**Novel Oral Antihypertensive Gets FDA's Blessing**

— Aprocitentan becomes the first endothelin receptor antagonist for BP lowering

The FDA has approved aprocitentan (Tryvio), making it the first endothelin receptor antagonist for the treatment of high blood pressure (BP), [Idorsia Pharmaceuticals announced](https://www.idorsia.com/investors/news-and-events/media-releases/media-release-details?id=3195250) on Wednesday. The once-daily oral medication is indicated in combination with other antihypertensive drugs to lower BP in adult patients who do not have their BP controlled with other therapies.

It is believed that some people may respond better to the drug's novel mechanism, as aprocitentan is a dual endothelin receptor antagonist that works differently than conventional diuretics, renin-angiotensin-aldosterone system antagonists, calcium channel blockers, and beta-blockers used to lower BP. Approval was supported by the phase III [PRECISION trial](https://www.medpagetoday.com/meetingcoverage/aha/101655), which included over 700 people with treatment-resistant hypertension. "*We have had to wait for over 30 years to see the approval of an oral anti-hypertensive agent that works on a new therapeutic pathway, so Tryvio provides transformational progress in the field of systemic hypertension*. *Today, we are not able to reduce blood pressure below recommended levels in at least 10% of the hypertensive patients we treat. As well, it is often patients at high risk of adverse cardiovascular outcomes and typically with comorbidities who pose this challenge*" said PRECISION investigator Michael Weber, MD.

Hypertension is a known risk factor for heart disease and stroke. An estimated [48% of adults in the U.S. have hypertension](https://www.cdc.gov/bloodpressure/facts.htm) and of this group, [over 75% are said to have uncontrolled BP](https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html), defined as BP over 130/80 mm Hg. To help address the unmet need for BP control, the FDA approved 2 device-based therapies for hypertension last November: the [Paradise ultrasound renal denervation system](https://www.medpagetoday.com/cardiology/hypertension/107227) and the [Symplicity Spyral renal denervation system](https://news.medtronic.com/fda-approves-medtronic-symplicity-spyral-renal-denervation-system-for-high-blood-pressure-newsroom%22%20%5Co%20%22Opens%20in%20a%20new%20tab%20or%20window%22%20%5Ct%20%22_blank).

In the PRECISION study, both 12.5 mg and 25 mg doses of aprocitentan lowered systolic BP in people starting at a systolic BP of 140 mm Hg or higher by approximately 4 mm Hg over placebo at week 4, with a sustained effect at week 40. Trial participants were then all put on the 25 mg dose for 8 months and re-randomized in the third phase of the study to this higher dose of aprocitentan or placebo. Aprocitentan users withdrawn from therapy and placed on placebo for 4 weeks saw systolic BP rebound.

According to the [prescribing information](https://www.idorsia.us/dam/jcr%3Ad834ee09-2e6c-443d-b3ac-c111e38f0990/tryvio_pi.pdf), edema and anemia are the most common adverse events with aprocitentan, and the drug is contraindicated in pregnancy. In trials, edema was reportedly manageable with addition or uptitration of diuretic therapy.

Now that it has been approved, aprocitentan has a recommended dosage of 12.5 mg orally once daily, with or without food, according to Idorsia. The prescribing information notes the drug is not approved for use at the 25 mg dose due to having no meaningful reduction in BP as compared to the 12.5 mg dose along with the added risk of edema.

Outside observers had also aired [concerns about using 25 mg aprocitentan in high-risk individuals](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2823%2900275-1/fulltext), such as patients with diabetes, chronic kidney disease, or heart failure.

The manufacturer plans to have aprocitentan on U.S. shelves in the second half of 2024.