Clinical Policy: Sotatercept (Winrevair)

Reference Number: CP.PHAR.657
Effective Date: 03.26.24
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Sotatercept-csrk (Winrevair™) is an activin signaling inhibitor.

FDA Approved Indication(s)

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

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Winrevair is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pulmonary Arterial Hypertension (must meet all)**:**

1. Diagnosis of PAH;
2. Prescribed by or in consultation with a cardiologist or pulmonologist;
3. Age ≥ 18 years;
4. Failure of a calcium channel blocker (*see Appendix B*), unless member meets one of the following (a or b):
   a. Inadequate response or contraindication to acute vasodilator testing;
   b. Contraindication or clinically significant adverse effects to calcium channel blockers are experienced;
5. Member meets one of the following (a or b):
   a. Winrevair is prescribed concurrently with TWO or more of the following drug classes, unless clinically significant adverse effects are experienced for all or all are contraindicated (i, ii, and/or iii, see *Appendix F*)*:
      i. Endothelin-receptor antagonist (e.g., ambrisentan, bosentan, Opsumit®);
      ii. Phosphodiesterase-5 (PDE-5) inhibitor (e.g., sildenafil, tadalafil) or soluble guanylate cyclase stimulator (e.g., Adempas®);
      iii. Prostacyclin analogue or receptor agonist (e.g., epoprostenol, Ventavis®, Uptravi®, treprostinil);
   b. Winrevair is prescribed concurrently with at least one other PAH therapy (see *Appendix F*)* AND is intolerant to combination therapy with two or more PAH drug classes (see *Appendix F*);

**Prior authorization may be required*

6. Documentation of platelet count ≥ 50 x 10^9/L;
7. Member meets both of the following (a and b):
   a. Dose does not exceed 0.7 mg/kg per 3 weeks;
   b. Quantity does not exceed one kit (1-vial kit or 2-vial kit) per 3 weeks.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Pulmonary Arterial Hypertension (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. Member meets one of the following (a or b):
   a. Winrevair is prescribed concurrently with TWO or more of the following drug classes, unless clinically significant adverse effects are experienced for all or all are contraindicated (i, ii, and/or iii, *see Appendix F*)*:
      i. Endothelin-receptor antagonist (e.g., ambrisentan, bosentan, Opsumit);
      ii. PDE-5 inhibitor (e.g., sildenafil, tadalafil) or soluble guanylate cyclase stimulator (e.g., Adempas);
      iii. Prostacyclin analogue or receptor agonist (e.g., epoprostenol, Ventavis, Uptravi, treprostinil);
   b. Winrevair is prescribed concurrently with at least one other PAH therapy (see *Appendix F*)* AND is intolerant to combination therapy with two or more PAH drug classes (see *Appendix F*);

**Prior authorization may be required*

4. If request is for a dose increase, both of the following (a and b):
   a. New dose does not exceed 0.7 mg/kg per 3 weeks;
   b. New quantity does not exceed one kit (1-vial kit or 2-vial kit) per 3 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ETRA: endothelin receptor antagonist
FC: functional class
FDA: Food and Drug Administration
PA: physical activity
PAH: pulmonary arterial hypertension
PDE-5: phosphodieseterase-5
PH: pulmonary hypertension
WHO: World Health Organization

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Calcium Channel Blockers		
nifedipine (Adalat® CC, Procardia XL®)†	30 mg PO QD; may increase to 60 to 120 mg BID	240 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
diltiazem (Dilt-XR®, Cardizem® CD, Cartia XT®, Tiazac®, Cardizem® LA, Matzim® LA) †	60 mg PO BID; may increase to 120 to 360 mg BID	720 mg/day
amlodipine (Norvasc®)†	5 mg PO QD; may increase to 15 to 30 mg/day	30 mg/day
PDE-5 Inhibitors		
sildenafil (Revatio®, Liqrev®)	Tablet and oral suspension: 20 mg to 80 mg PO TID Injection: 10 mg TID as an IV bolus	Tablet and oral suspension: 240 mg/day Injection: 30 mg/day
tadalafil (Adcirca®, Alyq®, Tadliq®)	40 mg PO QD	40 mg/day
Soluble guanylate cyclase stimulator		
Adempas® (riogicuat)	1 to 2.5 mg PO TID	7.5 mg
Endothelin receptor antagonists		
ambrisentan (Letaris®)	5 mg PO QD	10 mg/day
bosentan (Tracleer®)	62.5 to 125 mg PO BID	250 mg/day
Opsumit® (macitentan)	10 mg PO QD	10 mg/day
Prostacyclin analogues or prostacyclin receptor agonists		
epoprostenol (Flolan®, Veletri®)	2 ng/kg/min IV, increased based on clinical response	Based on clinical response
Treprostinil (Orenitram®, Remodulin®, Tyvaso®, Tyvaso DPI®)	Varies	Varies
Ventavis® (iloprost)	2.5 to 5 mcg INH 6 to 9 doses per day	45 mcg/day
Uptravi® (selexipag)	Tablet: 200 to 1,600 mcg PO BID Injection: IV BID at a dose that corresponds to the patient's current dose of Uptravi tablets	Tablets: 3,200 mcg/day Injection: 3,600 mcg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
†Off-label

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: Pulmonary Hypertension: WHO Classification
- Group 1: PAH (pulmonary arterial hypertension)
- Group 2: PH due to left heart disease

