

Revolutionizing treatment: Opsynvi and Winrevair shake up the PAH market

Market Event Summary

Opsynvi and Winrevair approved for PAH

New approvals bring life to a saturated market

A crowded PAH landscape, but unmet need remains

- Pulmonary arterial hypertension (PAH) is a progressive pulmonary vascular disease, and patients often require treatment with multiple agents. Despite a vast array of treatment options, mortality rates in PAH remain high. The PAH market is highly competitive, making it challenging for new entrants to positively differentiate themselves. Innovative treatments and strong clinical evidence will be key contributors for success in this market, as current therapies focus only on vasodilation / vasoconstriction and not the underlying causes of PAH.

Opsynvi supports early combination therapy

- Johnson & Johnson's Opsynvi is a once-daily oral fixed-dose combination (FDC) tablet that combines the endothelin receptor antagonist (ERA) macitentan (Johnson & Johnson's Opsumit) and the phosphodiesterase-5 inhibitor (PDE-5i) tadalafil (United Therapeutics' Adcirca). Both monotherapy agents are well entrenched in the treatment landscape.
- Opsynvi was approved by the FDA based on results from the Phase 3 A DUE trial, which showed a significant decrease in pulmonary vascular resistance (PVR) compared with macitentan and tadalafil monotherapies. Its approval marks the first FDC product for PAH.
- Use of Opsynvi aligns with the ECS / ERS 2022 guidelines, advocating early combination therapy for adult PAH patients in WHO functional class II-III.
- Opsynvi is expected to be available in the United States in April 2024.

Winrevair offers a new treatment approach

- Merck & Co.'s Winrevair (sotatercept-csrk) is an activin signaling inhibitor that targets the bone morphogenetic protein (BMP) pathway by serving as a TGF- β ligand trap. Mutations in the *BMP2* gene are a prevalent cause of heritable PAH, emphasizing the importance of targeting the BMP pathway. Winrevair is dosed subcutaneously once every 3 weeks.
- Winrevair's approval marks a significant milestone for PAH. Its distinctive mechanism of action (MOA) provides a novel treatment option. Unlike other current therapies, its effects are not primarily driven through vasodilation.
- Winrevair's approval is supported by data from its Phase 3 STELLAR trial, where it showed substantial improvements in PVR and 6-minute walk distance (6MWD). Although it was not a primary endpoint of the trial, it also showed 84% risk reduction in time to clinical worsening or death compared with placebo.
- The approval is not accompanied with a boxed warning or any contraindications. However, there are warnings of the risk of erythrocytosis, severe thrombocytopenia, and serious bleeding.
- Winrevair will launch at a price of \$14,000 per vial, amounting to an annual cost of \$238,000, and is expected to be available in April 2024 in the United States.

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Clarivate's takeaways

- The reduced pill burden associated with Opsynvi is expected to improve treatment compliance and bring combination therapy to some patients sooner. However, challenges such as competition from generic monotherapies and physician reluctance about FDCs will limit its widespread adoption.
- In contrast, Winrevair, with its novel MOA and strong efficacy profile, will capture substantial patient share.
 - Its initial use will likely be reserved for later lines of treatment.
 - Although not listed as a contraindication, a warning of serious bleeding with concomitant prostacyclin therapy may hold back Winrevair use; prostacyclin therapy is a well-established treatment approach in PAH.
 - We will wait for the findings of Winrevair's ZENITH trial (due 2025) to confirm the encouraging mortality data it showed in the STELLAR trial.

How will the PAH market evolve?

- What impact will the launch of Winrevair and Opsynvi have on the PAH treatment landscape?
- How will Winrevair's clinical profile and market adoption impact future launches of PAH drugs?
- What restrictions will payers implement on the prescribing of Winrevair and Opsynvi?

Clarivate coverage of pulmonary hypertension

- Disease Landscape & Forecast: Pulmonary hypertension - G7
- Epidemiology: Diagnosed incidence and prevalence data for various population segments of pulmonary hypertension across the G7 markets
- Current Treatment: Physician Insights: US - Explores the current prescribing trends of pulmonologists and cardiologists treating pulmonary arterial hypertension
- Current Treatment: Physician Insights: EU5 - Explores the current prescribing trends of pulmonologists and cardiologists treating pulmonary arterial hypertension
- Current Treatment: Treatment Algorithms: US - Explores the current prescribing trends of pulmonologists and cardiologists treating pulmonary arterial hypertension
- Unmet Need: Pulmonary arterial hypertension: US and EU5

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