



Sotatercept for Pulmonary Arterial Hypertension: Final Policy Recommendations

January 8, 2024

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the December 1, 2023 Midwest CEPAC public meeting on the use of sotatercept for the treatment of Pulmonary Arterial Hypertension. At the meeting, ICER presented the findings of its revised report on these treatments and the Midwest CEPAC voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations, and long-term value for money at current prices. Following the votes, ICER convened a Policy Roundtable of two patient representatives, one clinical expert, and two payer representatives to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed [here](#), and a recording of the voting portion of the meeting can be accessed [here](#). More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the appendix of this document. ICER's report on these treatments, which includes the same policy recommendations, can be found [here](#).

The roundtable discussion was facilitated by Dr. Steven Pearson. The main themes and recommendations from the discussion are organized by audience and summarized below.

Health Equity

All Stakeholders

Recommendation 1

All stakeholders have a responsibility and an important role to play in ensuring that effective new treatment options for patients with pulmonary arterial hypertension (PAH) are introduced in a way that will help reduce health inequities.

PAH is a severe, devastating disease affecting at least 50,000 persons in the US.¹ Current therapies improve symptoms and functional status for patients, but are not disease modifying, may be burdensome to administer, and can have debilitating side effects. New treatments, particularly those that are well-tolerated and may be disease-modifying, remain a significant unmet need. The clinical expert at the public meeting estimated that up to 50% of PAH patients may be eligible for sotatercept treatment. Therefore, efforts are needed to ensure that new therapies for PAH such as

sotatercept are accessible in a way such that they improve the health of patients and families without aggravating existing health inequities.

Clinical and patient experts highlighted that because of the rarity of PAH, as well as the severity of disease and the complexity of treatment, persons with PAH should ideally receive care from PAH specialists. However, because of both the number and geographic distribution of PAH specialists in the US, many patients need to travel long distances to access a PAH specialist or a Center of Excellence. This may contribute to delays in diagnosis and result in a more severe disease state at diagnosis, which can impact outcomes. Additionally, the distance to obtain care can be a tremendous burden for patients not only due to travel time, but also because of their need for high amounts of oxygen supplementation, which require transporting large, heavy tanks (as their oxygen requirements are too high for portable concentrators, and liquid oxygen is often not readily available due to limited reimbursement that has led to an 80% decrease in the use of liquid oxygen in the last decade²). Additionally, clinical experts highlighted that while they are willing to coordinate care with local clinicians, they are often not adequately compensated for this time, which adds to the barriers to appropriate expert care.

High costs of new therapies may also worsen disparities in accessing treatment. Current treatments are already expensive - patient experts described high out-of-pocket costs, in part due to the rising prevalence of co-insurance, copay accumulator programs, and high deductible health plans. This leads to a reliance on grants and manufacturer assistance, both of which are limited resources. Additionally, there is a concern that because clinical practice guidelines are not frequently updated and payers often base coverage policies on guidelines, there may be a delay in insurer coverage of a new third- or fourth-line drug such as sotatercept because it has not yet been incorporated into guidelines.

To address these concerns:

Manufacturers should take the following actions:

- Set the price for new treatments like sotatercept in **fair alignment with independent analyses of the long-term benefit for** patients.
- Work with **payors, specialty pharmacies, and clinicians to rapidly transition sotatercept to home-based administration**. Since access to PAH specialty centers may be limited, home-based administration of sotatercept could help decrease disparities in access to treatment.
- Work with payors to ensure that the combination of benefit design and financial assistance programs results in sotatercept being affordable for all patients.

Payers should take the following actions:

- Ensure that **benefit designs** developed in conjunction with employers and other plan sponsors do not create requirements for out-of-pocket spending that create major barriers to appropriate access for patients.
- Given that many patients with PAH will need to travel to obtain appropriate diagnosis and treatment, payers should consider **wraparound coverage**, including transportation, to ensure equal access to treatment. Geographical and income constraints should not undermine the tenets of fair access to which all patients have a fundamental right.
- Payers should understand that the diagnosis and care of PAH patients involves highly specialized knowledge and the need to work with expert clinicians, often at Centers of Excellence. Thus, they should work with clinicians to **ensure good access to specialists**, either via Centers of Excellence, telemedicine, and/or a hub-and-spoke system of local clinicians consulting with specialists, given the limited resource of PAH experts. When necessary, payers – including state Medicaid programs – should help facilitate care across state lines, including ensuring that their networks include clinicians who are licensed in the appropriate states. Specialists should receive adequate compensation for consultation with local clinicians to ensure that patients with PAH who live far from specialty centers can obtain care locally that is guided by the appropriate specialists.
- Payers should help advocate for and implement **reform of supplemental oxygen reimbursement policies**. Some PAH patients have very high oxygen flow needs, and their needs are best met with liquid oxygen, which allows for more mobility and a better quality of life. However, liquid oxygen requires specialized transportation infrastructure, more frequent deliveries, and more expensive equipment for use. Because all forms of oxygen are currently reimbursed similarly, more expensive forms such as liquid oxygen are not easily accessible.

Clinicians and Clinical specialty societies should take the following actions:

- Clinical specialty societies should be aware that payers rely heavily on clinical practice guidelines to craft coverage policies. Thus, societies should consider **rapid, focused updates to clinical practice guidelines** when new, effective therapies that may substantially change treatment recommendations become available.
- Clinicians and clinical specialty societies should ensure that PAH clinicians and/or Centers of Excellence have adequate geographical distribution and that clinicians are licensed and accredited with insurance plans across state lines such that access to care is not impeded either by geography or by insurance coverage.

- Clinical specialty societies should continue to use their voice to help advocate for more patient-centered oxygen therapy, including ensuring that clinical practice guidelines recommendations recognize the necessity of assessing patients' mobility needs, advocating for the reimbursement of oxygen education and equipment assessment, and advocating for the reform of the reimbursement policy for supplemental oxygen, which currently does not account for the differential costs between types of supplemental oxygen.³

Patients and Patient Groups should take the following actions:

- Continue to advocate for **better oxygen access**, as exemplified by the Four Pillars of Oxygen Reform³ advocated by the Pulmonary Hypertension Association, among others. This includes ensuring access to liquid oxygen when medically necessary.

Policymakers should take the following actions:

- **Continue COVID pandemic-era expansion of telemedicine policies** to allow for inter-state consultations and reimbursement for telehealth. The diagnosis and care of patients with PAH requires specialized knowledge and optimal care should take place in specialized centers. However, because of a shortage of PAH specialists and centers, in order to facilitate timely diagnosis and treatment of PAH, COVID-era policies relaxing rules for telemedicine and inter-state consultations should be continued.
- Medicare policymakers should **set differential reimbursement rates such that more expensive forms of oxygen (e.g., liquid oxygen) are accessible to patients who need it.**
- Create exceptions to allow manufacturers to raise prices above the caps set by the Inflation Reduction Act when a drug is priced at launch in fair alignment with its value and subsequently generates new evidence of additional or sustained benefit that increases the drug's clinical value. This would encourage manufacturers to engage in value-based pricing while incentivizing them to continue to generate long-term evidence of a drug's benefits.

Payers

Given that sotatercept has only been tested over a relatively short duration as an add-on therapy in a subset of patients with PAH, and that it is likely to be very expensive, it is reasonable for payers to use prior authorization as a component of coverage. Prior authorization criteria should be based on the FDA label, clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers and patients.

Coverage Criteria: General

ICER has previously described general criteria for fair coverage policies that should be considered as cornerstones of any drug coverage policy: [Cornerstones of 'fair' drug coverage: appropriate cost sharing and utilization management policies for pharmaceuticals.](#)

Drug-Specific Coverage Criteria: Sotatercept

No coverage criteria or other limits on the utilization of sotatercept should undermine the tenets of fair access to which all patients have a fundamental right. To explore the appropriate application of evidence to coverage policy, and to reflect the views of patient experts and clinicians on specific ways that payers might appropriately use coverage policy to manage resources prudently, we present the following perspectives on specific elements of cost sharing and coverage criteria for sotatercept.

Coverage Criteria

- **Age:** Age criteria are likely to follow the FDA label, which is likely to follow the clinical trial eligibility criteria of adults ≥ 18 years old. There are ongoing trials studying the use of sotatercept in children and adolescents with PAH; until those data are available, payers should have efficient mechanisms for clinicians to seek coverage exceptions for patients with serious unmet need who are near the cutoff for the age necessary for coverage.
- **Clinical eligibility:** It is difficult to predict at this time whether the FDA will grant a broad label for sotatercept to treat PAH in adults or whether the FDA will specify a narrower approval in line with key clinical trial eligibility criteria. Trials have suggested a very favorable safety profile, which would support a broader label, but the existence of various etiologic subpopulations of PAH, and the pivotal trial design of sotatercept as an add-on therapy to background treatments, would favor a more specified label.

Even if the FDA chooses to approve sotatercept under a broader label, payers are likely to apply some or all of the eligibility criteria from the pivotal trial, especially those related to ensuring an appropriate diagnosis of PAH and those that stipulate a range of severity within which the drug has been evaluated. Key eligibility criteria that are likely to be considered for coverage criteria include:

- WHO Group 1 PAH classification: idiopathic, heritable, drug or toxin-induced, and associated (e.g., connective tissue disease, congenital heart disease). Notably, patients with PAH as a result of portal hypertension or HIV were not included. The clinical expert at the public meeting advised that it was not clear why patients with

HIV-related PAH were excluded, and that the general etiology of their PAH seems reasonably likely amenable to treatment with sotatercept.

- Symptomatic PAH in WHO- FC II or III. Clinical experts advised that treating patients in Functional Class I or IV with sotatercept did not currently seem reasonable based on existing evidence; however, ongoing trials are testing sotatercept in both newly diagnosed PAH patients and those in WHO FC-IV. Given sotatercept's favorable safety profile and novel mechanism of action, payers should have efficient mechanisms for clinicians to seek coverage exceptions for patients in these situations with serious unmet need and should be prepared to update their coverage criteria as new evidence emerges.
- On stable doses of background PAH therapy and diuretics. Clinical guidelines currently recommend that low and intermediate risk patients should be initiated on combination therapy with phosphodiesterase-5 inhibitor (PDE5i) and endothelin receptor antagonist (ERA); those with high-risk disease should be initiated on triple therapy with the addition of an IV or SC prostacyclin analogue. Payers may consider requesting documentation that these agents have been prescribed, but, for patients newly diagnosed, clinical experts advised that it would not be appropriate to require a trial of these other agents before starting sotatercept, therefore no formal step therapy was judged to be reasonable.
- Peripheral vascular resistance ≥ 5 Wood Units and a pulmonary capillary wedge pressure or left ventricular end-diastolic pressure of ≤ 15 mmHg from right heart catheterization. The findings from catheterization were viewed by experts as parts of the usual evaluation of patients with PAH and therefore not unreasonable to include in coverage criteria.
- **Exclusion criteria:** Exclusion criteria will most likely mirror the long list of clinical trial exclusion criteria, which were focused on the accurate diagnosis of PAH and safety considerations, with the following exceptions:
 - As noted, although the pivotal trial excluded patients with HIV-associated PAH, the clinical expert at the public meeting did not think there was a reasonable clinical rationale to exclude this class of patients from treatment.
 - Payers should not require the evaluation or treatment of obstructive sleep apnea (OSA) as part of the criteria for sotatercept access. Although untreated OSA may potentially exacerbate pulmonary hypertension, underlying PAH will need to be treated whether or not a patient has OSA. Additionally, there are substantial barriers to timely access of diagnostics and treatment for OSA (e.g., sleep study,

continuous positive airway pressure machine) and requiring this step could significantly delay treatment for PAH.

- **Dose:** The dose of sotatercept is 0.7 mg delivered subcutaneously every three weeks, after one initial dose of 0.3 mg.
- **Duration of coverage and renewal criteria:** Initial coverage will likely be for a period of six to 12 months, which is long enough for dose titration, assessment of side effects, or disease progression.
- **Provider restrictions:** Clinical experts agree that it is reasonable to restrict prescriptions for sotatercept to PAH specialists. Specialty clinicians are better suited to identify patients who are most likely to benefit, provide sufficient information for patients to make a well-informed decision, and monitor for response and side effects. Because some patients may not have ready access to a PAH specialist, payers may consider allowing prescription by generalist physicians working in consultation with specialists.

Step Therapy

As noted earlier, first-line therapy for low to intermediate risk PAH is the combination of a PDE5i and an ERA.⁴ Thus, sotatercept will likely be used as a third-line or fourth-line agent. However, given its different mechanism of action from other third- and fourth-line agents, clinical experts did not deem it reasonable to require a trial of therapies, including a different third-line agent (e.g., prostacyclin, selexipag), prior to initiating sotatercept therapy. The clinical expert at the public meeting and patient representatives stated that delayed and restricted access to treatment due to step therapy requirements for patients with PAH could lead to clinical deterioration.

Manufacturers

Manufacturers should therefore price novel treatments in accordance with the demonstrated benefits to patients. In settings of some uncertainty, initial pricing should err on the side of being more affordable, based on the data currently available from rigorously conducted clinical trials and/or real-world evidence. This would allow more patients access, generating additional data on the real-world effectiveness of novel treatments that could be used in future assessment updates. With accumulation of evidence of substantial patient benefit, manufacturers should be allowed to increase pricing in accordance with benefit.

For example, the clinical expert at the public meeting estimated that 50% of patients with PAH – around 30,000 people in the US – would be potentially eligible for sotatercept therapy. If the treatment was priced at \$40,000 per year and if all eligible patients were treated, sotatercept would be considered a “blockbuster drug” (over \$1 billion USD in annual sales, though this does not account for research and development costs, which may be higher for rare disease therapies). If long-term follow-up data establish a substantial mortality benefit for sotatercept, then the price for sotatercept could be adjusted upward to a price in fair alignment with the additional demonstrated benefit.

Recommendation 2

Although outcomes-based agreements should be considered for many newly launched drugs with substantial uncertainty and high costs, sotatercept does not appear to be an ideal candidate, and the manufacturer should focus instead on setting a lower launch price to reflect underlying uncertainty.

Given the sotatercept may slow the progression of PAH without consistent improvements in patient biometric or qualitative outcomes in the short-term, it seems that it is currently not feasible to identify clinical outcomes that would clearly differentiate between patients who are benefitting from treatment from those who are not. One could assume, however, that if patients discontinue treatment, or if they do progress to lung transplant, that the treatment has not provided adequate benefit. The long time-course of these outcomes, however, also make it seem unlikely that sotatercept will be a good candidate for an outcomes-based agreement.

Researchers/Regulators

Recommendation 1

Researchers and regulators, in collaboration with manufacturers, clinicians, clinical specialty societies, and patient organizations, should focus on developing better quality of life measures for PAH.

Current patient-reported quality of life measures for PAH may not fully capture the burden of PAH and may not demonstrate adequate discrimination to show small changes in quality of life. For example, although the PAH-SYMPACT questionnaire was developed specifically for PAH patients with patient input, patient experts who participated in the STELLAR trial reported that it was difficult to rate their symptoms, which may have contributed to the minimal changes seen in the scale during the trial. Additionally, PAH-SYMPACT does not have a robust measure of caregiver burden. Development of more robust quality of life measures for PAH should be prioritized by all relevant stakeholders and should be a collaborative effort between researchers, patients and clinicians, and be supported by manufacturers, regulators, and funders like the National Institute of Health and Patient-Centered Outcomes Research Institute.

Recommendation 2

Future PAH research should focus on developing evidence on the relative effectiveness of sotatercept in populations underrepresented in the clinical trials. Another important question that should be the subject of future research is whether it is safe to withdraw treatments if patients' symptoms have improved, particularly in light of the potential disease modification effect of sotatercept.

Clinical trial populations do not always reflect the diversity of the overall population, leaving questions about the efficacy of a new treatment in a particular subpopulation. For example, in the STELLAR trial, patients with connective tissue disease, drug or toxin-mediated, and congenital heart disease associated PAH were underrepresented relative to the overall US PAH population.⁵ Additionally, prior treatments for PAH have not been classified as disease-modifying. Because the mechanism of action of sotatercept suggests that disease modification is possible, it raises the question of whether, as patients improve, medications can be safely withdrawn. Thus, additional evidence generation is necessary. Manufacturers and funders such as Patient-Centered Outcomes Research Institute should support the development of well-designed observational studies and other real world evidence sources to answer such questions.

References

1. Levine DJ. Pulmonary arterial hypertension: updates in epidemiology and evaluation of patients. *Am J Manag Care*. 2021;27(3 Suppl):S35-S41.
2. American Lung Association. Why We Urgently Need Supplemental Oxygen Reform. <https://www.lung.org/blog/supplemental-oxygen-reform>. Published 2023. Accessed December 6, 2023.
3. Four Pillars for Oxygen Reform. 2022.
4. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-3731.
5. 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

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the December 1, 2023 public meeting of Midwest CEPAC.

Appendix Table 1. ICER Staff and Consultants and COI Disclosures

| ICER Staff and Consultants* | |
|--|--|
| Sarah Emond, MPP , President-Elect, ICER | Dmitriy Nikitin, MSPH , Senior Research Lead, Evidence Synthesis, ICER |
| