Winrevair™
(sotatercept-csrk)

Date of Origin: 08/01/2024 **Effective Date: 08/01/2024**
Last Review Date: 08/01/2024
Dates Reviewed: 08/01/2024

Developed By: Medical Criteria Committee

I. Length of Authorization

- Initial: Six Months
- Renewal: 12 months

II. Dosing Limits

A. Max Units (per dose and over time) [Medical Benefit]:

- 120 mg every 3 weeks*

*Injection volume should be rounded to the nearest 0.1mL

III. Initial Evaluation

I. **Sotatercept-csrk (Winrevair)** may be considered medically necessary when the following criteria are met:

A. Member is 18 years of age or older; **OR**
B. Medication is prescribed by, or in consultation with, cardiologist or pulmonologist; **AND**
C. A diagnosis of one of the following:
1. **Pulmonary arterial hypertension (PAH) (WHO Group 1)**; **AND**
a. An acute vasoreactivity test has been performed; **AND**
i. Results were negative; **OR**
ii. Results were positive; **AND**
1. Treatment with a calcium channel blocker (CCB) (e.g. amlodipine, diltiazem, felodipine, nifedipine, nicardipine, or verapamil) has been ineffective after three months of therapy, unless contraindicated, or not tolerated; **AND**
b. The request is for sotatercept (Winrevair); **AND**
i. Member has WHO functional class II or III symptoms; **AND**
ii. Provider attestation that the member has, or will receive, training from a healthcare professional on how to reconstitute, prepare, measure, and inject sotatercept (Winrevair); **AND**
iii. Treatment with one agent in each of the following groups has been ineffective, contraindicated, or not tolerated:

1. Endothelin receptor antagonist [e.g., bosentan (Tracleer), ambrisentan (Letairis), or macitentan (Opsumit)]
2. Phosphodiesterase type 5 (PDE5 inhibitor) [e.g., sildenafil, tadalafil] or riociguat (Adempas)
3. Prostacyclin agonist [e.g., treprostinil (Remodulin, Tyvaso, Orenitram), selexipeg (Uptravi)]; **AND**

iv. Provider attestation that the member will be continuing background therapy with at least two other PAH medications, unless contraindicated or not tolerated; **OR**

II. Sotatercept (Winrevair) is considered investigational when used for all other conditions including but not limited to:
   A. Pulmonary hypertension (PH) WHO Groups II-V
      - Group II - Left heart disease, including congestive heart failure (CHF)
      - Group III - Lung diseases, including chronic obstructive pulmonary disease (COPD), bronchiectasis, and idiopathic pulmonary fibrosis (IPF); Other lung disease with mixed obstruction and restriction (e.g., pulmonary fibrosis with emphysema; Hypoxia without lung disease (e.g., high altitude, sleep-disordered breathing, obesity hypoventilation)
      - Group IV - Chronic thrombotic and/or embolic disease
      - Group V – Sarcoidosis
   B. Chronic thromboembolic pulmonary hypertension (CTEPH)
   C. Newly diagnosed PH (i.e., treatment naïve)
   D. Myeloproliferative disorders/Myelofibrosis
   E. Anemia

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**

II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. Member has exhibited improvement or stability of disease symptoms (e.g. improved exercise capacity and tolerance, reduced number of hospitalizations, improvement in WHO functional class)

Supporting Evidence

I. Patients with PH are classified into five clinical groups based on cause of PH.
   a. Group 1: pulmonary **arterial** hypertension (PAH) which has several causes (e.g., inheritable causes, drugs, connective tissue disease)
   b. Group 2: PH due to left-sided heart disease
   c. Group 3: PH due to chronic lung disorders and hypoxemia
   d. Group 4: PH due to pulmonary artery obstructions
   e. Group 5: PH due to unidentified mechanisms

II. Pulmonary Hypertension (PH0 is a progressive and life-threatening disease. The medications as well as the disease state should be managed by a specialist.

III. The American College of Chest Physicians (CHEST) guideline for Therapy for PAH in adults suggests that patients with PAH, in the absence of contraindications, should undergo acute vasoreactivity testing using a short-acting agent at a medical center with experience in the performance and interpretation of vasoreactivity testing. Contraindications to acute vasoreactivity testing include low systemic BP, low CO, or the presence of FC IV symptoms. Patients who demonstrate acute vasoreactivity – in the absence of right-sided heart failure or contraindications to CCB therapy – according to consensus definition, should be considered candidates for a trial of therapy with an oral CCB. CCBs are considered primary therapy.

IV. Lacking head-to-head comparisons of pharmacologic agents for the treatment of PAH, there is insufficient evidence to determine if one agent is superior to another.

V. The safety and efficacy of sotatercept (Winrevair) was studied in the Phase 3, randomized, double-blind, placebo-controlled STELLAR trial in 323 adult patients with WHO group 1 PAH with functional class (FC) II or III symptoms over a period of 24 weeks. Patients continued their stable background therapy consisting of monotherapy, dual therapy, or triple therapy with medications that were available at the time of study enrollment, depending on the patient's disease severity. Approximately 60% of patients were receiving triple therapy with an PDE-5 inhibitor, ERA, and prostacyclin agonist, with nearly 40% receiving prostacyclin infusion therapy at inclusion. The primary efficacy outcome was the change in the 6-minute walk distance (6MWD) from baseline to week 24. Key secondary endpoints consisted of a multicomponent improvement at week 24 compared to baseline, and change from baseline in pulmonary vascular resistance, NT-proBNP level, and improvement in WHO functional class at week 24. All primary and key secondary endpoints met the threshold for statistical significance compared to placebo.

VI. While this was a well-designed randomized, double-blind, placebo-controlled trial with sotatercept (Winrevair) demonstrating statistical significance in the key primary and secondary endpoints, the trial utilized a surrogate endpoint as the primary endpoint and an unvalidated key secondary endpoint (MCI) that have not been shown to correlate with impact on morbidity/mortality. However, the positive impact on WHO-FC and 6MWD may be considered clinically meaningful for patients' functionality and quality of life. Based on this information, the overall quality of evidence is considered moderate. Additionally, the trial duration was limited to 24 weeks, the durability of response in this chronic disease state remains unknown and will be realized in real-world settings.

VII. The SOTERIA trial is an ongoing, long-term (7-year) open label follow-up study of patients who completed the initial phase 2 PULSAR or Phase 3 STELLAR clinical trial; all patients were continued or were initiated on sotatercept (Winrevair), if they were originally in the placebo arm. The interim one-year follow-up data suggests that there may be maintenance benefit in the 6MWD, NT-proBNP, and WHO-FC compared with study baseline, although there was a large variance around the mean for the 6MWD and NT-proBNP outcomes. Final readout of this data is anticipated around September 2027.

VIII. Most of the adverse events reported during the clinical trial were mild to moderate in severity, and fewer patients in the sotatercept (Winrevair) group (8.0%) experienced severe adverse events (AEs) compared to placebo (13.1%). The most common AEs reported during the clinical trial period for sotatercept (Winrevair) versus placebo, respectively, included thrombocytopenia (6.1% vs. 2.5%), bleeding events (21.5% vs. 12.5%), headache (20.2% vs. 15%), nausea (9.8% vs. 11.2%), telangiectasia

(10.4% vs. 3.1%), and dizziness (10.4% vs. 1.9%). A total of nine patients died through the data cut-off date: two patients (1.2%) in the sotatercept group due to acute myocardial infarction and intracranial hemorrhage, and seven patients (4.4%) in the placebo group due to cardiac arrest, cardiogenic shock, right ventricular failure, sepsis, PAH, and COVID.

IX. The American College of Cardiology (ACCF)/American Heart Association (AHA) guidelines indicate oral ERA or PDE-5 inhibitor therapy as first line treatment for lower risk PAH patients. There is insufficient safety and efficacy evidence to establish that any one oral therapy for PAH is clearly superior to another. Treatment guidelines support combination therapy of PDE, ERA, and prostanoid agents.

X. For patients with WHO functional class II or III 2019 American College of Chest Physicians (CHEST) guidelines recommend the combination of ambrisentan and tadalafil as first line therapy. This is based on data from the AMBITION trial. The trial involved 605 patients with WHO functional class II or III PAH. Patients were randomly assigned to receive once daily ambrisentan plus tadalafil or to either drug alone. Doses were titrated from 5-10 mg/day for ambrisentan and from 20-40 mg/day for tadalafil. Treatment with the combination was associated with an approximately 50% reduction in risk for clinical failure compared with either drug alone (*P* = .0002), with improved exercise ability as well as decreased disease progression and hospitalization.

XI. The 2019 CHEST guidelines recommend treatment naive PAH patients with WHO functional class II and III use combination therapy with ambrisentan and tadalafil to improve 6MWD. For patients who are unwilling or unable to tolerate combination therapy monotherapy with a currently approved ERA, PDE-5 inhibitor, or the soluble guanylate cyclase stimulator riociguat is advised. Guidelines suggest that parenteral or inhaled prostanoids may be chosen as initial therapy, in combination with tadalafil and ambrisentan, for treatment naive PAH patients with WHO FC III symptoms who present with a more severe phenotype, or as second line agents for PAH patients with WHO FC II symptoms who have not met their treatment goals on established dual therapy.

Billing Code/Availability Information

Jcode:

- J3490/J3590 – injection, sotatercept-csrk (Winrevair)

NDC:

- 45 mg vial – 1 mL syringe kit NDC: 0006-5090-01
- 60 mg vial – 1 1.3 mL syringe kit NDC: 0006-5091-01
- 45 mg vials (2) – 2 1 mL syringe kit NDC: 0006-5087-01
- 60 mg vials (2) – 2 1.3 mL syringe kite NDC: 0006-5088-01

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Appendix 1

I. Table 1: PAH Determinants of Prognosis (ACCF/AHA Guidelines)

Determinants of Risk	Lower Risk (Good Prognosis)	Higher Risk (Poor Prognosis)
Clinical evidence of RV failure	No	Yes
Progression of symptoms	Gradual	Rapid
WHO class†	II, III	IV
6MW distance‡	Longer (greater than 400 m)	Shorter (less than 300 m)
CPET	Peak VO2 greater than 10.4 mL/kg/min	Peak VO2 less than 10.4 mL/kg/min
Echocardiography	Minimal RV dysfunction	Pericardial effusion, significant RV enlargement/dysfunction, right atrial enlargement
Hemodynamics	RAP less than 10 mm Hg, CI greater than 2.5 L/min/m2	RAP greater than 20 mm Hg, CI less than 2.0 L/min/m2
BNP§	Minimally elevated	Significantly elevated
*Most data available pertains to IPAH. Little data is available for other forms of PAH. One should not rely on any single factor to make risk predictions.		
†WHO class is the functional classification for PAH and is a modification of the New York Heart Association functional class.		
‡6MW distance is also influenced by age, gender, and height.		
§As there is currently limited data regarding the influence of BNP on prognosis, and many factors including renal function, weight, age, and gender may influence BNP, absolute numbers are not given for this variable.		
6MW indicates 6-minute walk; BNP, brain natriuretic peptide. CI, cardiac index; CPET, cardiopulmonary exercise testing; peak VO2, average peak oxygen uptake during exercise; RAP, right atrial pressure; RV, right ventricle; and WHO, World Health Organization.		

Appendix 2 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
I27.20	Pulmonary arterial hypertension (PAH)

Appendix 3 – Dosage/Administration

Medication:	ICD-10 Description
Winrevair	• Starting dose: 0.3 mg/kg administered subcutaneously every 3 weeks. • After verifying acceptable Hgb and platelet count, increase to the target dose of 0.7 mg/kg. Continue treatment at 0.7 mg/kg every 3 weeks unless dosage adjustments are required due to hemoglobin increase or platelet count decrease (Refer to the prescribing information for specific dose modification criteria). **Note: Patients and caregivers may administer Winrevair when considered appropriate and when they receive training and follow-up from the healthcare provider.

Appendix 4 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA,HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corporation (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corporation (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Cahaba Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC