxicity are known effects of ERAs, including TRYVIO. Elevations in alanine transaminase (ALT) or aspartate aminotransferase (AST) of greater than 5-fold upper limit of normal (ULN) were observed rarely in patients treated with aprocitentan in the clinical trial, including cases with positive rechallenge. To reduce the risk of potential serious hepatotoxicity, measure serum aminotransferase levels and total bilirubin prior to initiation of treatment and repeat during treatment periodically and as clinically indicated.

PRECISION: Study design

TRYVIO was evaluated in the PRECISION trial, a multipart, blinded, randomized, parallel-group, phase 3 multicenter study of 730 adults with systolic blood pressure (SBP) ≥140 mm Hg who were prescribed ≥3 antihypertensive medications. Prior to randomization, all patients were switched to a standardized antihypertensive therapy consisting of an ARB, a CCB, and a diuretic, which were continued throughout the study. The primary efficacy endpoint was the change in sitting office SBP (SiSBP) from baseline to week 4, measured at trough by unattended automated office blood pressure (uAOBP).[1]

Key inclusion criteria[6]:

- ✔ Unattended SiSBP ≥140 mm Hg
- ✔ High blood pressure despite taking at least ≥3 antihypertensive medications, including a diuretic

Key exclusion criteria[6]:

- ✖ Confirmed hypertensive crisis (BP >180/120 mm Hg)*
- ✖ Major cardiovascular, renal, or cerebrovascular medical complications in the past 6 months or NYHA stage III-IV heart failure
- ✖ N-terminal pro-BNP levels ≥500 pg/mL
- ✖ eGFR <15 mL/min/1.73 m^2

Out of the 730 patients randomized, 162 had chronic kidney disease (eGFR 15 to <60 mL/min/1.73 m^2).[1,2]

At baseline, 63% of patients reported taking ≥4 antihypertensive medications.[1]

AOBPM = automated office blood pressure measurement; ARB = AT_1 receptor blocker; BNP = B-type natriuretic peptide; BP = blood pressure; CCB = calcium channel blocker; eGFR = estimated glomerular filtration rate; NYHA = New York Heart Association.

*Confirmed hypertensive crisis (grade 3) defined as SiSBP ≥180 mm Hg and/or sitting diastolic blood pressure (SiDBP) ≥110 mm Hg as measured by AOBPM at 2 different timepoints.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

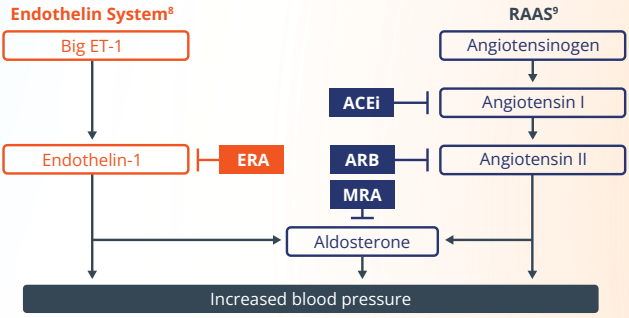
Hepatotoxicity (continued)

Do not initiate TRYVIO in patients with elevated aminotransferases (>3 × ULN) or moderate to severe hepatic impairment. Advise patients with symptoms suggesting hepatotoxicity (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, scleral icterus, jaundice, dark urine, fever, or itching) to immediately stop treatment with TRYVIO and seek medical attention.

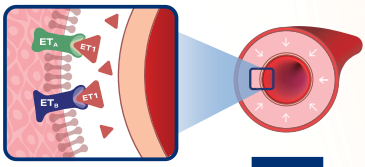
If sustained, unexplained, clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 × ULN, or if clinical symptoms of hepatotoxicity occur, discontinue TRYVIO.

Take a different path to help your patients lower their blood pressure

The endothelin system is one of several key pathways in hypertension and has not been successfully targeted by existing systemic hypertension therapies.[1-3,7]



TRYVIO mechanism of action (MOA)

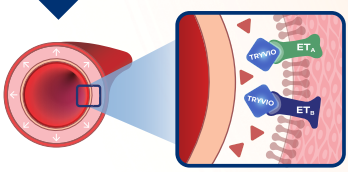


Hypertensive State

Overactivation of the endothelin system induces vasoconstriction and remodeling via binding of ET-1 to ET_A and ET_B receptors.[1,10,11]

The TRYVIO Effect

Aprocitentan inhibits the endothelin system by blocking ET_A and ET_B receptors.[1]



TRYVIO is the first and only dual ERA for combination treatment of patients with difficult-to-control hypertension.[1-3]

ACEi = angiotensin-converting enzyme inhibitor; ARB = AT_1 receptor blocker; eGFR = estimated glomerular filtration rate; ERA = endothelin receptor antagonist; ET-1 = endothelin-1; MRA = mineralocorticoid receptor antagonist; RAAS = renin-angiotensin-aldosterone system.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Fluid Retention

Fluid retention and peripheral edema are known effects of ERAs, including TRYVIO. Edema/fluid retention was reported in 9% of TRYVIO-treated patients compared with 18% of patients receiving aprocitentan 25 mg (twice the recommended dose) and 2% on placebo in the clinical trial, requiring additional diuretic use in some patients. Older age and chronic kidney disease are risk factors for edema/fluid retention with TRYVIO. TRYVIO has not been studied in patients with heart failure New York Heart Association stage III–IV, unstable cardiac function, or with NTproBNP ≥500 pg/mL. TRYVIO is not recommended in these patients.

Monitor for signs and symptoms of fluid retention, weight gain, and worsening heart failure. If clinically significant fluid retention develops, treat appropriately, and consider discontinuation of TRYVIO.

Please see full Prescribing Information, including BOXED Warning.

Dosing

Take the pressure down with once-daily dosing[1]

- Once-daily 12.5 mg dose taken with or without food
  - Taken day or night
  - No monitoring required
  - No clinically relevant drug-drug interactions were reported in clinical trials[1,2]

For illustrative purposes only

- No dose adjustment required in patients with mild to severe renal impairment (eGFR ≥15 mL/min)[1,*]
  - TRYVIO is not recommended in patients with kidney failure (eGFR <15 mL/min) or on dialysis
  - Patients with renal impairment are at increased risk of edema/fluid retention

- No evidence of increased incidence of hyperkalemia or hypotension was reported in clinical trials[1,2,4,5]

*Primarily metabolized by UGT1A1- and UGT2B7-mediated N-glucosidation and non-enzymatic hydrolysis.[1]

eGFR = estimated glomerular filtration rate.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hemoglobin Decrease

Decreases in hemoglobin concentration and hematocrit have occurred following administration of other ERAs and were observed in the clinical trial with TRYVIO. Hemoglobin decreases usually presented early, stabilized thereafter, and were reversible after discontinuation. A decrease in hemoglobin of >2 g/dL from baseline was observed in 7% of patients compared to 1% of placebo patients. A decrease to below 10.0 g/dL was observed in 3% of TRYVIO-treated patients compared to 0 patients taking placebo. Initiation of TRYVIO is not recommended in patients with severe anemia. Measure hemoglobin prior to initiation of treatment and periodically during treatment as clinically indicated.

Decreased Sperm Counts

TRYVIO, like other ERAs, may have an adverse effect on spermatogenesis. Counsel men about potential effects on fertility.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions (more frequent than placebo and ≥2% in TRYVIO-treated patients) are edema/fluid retention and anemia.

USE IN SPECIFIC POPULATIONS

Lactation

There are no data on the presence of aprocitentan in human milk, the effects on the breastfed infant, or the effect on milk production. Because of the potential for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment with TRYVIO.

Prescribing

TRYVIO is available through Walgreens Specialty Pharmacy*

Walgreens Specialty Pharmacy will automatically apply the appropriate savings program and determine coverage and out-of-pocket cost for your patients.

To get started, simply e-prescribe your patients' prescriptions with refills† in your EHR system to the Walgreens Specialty Pharmacy below:

Walgreens Specialty Pharmacy

NCPDP: 3974157

NPI# 1972560688

130 Enterprise Dr, Pittsburgh, PA 15275

Toll-free Phone Number: 888-347-3416

Fax Number: 877-231-8302

*Also available at other retail pharmacies. Patient must present the free trial and/or copay card when picking up their TRYVIO prescription.

†If prescribing to Walgreens Specialty Pharmacy, refills are not required for the patient to participate in the free trial offer; however, if the Rx is written with refills, Walgreens can determine insurance coverage while the free trial is initiated to help prevent future delays. Walgreens Specialty Pharmacy may request additional prescriptions if needed.

TRYVIO 30-day free trial and savings

Free Trial Offer:

30-DAY FREE TRIAL OFFER

New patients starting TRYVIO are eligible for a 30-day free trial offer,* regardless of insurance.

TRYVIO Savings:

TRYVIO™ (aprocitentan) 12.5mg tablets

TRYVIO SAVINGS PROGRAM

Commercially eligible patients may receive TRYVIO for as little as **$10**† per month.

No copay or free trial cards are needed if the prescription is sent to the Walgreen Specialty Pharmacy listed above.

EHR = electronic health record.

*Eligible patients only. Limitations apply. This offer is good for a 30-day (maximum 30 tablets; one-time use) free trial of TRYVIO at no cost to your patient. See full Terms and Conditions.

†Limitations apply. For commercially eligible patients only. This offer is not valid under Medicare, Medicaid, or any other federal or state program. Patient must be 18 years of age or older and a resident of the United States. See full Terms and Conditions.

IMPORTANT SAFETY INFORMATION (continued)
USE IN SPECIFIC POPULATIONS (continued)

Renal Impairment

TRYVIO is not recommended in patients with kidney failure (eGFR <15 mL/min) or on dialysis. Patients with renal impairment are at increased risk of edema/fluid retention.

Please see full Prescribing Information, including BOXED Warning.

TRYVIO™
(aprocitentan) 12.5mg tablets

TRYVIO is the first and only dual ERA indicated for systemic hypertension in combination with other drugs[1,2,4,5]

15.4 mm Hg
Systolic

Significantly reduced systolic BP in combination with other hypertension medications[1]

- Effect was consistent in reducing diastolic BP
- Efficacy and safety profile appeared to be consistent across subgroups

In clinical studies:

- **No clinically relevant drug-drug interactions were reported[1,2]**
- No evidence of increased incidence of hyperkalemia or hypotension was reported[1,2,4,5]
- The most frequent AEs were mild-to-moderate edema/fluid retention and anemia[1]

Once-daily, single dose 12.5-mg tablet[1]

AEs = adverse events; BP = blood pressure;
ERA = endothelin receptor antagonist.

IMPORTANT SAFETY INFORMATION (continued)
USE IN SPECIFIC POPULATIONS (continued)

Hepatic Impairment

TRYVIO is not recommended in patients with moderate and severe hepatic impairment (Child-Pugh class B and C) because these patients may be at increased risk for poor outcomes from hepatotoxicity.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see full Prescribing Information, including BOXED Warning.

For more information, visit **TRYVIOHCP.com**

References: 1. TRYVIO™ (aprocitentan) [prescribing information]. Radnor, PA: Idorsia Pharmaceuticals US Inc; 2025. **2.** Schlaich MP, Bellet M, Weber MA, et al; PRECISION investigators. Dual endothelin antagonist aprocitentan for resistant hypertension (PRECISION): a multicentre, blinded, randomised, parallel-group, phase 3 trial. *Lancet*. 2022;400(10367):1927-1937. Published correction appears in *Lancet.* 2023;401(10373):268. doi:10.1016/S0140-6736(23)00119-8 **3.** Dhillon S. Aprocitentan: first approval. *Drugs.* 2024;84(7):841-847. doi:10.1007/s40265-024-02053-0 **4.** Supplementary appendix to: Schlaich MP, Bellet M, Weber MA, et al; PRECISION investigators. Dual endothelin antagonist aprocitentan for resistant hypertension (PRECISION): a multicentre, blinded, randomised, parallel-group, phase 3 trial. *Lancet*. 2022;400(10367):1927-1937. doi:10.1016/S0140-6736(22)02034-7 **5.** Schiffrin EL, Fisher NDL. Diagnosis and management of resistant hypertension. *BMJ*. 2024;385:e079108. Published 2024 Jun 19. doi:10.1136/bmj-2023-079108 **6.** Danaietash P, Verweij P, Wang JG, et al. Identifying and treating resistant hypertension in PRECISION: A randomized long-term clinical trial with aprocitentan. *J Clin Hypertens* (Greenwich). 2022;24(7):804-813. doi:10.1111/jch.14517 **7.** Clozel M. Aprocitentan and the endothelin system in resistant hypertension. *Can J Physiol Pharmacol.* 2022;100(7):573-583. doi:10.1139/cjpp-2022-0010 **8.** Dhaun N, Goddard J, Kohan DE, et al. Role of endothelin-1 in clinical hypertension: 20 years on. *Hypertension.* 2008;52(3):452-459. doi:10.1161/HYPERTENSIONAHA.108.117366 **9.** Te Riet L, van Esch JH, Roks AJ, et al. Hypertension: renin-angiotensin-aldosterone system alterations. *Circ Res*. 2015;116(6):960-975. doi:10.1161/CIRCRESAHA.116.303587 **10.** Heidari Nejad S, Azzam O, Schlaich MP. Dual endothelin antagonism with aprocitentan as a novel therapeutic approach for resistant hypertension. *Curr Hypertens Rep*. 2023;25(10):343-352. doi:10.1007/s11906-023-01259-z **11.** Kostov K. The causal relationship between endothelin-1 and hypertension: focusing on endothelial dysfunction, arterial stiffness, vascular remodeling, and blood pressure regulation. *Life (Basel)*. 2021;11(9):986. doi:10.3390/life11090986

idorsia

US-AP-00154 02/26 **idorsia.us**