

# PRODUCT PROFILE

## **WINREVAIR** Sotatercept-csrk, for injection, for subcutaneous use

### **Manufacturer**

Merck Sharp & Dohme LLC

### **Indication**

Sotatercept is indicated for the treatment of adults with pulmonary arterial hypertension (PAH; WHO [World Health Organization] Group 1) to increase exercise capacity, improve WHO functional class (FC) and reduce the risk of clinical worsening events.<sup>1</sup>

### **Dosing and Administration**

- Sotatercept is administered subcutaneously every 3 weeks based on patient body weight, starting at 0.3 mg/kg. After confirming acceptable hemoglobin and platelet counts, increase to 0.7 mg/kg every 3 weeks unless dosage adjustments are needed; do not initiate treatment if platelet count is less than 50,000/mm<sup>3</sup>.<sup>1</sup>

### **Storage and Handling**

- Store vials refrigerated at 2 C to 8 C (36 F to 46 F) in their original carton and do not freeze; the kit should remain refrigerated until use but can be kept at up to 25 C (77 F) for up to 24 hours.<sup>1</sup>

### **Safety/Warnings**

- Sotatercept may increase hemoglobin. Severe erythrocytosis may increase the risk of thromboembolic events or hyperviscosity syndrome.<sup>1</sup>
- Sotatercept may decrease platelet count. Severe thrombocytopenia may increase the risk of bleeding.<sup>1</sup>
- Serious bleeding (e.g., gastrointestinal, intracranial hemorrhage) was reported in 4% of patients taking sotatercept and 1% of patients taking placebo.<sup>1</sup>
- Animal studies indicate that sotatercept may cause fetal harm during pregnancy and impair both female and male fertility.<sup>1</sup>
- The most commonly reported adverse reactions (occurring in ≥ 10% of sotatercept-treated patients and at least 5% more than placebo) were headache (24.5%), epistaxis (22.1%), rash (20.2%), telangiectasia (16.6%), diarrhea (15.3%), dizziness (14.7%) and erythema (13.5%).<sup>1</sup>

### **Disease State Background**

PAH is a rare, progressive condition in which the small arteries in the lungs become thickened and narrowed, obstructing blood flow and causing increased lung blood pressure. It leads to high morbidity and a shortened lifespan.<sup>2</sup> The American Heart Association recommends early diagnosis to begin supportive treatment to reduce morbidity and to avoid shortened lifespans.<sup>3</sup> Although PAH has been linked to genetic and environmental factors in some cases the majority of cases (approximately 50% to 60%) remain idiopathic, with no discernable underlying cause.<sup>4,5,6,7</sup> An estimated 500 to 1000 cases are diagnosed in the United States each year.<sup>8</sup> PAH, more common in women aged 30 to 60 years, disproportionately affects Black and Hispanic women.<sup>8</sup>

### **Place in Therapy**

Currently, no cure exists for PAH and many patients experience poor outcomes after experiencing an aggressive and progressive disease course.<sup>9</sup> Historically available treatments delay progression but mainly address symptoms rather than treat the underlying pathophysiology and disease mechanism.<sup>7</sup> Sotatercept is the first FDA-approved therapy with a mechanism of action directly targeting the underlying cause of PAH.<sup>10</sup> In clinical trials, sotatercept was shown to significantly improve exercise capacity and other secondary outcome measures in addition to background PAH therapy compared with background PAH therapy alone.<sup>11</sup>

## Managed Care Considerations

Sotatercept represents a novel therapy class and expands options for patients. The American College of Chest Physicians (CHEST) guidelines suggest that dual combination therapy is superior to monotherapy to improve 6-minute walk testing (6WMT) and to reduce mortality for treatment-naïve PAH patients with WHO Functional Class II and III.<sup>12</sup> Mortality rates for patients with PAH remain high, with 3-year mortality rates reaching up to 55% for high-risk groups. Despite lower mortality rates among patients treated with combination therapy compared with monotherapy (7% vs 13%, respectively), no difference was observed in a study between groups after 2 and 3 years.<sup>13</sup>

## Market Insights

- Patients with PAH have faced limited treatment options and poor outcomes. Sotatercept, the first FDA-approved activin signaling inhibitor, improves the 6WMT and reduces mortality, offering a potential new standard of care as either add-on or first-line therapy. It targets the underlying cause of PAH, potentially reversing disease pathology and improving quality of life.
- Phase 3 trials show significant benefits, including improved exercise capacity at 24 weeks. Prior to sotatercept, no therapies targeted the abnormal pulmonary vasculature driving PAH.<sup>11</sup>

## REFERENCES

1. Winrevair. Merck Sharp & Dohme LLC; 2024. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2024/761363s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761363s000lbl.pdf)
2. Beshay S, Sahay S, Humbert M. Evaluation and management of pulmonary arterial hypertension. *Respir Med*. 2020;171:106099. doi:10.1016/j.rmed.2020.106099
3. Maron BA. Revised definition of pulmonary hypertension and approach to management: a Clinical Primer. *J Am Heart Assoc*. 2023;12(8):e029024. doi:10.1161/jaha.122.029024
4. Rhodes CJ, Batai K, Bleda M, et al. Genetic determinants of risk in pulmonary arterial hypertension: international genome-wide association studies and meta-analysis. *Lancet Respir Med*. 2019;7(3):227-238. doi:10.1016/S22132600(18)30409-0
5. Callejo M, Barberá JA, Duarte J, Perez-Vizcaino F. Impact of nutrition on pulmonary arterial hypertension. *Nutrients*. 2020;12(1):169. doi:10.3390/nu12010169
6. Sydykov A, Mamazhakypov A, Maripov A, et al. Pulmonary hypertension in acute and chronic high altitude maladaptation disorders. *Int J Environ Res Public Health*. 2021;18(4):1692. doi:10.3390/ijerph18041692
7. Humbert M, Kovacs G, Hoeper MM, et al; ESC/ERS Scientific Document Group. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-3731. doi:10.1093/eurheartj/ehac237
8. Learn about pulmonary arterial hypertension. American Lung Association. Updated June 7, 2024. Accessed August 7, 2024. <https://www.lung.org/lung-health-diseases/lung-disease-lookup/pulmonary-arterial-hypertension/learn-about-pulmonary-arterial-hypertension>
9. Gale S. The evolving treatment landscape of pulmonary arterial hypertension. *Am J Manag Care*. 2021;27(suppl 3):S42-S52. doi:10.37765/ajmc.2021.88610
10. FDA approves Merck's Winrevair (sotatercept-csrk), a first-in-class treatment for adults with pulmonary arterial hypertension (PAH, WHO\* Group 1). Press release. Merck. March 26, 2024. Accessed August 7, 2024. <https://www.merck.com/news/fda-approves-mercks-winrevair-sotatercept-csrk-a-first-in-class-treatment-for-adults-with-pulmonary-arterial-hypertension-pah-who-group-1/>
11. Hoeper MM, Badesch DB, Ghofrani HA, et al. Phase 3 trial of sotatercept for treatment of pulmonary arterial hypertension. *N Engl J Med*. 2023;388(16):1478-1490. doi:10.1056/NEJMoa2213558
12. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults: update of the CHEST guideline and expert panel report. *Chest*. 2019;155(3):565-586. doi:10.1016/j.chest.2018.11.030
13. Chang KY, Duval S, Badesch DB, et al; PHAR Investigators. Mortality in pulmonary arterial hypertension in the modern era: early insights from the Pulmonary Hypertension Association Registry. *J Am Heart Assoc*. 2022;11(9):e024969. doi:10.1161/JAHA.121.024969