Oscar Clinical Guideline: Winrevair (sotatercept-csrk) (PG207, Ver. 2)

Winrevair (sotatercept-csrk)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Pulmonary arterial hypertension (PAH) is a rare, progressive disorder characterized by abnormally high blood pressure in the pulmonary arteries due to pathologic remodeling and narrowing of the small pulmonary arteries. This increased pulmonary vascular resistance strains the right side of the heart, eventually leading to right ventricular failure and premature death. PAH is classified as World Health Organization (WHO) Group 1 within the broader pulmonary hypertension categorization.

Current treatments for PAH target the prostacyclin, endothelin, and nitric oxide pathways to promote vasodilation and slow disease progression. These include endothelin receptor antagonists, phosphodiesterase-5 inhibitors, soluble guanylate cyclase stimulators, and prostacyclin pathway agents. However, despite combination therapy with these medications, PAH still carries high morbidity and mortality. Median survival is only 5-7 years after diagnosis, highlighting the need for novel treatment options.

Winrevair (sotatercept-csrk) is a first-in-class fusion protein that acts as a ligand trap to bind and inhibit activins and growth differentiation factors involved in the pathogenesis of PAH. By modulating signaling in the TGF-**β**/BMP pathway, Winrevair (sotatercept-csrk) has the potential to rebalance vascular homeostasis and inhibit or reverse pulmonary vascular remodeling. In the pivotal phase 3 STELLAR trial, Winrevair (sotatercept-csrk) significantly improved exercise capacity, hemodynamics, and clinical outcomes when added to standard combination therapy in patients with PAH. Winrevair (sotatercept-csrk) is indicated to improve exercise capacity, WHO functional class, and reduce the risk of clinical worsening events in adults with PAH.

Definitions

"**Pulmonary arterial hypertension (PAH)**" refers to a rare, progressive disorder characterized by abnormally high blood pressure in the pulmonary arteries that supply blood to the lungs. It is caused by pathologic narrowing and obstruction of the small pulmonary arteries. PAH is classified as WHO Group 1 pulmonary hypertension.

"**WHO functional class (FC)**" is a system to categorize the severity of functional impairment in patients with PAH based on symptom burden and activity limitation. WHO FC ranges from I to IV, with higher classes reflecting more severe symptoms and limitations.

"**6-minute walk distance (6MWD)**" is an objective measure of submaximal exercise capacity. It quantifies the distance an individual is able to walk on a flat, hard surface over a period of 6 minutes.

"**Right heart catheterization (RHC)**" refers to the gold standard diagnostic test used to definitively diagnose PAH and differentiate it from other types of pulmonary hypertension. RHC directly measures pressures in the right side of the heart and pulmonary arteries. PAH is defined hemodynamically by a mean pulmonary artery pressure (mPAP) ≥ 25 mmHg, pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg, and pulmonary vascular resistance (PVR) > 3 Wood units.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Winrevair (sotatercept-csrk)** medically necessary when **ALL** of the following criteria are met:

1. Prescribed by or in consultation with a cardiologist or pulmonologist with expertise in treating PAH; ***AND***
2. The member is 18 years of age or older; ***AND***

3. The member has a confirmed diagnosis of WHO Group 1 pulmonary arterial hypertension (PAH) that is classified as **ANY** of the following:
    a. Idiopathic; ***or***
    b. Heritable; ***or***
    c. Drug- or toxin-induced; ***or***
    d. Associated with connective tissue disease; ***or***
    e. Associated with corrected congenital systemic-to-pulmonary shunts (≥1 year after repair); ***AND***
4. The member's diagnosis has been confirmed by right catheterization showing **ALL** of the following:
    a. Mean pulmonary artery pressure (mPAP) > 20 mmHg at rest; ***and***
    b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg; ***and***
    c. Pulmonary vascular resistance (PVR) > 2 Wood units; ***AND***
5. The member has a World Health Organization (WHO) functional classification of either:
    a. Class II [Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.]; ***or***
    b. Class III [Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.]; ***AND***
6. The member is currently receiving a stable dose of at least two PAH-specific medications from **TWO** of the following drug classes for at least 90 days:
    a. Endothelin receptor antagonist (ERA) [e.g. bosentan, ambrisentan, macitentan]; ***and/or***
    b. Phosphodiesterase-5 inhibitor (PDE5i) [e.g. sildenafil, tadalafil]; ***and/or***
    c. Soluble guanylate cyclase (sGC) stimulator [e.g. riociguat]; ***AND***
7. The member does **NOT** have ANY of the following:
    a. HIV-associated PAH; ***or***
    b. Portopulmonary hypertension; ***or***
    c. Schistosomiasis-associated PAH; ***or***
    d. Pulmonary veno-occlusive disease; ***or***
    e. WHO Group 2, 3, 4 or 5 pulmonary hypertension; ***or***
        i. *Group 2: PH due to left heart disease.*
        ii. *Group 3: PH due to lung diseases and/or hypoxia.*
        iii. *Group 4: PH due to pulmonary artery obstructions.*
        iv. *Group 5: PH with unclear and/or multifactorial mechanisms.*
    f. Platelet count < 50,000/mm3 (50×10^9/L); ***AND***

8. Winrevair (sotatercept-csrk) is being prescribed at a dose and frequency that is within FDA approved labeling **OR** is supported by compendia or evidence-based published dosing guidelines for the requested indication.
    - *Starting dose: 0.3 mg/kg subcutaneously every 3 weeks*
    - *Target maintenance dose: 0.7 mg/kg subcutaneously every 3 weeks*

If the above prior authorization criteria are met, the requested product will be authorized for 6-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12-months will be granted if the member has recent (within the last 3 months) clinical chart documentation demonstrating **ALL** of the following criteria:

1. Continues to meet the Initial Authorization criteria; ***AND***
2. Documentation of positive clinical response as demonstrated by at least **ONE** of the following:
    a. Improvement or maintenance in 6-minute walk distance; ***or***
    b. Improvement in WHO functional class; ***or***
    c. Reduction in hospitalizations for PAH; ***or***
    d. Improvement in hemodynamic parameters; ***AND***
3. There is no recorded evidence of unacceptable toxicity or adverse reactions from the drug (e.g. severe thrombocytopenia, serious bleeding).

Experimental or Investigational / Not Medically Necessary

Winrevair (sotatercept-csrk) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Pulmonary hypertension (PH) classified in WHO Groups 2-5, including:
    - PH due to left heart disease (Group 2).
    - PH due to lung diseases and/or hypoxia (Group 3).
    - Chronic thromboembolic PH (CTEPH) (Group 4).
    - PH with unclear or multifactorial etiologies (Group 5).
- Specific PAH etiologies/subgroups that were excluded from or not evaluated in the pivotal clinical trials, including:
    - PAH associated with portal hypertension.

    - HIV-associated PAH.
    - Schistosomiasis-associated PAH.
    - Pulmonary veno-occlusive disease (PVOD).
- Treatment of pediatric PAH (patients <18 years old).
- Patients with WHO functional class I or IV symptoms.

Rationale: Winrevair (sotatercept-csrk) has not been adequately studied for safety and efficacy in the above patient populations and clinical scenarios. Its FDA approval and pivotal trial data are limited to use in adults with WHO Group 1 PAH classified as idiopathic, heritable, drug-induced, or associated with connective tissue diseases or congenital heart disease. Patients had WHO FC II or III symptoms despite combination therapy with two or more PAH-specific drug classes.

- There is a lack of robust clinical trial data supporting the use of Winrevair (sotatercept-csrk) for non-Group 1 PH etiologies or the specific PAH subgroups listed above that were excluded from the STELLAR trial. Pediatric PAH patients were not included in the clinical development program. Winrevair (sotatercept-csrk) has not been evaluated in FC I or IV patients.
- The above Plan position is based on the best currently available clinical evidence for Winrevair (sotatercept-csrk) in PAH. As additional trials are published, the Plan will modify these policy statements accordingly to reflect any relevant changes in the evidence base and/or guideline recommendations. Until such time, Winrevair (sotatercept-csrk) use outside of its FDA-approved indication and pivotal trial population is considered experimental, investigational and unproven.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*

I27.0	Primary Pulmonary Hypertension

Appendix

Table 1: Clinical Classification of Pulmonary Hypertension

Group 1: PAH 1.1 Idiopathic 1.1.1 Long-term responders to calcium channel blockers 1.2 Heritable# 1.3 Associated with drugs and toxins# 1.4 Associated with: 1.4.1 connective tissue disease 1.4.2 HIV infection 1.4.3 portal hypertension 1.4.4 congenital heart disease 1.4.5 schistosomiasis 1.5 PAH with features of venous/capillary (PVOD/PCH) involvement 1.6 Persistent PH of the newborn
Group 2: PH associated with left heart disease 2.1 Heart failure: 2.1.1 with preserved ejection fraction 2.1.2 with reduced or mildly reduced ejection fraction 2.1.3 cardiomyopathies with specific aetiologies¶ 2.2 Valvular heart disease: 2.2.1 aortic valve disease 2.2.2 mitral valve disease 2.2.3 mixed valvular disease 2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH
Group 3: PH associated with lung diseases and/or hypoxia 3.1 COPD and/or emphysema 3.2 Interstitial lung disease 3.3 Combined pulmonary fibrosis and emphysema 3.4 Other parenchymal lung diseases+ 3.5 Nonparenchymal restrictive diseases: 3.5.1 hypoventilation syndromes 3.5.2 pneumonectomy 3.6 Hypoxia without lung disease (e.g. high altitude) 3.7 Developmental lung diseases
Group 4: PH associated with pulmonary artery obstructions 4.1 Chronic thromboembolic PH 4.2 Other pulmonary artery obstructions§

Group 5: PH with unclear and/or multifactorial mechanisms 5.1 Haematological disorders*ƒ* 5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis and neurofibromatosis type 1 5.3 Metabolic disorders## 5.4 Chronic renal failure with or without haemodialysis 5.5 Pulmonary tumour thrombotic microangiopathy 5.6 Fibrosing mediastinitis 5.7 Complex congenital heart disease

PAH: pulmonary arterial hypertension; PVOD: pulmonary veno-occlusive disease; PCH: pulmonary capillary haemangiomatosis. #: patients with heritable PAH or PAH associated with drugs and toxins might be long-term responders to calcium channel blockers; ¶: hypertrophic, amyloid, Fabry disease and Chagas disease; +: parenchymal lung diseases not included in group 5; §: other causes of pulmonary artery obstructions include sarcomas (high- or intermediate-grade or angiosarcoma), other malignant tumours (e.g. renal carcinoma, uterine carcinoma, germ-cell tumours of the testis), nonmalignant tumours (e.g. uterine leiomyoma), arteritis without connective tissue disease, congenital pulmonary arterial stenoses and hydatidosis; ƒ: including inherited and acquired chronic haemolytic anaemia and chronic myeloproliferative disorders; ##: including glycogen storage diseases and Gaucher disease.

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