Drug Coverage Policy

Effective Date……6/15/2026
Coverage Policy Number……IP0645
Policy Title……Winrevair

Pulmonary Arterial Hypertension – Winrevair

- Winrevair™ (sotaterept-csrk subcutaneous injection – Merck)

INSTRUCTIONS FOR USE
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OVERVIEW
Winrevair, an activin signaling inhibitor, is indicated for the treatment of **pulmonary arterial hypertension (PAH)** World Health Organization (WHO) Group 1 in adults to increase exercise

capacity, improve WHO functional class (FC), and reduce the risk of clinical worsening events, including hospitalization for PAH, lung transplantation, and death.[1]

Disease Overview
PAH is a serious but rare condition with an estimated prevalence of 10.6 cases per 1 million adults in the US.[2] It is classified within WHO Group 1 pulmonary hypertension among the five different groups that are recognized. In this progressive disorder, the small arteries in the lungs become narrow, restricted, or blocked. This causes the heart to work harder to pump blood, leading to activity impairment. Although the mean age of diagnosis is between 36 and 50 years, patients of any age may be affected. PAH is defined as a mean pulmonary artery pressure (mPAP) > 20 mmHg (at rest) with a pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg and a pulmonary vascular resistance > 2 Wood units measured by cardiac catheterization.[3,4] Despite the introduction of many PAH-specific therapies, mortality associated with PAH remains high. When stratified into intermediate and high-risk PAH, the 3-year mortality rate was reported as 18% to 20% for intermediate risk and 28% to 55% for high-risk PAH.[5]

Winrevair has been previously evaluated in STELLAR; eligible patients had WHO Functional Class II or Class III PAH.[7] However, Winrevair was more recently evaluated in ZENITH, which enrolled patients with WHO Functional Class III or Class IV PAH.[8] This new data supports its use in this functional class.

Guidelines
Various guidelines for PAH are available; Winrevair is addressed in an expert consensus document from the World Symposium on Pulmonary Hypertension (WSPH).

- In 2024, the WSPH provided an updated treatment algorithm based on individual risk assessment.[7] Generally, combination therapy with a phosphodiesterase type 5 (PDE5i) and endothelin receptor antagonist (ERA) are recommended as initial therapy in patients considered low risk. Patients with severe PAH and classified as high-risk at the time of diagnosis should receive a parenteral prostacyclin in combination with an ERA and a PDE5i. Winrevair may be considered as add-on therapy in patients who are at intermediate-low risk, intermediate-high risk, and high-risk for decompensation.
- In 2022, the European Society of Cardiology and the European Respiratory Society (ESC/ERS) updated guidelines on the diagnosis and management of PAH in adults.[3] The treatment algorithm for PAH has been simplified, with a clear focus on individual risk assessment, cardiopulmonary comorbidities, and treatment goals. Generally, combination therapy with a PDE5i and ERA are recommended as initial therapy in patients considered low-risk. If low-risk status is not achieved within 3 to 6 months, the addition of a prostacyclin analogue is recommended. Combination therapy including an intravenous (IV) prostacyclin analogue is recommended as initial therapy in patients considered high-risk.
- The CHEST guidelines (2019) use the patient's functional class (FC) to determine disease severity instead of the comprehensive risk assessment.[6] The guidelines recommend initiating combination oral therapy with an ERA and a PDE5i for patients with mild or moderate disease (FC II or III) or IV prostacyclin therapy for patients with severe disease (FC III with rapid disease progression or FC IV). Patients who remain symptomatic despite initial treatment should be treated with a second or third agent.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Winrevair. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with these products as well as the monitoring required for adverse events and

long-term efficacy, approval requires these agents to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for initiation of therapy as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and catheterization laboratory reports. For a patient case in which the documentation requirement of the right heart catheterization upon Prior Authorization coverage review for a different medication indicated for WHO Group 1 PAH has been previously provided, the documentation requirement in this *Pulmonary Arterial Hypertension – Winrevair* policy is considered to be met.

Winrevair is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) Group 1.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv and v):
     - **i.** Patients is ≥ 18 years of age; AND
     - **ii.** Patient meets the following (a and b):
       - **a)** The patient has had a right heart catheterization **[documentation required]** (see documentation section above)**;** AND
       - **b)** The results of the right heart catheterization confirmed the diagnosis of WHO Group 1 PAH; AND
     - **iii.** Patient meets ONE of the following (a or b):
       - **a)** According to the prescriber, patient is intermediate-high risk or high risk; OR
       - **b)** According to the prescriber, patient is low-risk or intermediate-low risk and has tried or is currently receiving one or more agents for PAH from the following different categories (either alone or in combination with another therapy) for ≥ 60 days ([1], [2], [3], or [4]):
         - **(1)** Phosphodiesterase type 5 (PDE5) inhibitors; OR
         - **(2)** Endothelin receptor antagonists (ERAs); OR
         - **(3)** Adempas (riociguat tablets); OR
         - **(4)** Prostacyclin analogs/mimetics; AND

           Note: Examples of phosphodiesterase type 5 (PDE5) inhibitors include sildenafil and tadalafil. Endothelin receptor antagonists (ERAs) include bosentan, ambrisentan, Opsumit (macitentan tablets). Prostacyclin analogs/mimetics include Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil oral inhalation powder), treprostinil injection, epoprostenol injection, Uptravi (selexipag tablets) and Yutrepia (treprostinil inhalation powder).
     - **iv.** The medication is prescribed by or in consultation with a cardiologist or a pulmonologist.
   - **B)** Patient is Currently Receiving Winrevair. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has had a right heart catheterization; AND

         Note: This refers to prior to starting therapy with a medication for WHO Group 1 PAH.
       - **b)** Results of the right heart catheterization confirmed the diagnosis of WHO Group 1 PAH; AND

ii. The medication is prescribed by or in consultation with a cardiologist or a pulmonologist.

Conditions Not Covered

Winrevair for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Winrevair® subcutaneous injection [prescribing information]. Rahway, NJ: Merck; October 2025.
2. Ruopp NF, Cockrill BA. Diagnosis and treatment of pulmonary arterial hypertension. A review. *JAMA*. 2022;327(14):1379-1391.
3. Humbert M, Kovacs G, Hoeper MM, et al, for the 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.
4. Maron B. Revised definition of pulmonary hypertension and approach to management: a clinical primer. *J Am Heart Assoc*. 2023 April 7. [epub ahead of print].
5. 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 May 3;11(9):e024969. doi: 10.1161/JAHA.121.024969.
6. 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.
7. Chin KM, Gaine SP, Gerges C, et al. Treatment algorithm for pulmonary arterial hypertension. *Eur Respir J.* 2024 Oct 31;64(4):2401325. doi: 10.1183/13993003.01325-2024.
8. 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.
9. Humbert M, McLaughlin VV, Badesch DB, et al. Sotatercept in patients with pulmonary arterial hypertension at high risk for death. *N Engl J Med.* 2025 March 31. [Online ahead of print].

Revision Details

Summary of Changes	Review Date	Effective Date
New policy	7/3/2024	08/15/2024
Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1: To the requirement of Functional Class PAH, Class IV was added; previously, only Functional Class II and III were listed. Additionally, documentation required was added to the policy to align with ESI policy.	6/18/2025	8/1/2025
Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1: Initial Therapy Clarified documentation requirements. **Added** Yutrepia as an example of an inhaled prostacyclin.	10/2/2025	11/15/2025
Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) Group 1: The requirement that the	4/16/2026	6/15/2026

patient is in Functional Class II, III, or IV was removed. A requirement that, according to the prescriber, the patient is intermediate or high-risk or is low-risk or intermediate-low risk was added. For a patient with low-risk or intermediate-low risk, a requirement and associated Note was added for documentation that the patient has tried or is currently receiving one or more agents from the following different categories (either alone or in combination with another therapy) for ≥ 60 days: PDE5 inhibitors, ERAs, Adempas, or prostacyclin analogs/mimetics. The previous requirement for systemic therapy that applied to all patients was removed.		

The policy effective date is in force until updated or retired.

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