- Group 3: PH due to lung disease and/or hypoxemia
- Group 4: CTEPH (chronic thromboembolic pulmonary hypertension)
- Group 5: PH due to unclear multifactorial mechanisms

Appendix E: Pulmonary Hypertension: WHO/NYHA Functional Classes (FC)

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
Monitoring for progression of PH and treatment of co-existing conditions	I	Comfortable at rest	No limitation	Ordinary PA does not cause undue dyspnea or fatigue, chest pain, or near syncope.	
Advanced treatment of PH with PH-targeted therapy - *see Appendix F***	II	Comfortable at rest	Slight limitation	Ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	
	III	Comfortable at rest	Marked limitation	Less than ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	
	IV	Dyspnea or fatigue may be present at rest	Inability to carry out any PA without symptoms	Discomfort is increased by any PA.	Signs of right heart failure

*PH supportive measures may include diuretics, oxygen therapy, anticoagulation, digoxin, exercise, pneumococcal vaccination. **Advanced treatment options also include calcium channel blockers.

Appendix F: Pulmonary Hypertension: Targeted Therapies

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
Reduction of pulmonary arterial pressure through vasodilation	Prostacyclin* pathway agonist **Member of the prostanoid class of fatty acid derivatives.*	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		Synthetic prostacyclin analog	Treprostinil	Orenitram (oral tablet) Remodulin (IV) Tyvaso (inhalation)
			Iloprost	Ventavis (inhalation)
		Non-prostanoid prostacyclin	Selexipag	Uptravi (oral tablet)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
		receptor (IP receptor) agonist		
	Endothelin receptor antagonist (ETRA)	Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)
		Nonselective dual action receptor antagonist	Bosentan	Tracleer (oral tablet)
			Macitentan	Opsumit (oral tablet)
	Nitric oxide-cyclic guanosine monophosphate enhancer	Phosphodiesterase type 5 (PDE5) inhibitor	Sildenafil	Revatio (IV, oral tablet, oral suspension)
			Tadalafil	Adcirca (oral tablet)
		Guanylate cyclase stimulant (sGC)	Riociguat	Adempas (oral tablet)

Appendix G: Dose Rounding Guidelines for Weight-Based Doses

Recommended Dosage	Weight-based Recommended Dose Range	Vial Quantity Recommendation
Initial: 0.3 mg/kg	7.5 to 47.49 mg	45 mg kit (containing 1 x 45 mg vial)
	47.5 to 57.49 mg	60 mg kit (containing 1 x 60 mg vial)
Target: 0.7 mg/kg	7.5 to 47.49 mg	45 mg kit (containing 1 x 45 mg vial)
	47.5 to 62.49 mg	60 mg kit (containing 1 x 60 mg vial)
	62.5 to 92.49 mg	90 mg kit (containing 2 x 45 mg vials)
	92.5 to 122.49 mg	120 mg kit (containing 2 x 60 mg vials)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PAH	Starting dose of 0.3 mg/kg with a target dose of 0.7 mg/kg administered subcutaneously every 3 weeks* **Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses*	0.7 mg/kg every 3 weeks

VI. Product Availability

Single-dose vials (in kits containing 1 vial or 2 vials): 45 mg, 60 mg

VII. References

1. Winrevair Prescribing Information. Rahway, NJ: Merck Sharp & Dohme LLC. March 2024. Available at: www.winrevair.com. Accessed November 20, 2024.
2. Hoeper MM, Badesch DB, Ghofrani HA, et al. Phase 3 Trial of Sotatercept for Treatment of Pulmonary Arterial Hypertension. *N Engl J Med.* 2023 Apr 20;388(16):1478-1490. doi: 10.1056/NEJMoa2213558.

3. Humbert M, McLaughlin V, Gibbs JSR, et al. Sotatercept for the Treatment of Pulmonary Arterial Hypertension. *N Engl J Med.* 2021 Apr 1;384(13):1204-1215. doi: 10.1056/NEJMoa2024277.
4. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association - developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009; 53(17): 1573-1619.
5. 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: https://doi.org/10.1016/j.chest.2018.11.030.
6. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol.* 2013; 62(25): Suppl D92-99.
7. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Kardiol Pol*. 2015;73(12):1127-206. doi: 10.5603/KP.2015.0242
8. Simmonneau G, Montani D, Celermajer D, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019; 53:1801913.
9. Sitbon O, Humber M, Jais X, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation.* 2005;111(23);3105;11.
10. Yaghi S, Novikov A, Trandafirescu T. Clinical update on pulmonary hypertension. *J Investig Med.* 2020; 0:1-7. doi:10.1136/jim-2020-001291.
11. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *European Heart Journal*, Volume 43, Issue 38, 7 October 2022, Pages 3618–3731, https://doi.org/10.1093/eurheartj/ehac237.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	10.24.23	02.24
Drug is now FDA approved – criteria updated per FDA labeling: added documentation of platelet count ≥ 50 x 10^9/L; added quantity limit of one kit per 21 days; added Appendix G for recommended vial quantity based on weight-based dose range; references reviewed and updated.	04.03.24	
1Q 2025 annual review: added bypass to use Winrevair with PAH monotherapy if intolerant to two or more PAH drug classes; in Appendix B per Clinical Pharmacology, removed commercially unavailable branded products, updated dosing regimens; clarified drugs used for off-label indications; references reviewed and updated.	11.20.24	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.