Media Release
November 15, 2024

Idorsia's once-daily TRYVIO™ (aprocitentan) is now available in the U.S., advancing treatment options for millions of patients with difficult-to-control hypertension

- Once-daily TRYVIO, now available to prescribe in the U.S., is 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 medications.
- TRYVIO is the first-and-only dual endothelin receptor antagonist (ERA) for the treatment of systemic hypertension.
- Idorsia to present new data on TRYVIO at American Heart Association's Scientific Sessions and will have a TRYVIO commercial and medical booth at #1705

Radnor, PA – November 15, 2024
Idorsia Pharmaceuticals U.S. Inc. today announced that TRYVIO™ (aprocitentan) is now available in the U.S. 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. In the United States, nearly 120 million adults – or about half of the adult population – have hypertension.[1] Of those diagnosed and treated with existing standards of care, only ~50% achieve blood pressure control at a goal of <130/80 mm Hg.[1]

TRYVIO was approved by the U.S. FDA based on the Phase 3 PRECISION trial which demonstrated that TRYVIO reduced systolic blood pressure by 15.4 mm Hg from baseline at 4 weeks (primary endpoint) when added to standardized background therapy of at least three antihypertensive drugs, including a diuretic (see full PRECISION phase 3 study design below).[2] TRYVIO was well-tolerated, and its safety profile established over a 48-week study. The most frequently reported adverse reactions were edema/fluid retention and anemia.[2] TRYVIO has a boxed warning for embryo-fetal toxicity.

Tosh Butt, President and General Manager of Idorsia U.S. commented:
"Today, hypertension is the leading modifiable risk factor for cardiovascular disease and mortality in the world. TRYVIO's availability in the U.S. is an important milestone for the millions of patients who require novel approaches to control their blood pressure. Idorsia has delivered a treatment addressing a previously unaddressed therapeutic pathway in systemic hypertension for the first time in over three decades, giving hope to patients whose existing therapies are not adequate. We are enormously proud to bring this important medication to the medical community and the patients they serve."

Michael A. Weber, MD, Professor of Medicine, Division of Cardiovascular Medicine State University of New York, commented:
"Uncontrolled hypertension can increase the risk of life-threatening conditions, such as major adverse cardiovascular and cerebrovascular events. For patients with comorbid conditions such as diabetes, chronic kidney disease, and heart failure, these issues pose an increased burden. TRYVIO provides physicians with a therapeutic option targeting a previously unaddressed pathway to address the millions of patients with hypertension whose blood pressure is not adequately controlled despite being treated with the existing standards of care."

TRYVIO is the only FDA-approved treatment for systemic hypertension targeting endothelin system, a key pathway in the pathophysiology of hypertension. TRYVIO is a 12.5mg oral, once-daily medication that can be taken with or without food. No dose adjustment for patients with renal impairment (eGRF ≥ 15 mL/min) is required.[2] TRYVIO is not recommended in patients with kidney failure (eGFR <15 mL/min). Patients with renal impairment are at increased risk of edema/fluid retention.

TRYVIO is only available through a risk evaluation and mitigation strategy (REMS) program because of the risk of embryo-fetal toxicity. Prescribers must complete a one-time enrollment in the TRYVIO REMS program in order to prescribe.[2] No patient enrollment or reporting is required. TRYVIO is exclusively available to prescribe through Walgreens Specialty Pharmacy.

To learn more about this important treatment option and how to prescribe, please visit TRYVIOhcp.com.

About PRECISION Phase 3 Clinical Study[3,4]

The efficacy of TRYVIO (aprocitentan) was evaluated in a multipart, Phase 3 multicenter study (PRECISION, NCT03541174) in adults with systolic blood pressure (SBP) ≥140 mm Hg who were prescribed at least three antihypertensive medications. The trial included a placebo run-in period, which was followed by three parts as described below. Prior to the placebo run-in period, all patients were switched to standard background antihypertensive therapy consisting of an angiotensin receptor blocker, a calcium channel blocker, and a diuretic, which was continued throughout the study. Patients with concomitant use of beta-blockers continued this treatment throughout the study.

Following the 4-week placebo run-in period, 730 patients were randomized equally to aprocitentan at either 12.5 mg, 25 mg, or placebo once daily during the initial 4-week double-blind (DB) treatment period (part 1). At the end of 4 weeks, all patients entered the single-blind treatment period (part 2) where they received 25 mg aprocitentan once daily for 32 weeks. At the end of the 32 weeks, patients were re-randomized to receive either 25 mg aprocitentan or placebo, once daily, during a 12-week DB-withdrawal period (part 3).

The primary efficacy endpoint was the change in sitting SBP (SiSBP) from baseline to Week 4 during part 1, measured at trough by unattended automated office blood pressure (uAOBP).

The key secondary endpoint was the change in SiSBP measured at trough by uAOBP from Week 36 (i.e., prior to randomized withdrawal to 25 mg aprocitentan or placebo in part 3) to Week 40.

Patients had a mean age of 62 years (range 24 to 84 years) and 60% were male. Patients were White (83%), African American (11%) or Asian (5%). Approximately 10% were Hispanic. The mean body mass index (BMI) was 34 kg/m2 (range 18 to 64 kg/m2). At baseline, 19% of patients had an eGFR 30–59 mL/min/1.73 m2 and 3% had an eGFR 15–29 mL/min/1.73 m2. At baseline, 24% of patients had a urine albumin-to-creatinine ratio (UACR) of 30–300 mg/g and 13% had a UACR >300 mg/g. Approximately 54% of patients had a medical history of diabetes mellitus, 31% ischemic heart disease, and 20% congestive heart failure. At baseline, 63% of patients reported taking four or more antihypertensive medications.

TRYVIO 12.5 mg was statistically superior to placebo in reducing SiSBP at Week 4 (part 1). The treatment effect was consistent for sitting diastolic BP (SiDBP).

The persistence of the BP-lowering effect of TRYVIO was demonstrated in part 3 of the trial, in which patients on aprocitentan were re-randomized to placebo or 25 mg aprocitentan following a period during which all patients were treated with 25 mg. In patients re-randomized to placebo, the mean

SiSBP increased, whereas in patients re-randomized to 25 mg aprocitentan the mean effect on SiSBP was maintained and was statistically superior to placebo at Week 40. The treatment effect was consistent for SiDBP.

Most of the BP-lowering effect occurred within the first two weeks of treatment with TRYVIO. TRYVIO is not approved for use at a 25 mg dose. The efficacy for the 25 mg aprocitentan dose as measured in the primary end point of change in sitting SBP (SiSBP) from baseline to Week 4 in part 1, was similar to the 12.5 mg dose and thus aprocitentan 12.5 mg is the approved dose.

TRYVIO's BP-lowering effect appeared consistent among subgroups defined by age, sex, race, BMI, baseline eGFR, baseline UACR, medical history of diabetes, and between BP measurement methodologies (uAOBP and ambulatory BP measurements).

The most frequently reported adverse reactions to TRYVIO during the 4-week double-blind placebo-controlled treatment period (part 1) of the PRECISION study were edema/fluid retention and anemia. During the initial 4-week double-blind placebo-controlled treatment period (part 1), 0.8% of patients experienced an adverse reaction of hypersensitivity (i.e., rash, erythema, allergic edema) on TRYVIO compared to no reports in patients treated with placebo. One patient experienced allergic dermatitis requiring hospitalization while receiving aprocitentan 25 mg. TRYVIO is contraindicated in patients who are hypersensitive to aprocitentan or any of its excipients. Use of TRYVIO is contraindicated in pregnancy.

Lowering BP reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes. There are no controlled trials demonstrating reduction of risk of these events with TRYVIO.

Important Safety Information

TRYVIO may cause serious side effects, including:

TRYVIO can cause major birth defects if used by pregnant patients and has a BOXED Warning for embryo-fetal toxicity.

- People who can become pregnant must not be pregnant when they start taking TRYVIO or become pregnant during treatment with TRYVIO or for 1 month after stopping treatment with TRYVIO.
- People who can become pregnant should have a negative pregnancy test before starting treatment with TRYVIO, each month during treatment with TRYVIO, and 1 month after stopping TRYVIO.
- People who can become pregnant should use acceptable birth control before starting treatment with TRYVIO, during treatment with TRYVIO, and for 1 month after stopping TRYVIO because the medicine may still be in your body.
- People can only receive TRYVIO through a restricted program called the TRYVIO REMS. If you are a person who can become pregnant, your healthcare provider will talk to you about pregnancy testing recommendations and the need to use acceptable birth control, the benefits and risks of TRYVIO, and the need to report suspected pregnancy right away to your healthcare provider.

What is TRYVIO?

TRYVIO is a prescription medicine used to treat high blood pressure (hypertension) in adults who are taking other high blood pressure medicines and whose blood pressure is not well controlled.

Do not take TRYVIO if you are

- pregnant or currently trying to become pregnant.
- allergic to aprocitentan or any of the ingredients in TRYVIO.

Before taking TRYVIO, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- have heart failure
- have anemia
- have kidney problems or get dialysis
- are pregnant or plan to become pregnant during treatment with TRYVIO. TRYVIO can cause serious birth defects.
- are breastfeeding or plan to breastfeed. It is not known if TRYVIO passes into your breastmilk. Do not breastfeed if you take TRYVIO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

TRYVIO may cause other serious side effects, including:

- Liver problems. TRYVIO may cause liver problems. Your healthcare provider should do blood tests to check your liver before starting treatment and as needed during treatment with TRYVIO. Tell your healthcare provider if you have any of the following symptoms of liver problems during treatment with TRYVIO:
    - nausea or vomiting
    - pain in the upper right stomach
    - tiredness
    - loss of appetite
    - yellowing of your skin or whites of your eyes
    - dark urine
    - fever
    - itching
- Fluid retention. Fluid retention and swelling are common during treatment with TRYVIO and can be serious. Tell your healthcare provider right away if you have any unusual weight gain, trouble breathing, or swelling of your ankles or legs. Your healthcare provider may treat you with other medicines (diuretics) if you develop fluid retention or swelling.
- Low red blood cell levels (anemia). Anemia is common during treatment with TRYVIO and can be serious. Your healthcare provider will do blood tests to check your red blood cells before starting and as needed during treatment with TRYVIO.
- Decreased sperm count. TRYVIO may cause decreased sperm counts in males and may affect the ability to father a child. Tell your healthcare provider if being able to have children is important to you.

Your healthcare provider may stop treatment with TRYVIO if you develop certain side effects. Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of TRYVIO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

For more information see the Full Prescribing Information including BOXED Warning (PI and Medication Guide).

Notes to the editor

References

1. Million Hearts. Estimated hypertension prevalence, treatment, and control among U.S. adults. Accessed 29 January 2024. https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html
2. TRYVIO®(aprocitentan) [prescribing information]. Radnor, PA: Idorsia Pharmaceuticals US Inc; 2024
3. Danaietash P et al. Identifying and treating resistant hypertension in PRECISION: A randomized long-term clinical trial with aprocitentan. J Clin Hypertension 2022 Jul;24(7):804-813.
4. Schlaich MP, et al. A randomized controlled trial of the dual endothelin antagonist aprocitentan for resistant hypertension. The Lancet, 2022; Dec 3;400(10367):1927-1937.

About Idorsia US

Idorsia US, an affiliate of Idorsia, is reaching out for more – we have more ideas, we see more opportunities, and we want to help more patients. To achieve this, we will help develop Idorsia into a leading biopharmaceutical company, with a strong scientific core. With commercial operations based outside of Philadelphia, PA, one of densest communities of life sciences talent in the world, we are helping to realize the company's ambition of bringing innovative medicines from bench to bedside. Our goal is to build a commercial footprint that will deliver Idorsia's deep pipeline of products from its R&D engine to the US market – with the potential to change the lives of many patients.

About Idorsia

Idorsia Ltd is reaching out for more – We have more ideas, we see more opportunities and we want to help more patients. In order to achieve this, we will develop Idorsia into a leading biopharmaceutical company, with a strong scientific core.

Headquartered near Basel, Switzerland – a European biotech-hub – Idorsia is specialized in the discovery, development, and commercialization of small molecules to transform the horizon of therapeutic options. Idorsia has a 25-year heritage of drug discovery, a broad portfolio of innovative drugs in the pipeline, an experienced team of professionals covering all disciplines from bench to bedside, and commercial operations in Europe and North America – the ideal constellation for bringing innovative medicines to patients.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 750 highly qualified specialists dedicated to realizing our ambitious targets.

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