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 (see Appendix

A, table 1). PAH is further grouped into functional class (I-IV), where high value functional classes indicate worsening impairment on physical activity due to PAH.

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. Additional therapies include diuretics and calcium channel blockers. 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 (e.g., 6 minute walking distance, WHO functional class) when added to standard monotherapy or combination therapy in those 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

"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.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"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.

"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.

"[s]" indicates state mandates may apply.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Pulmonary Arterial Hypertension

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 World Health Organization (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 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 (2) of the following drug classes for at least 90 days[s]:
    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/or*
    d. Prostacyclin analogues or receptor agonists [e.g., treprostinil, illoprost, epoprostenol, selexipag]; *AND*
7. The member meets ALL of the following:
    a. No evidence of HIV-associated PAH; *or*
    b. No evidence of pulmonary hypertension; *or*
    c. No evidence of Schistosomiasis-associated PAH; *or*
    d. No evidence of Pulmonary veno-occlusive disease; *or*
    e. No evidence of 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. No evidence of 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*
    - *The recommended 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 up to 6-months.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Pulmonary Arterial Hypertension

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

1. The member continues to meet the applicable Initial Authorization criteria; *AND*
2. Chart Documentation of positive clinical response as demonstrated by at least ONE (1) of the following:
    a. Improvement or maintenance in 6-minute walk distance (6MWD); *or*
    b. Improvement in or maintenance of WHO functional class; *or*

c. Reduction in hospitalizations for PAH; *or*
d. Improvement in hemodynamic parameters (e.g., pulmonary vascular resistance [PVR], pulmonary artery wedge pressure); *AND*

3. There is no recorded evidence of unacceptable toxicity or adverse reactions from the drug (e.g. severe thrombocytopenia, serious bleeding).

If the above prior reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Experimental or Investigational / Not Medically Necessary[s]

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 (the below WHO Groupings were explicitly included from the pivotal trial and evidence to support the safety and efficacy of Winrevair [sotatercept-csrk] in these populations is lacking):
    - 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 (the below diagnosis were explicitly included from the pivotal trial and evidence to support the safety and efficacy of Winrevair [sotatercept-csrk] in these populations is lacking):
    - PAH associated with portal hypertension.
    - HIV-associated PAH.
    - Schistosomiasis-associated PAH.
    - Pulmonary veno-occlusive disease (PVOD).
- Treatment of pediatric PAH (those less than 18 years of age). Winrevair (sotatercept-csrk) has not been studied in a pediatric population.
- Patients with WHO functional class (FC) I or IV symptoms. Those with WHO FC I (one) or IV (four) were not included in the pivotal trial and evidence to support the safety and efficacy of Winrevair (sotatercept-csrk) in those populations is lacking.
- 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

Table 1	
CPT/HCPCS codes for pulmonary arterial hypertension 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

Table 2	
ICD-10 diagnosis codes considered medically necessary for pulmonary arterial hypertension with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
I27.0	Primary Pulmonary Hypertension

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Appendix A

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

COPD: chronic obstructive pulmonary disease; PAH: pulmonary arterial hypertension; PH: pulmonary 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.

Clinical Guideline Revision / History Information

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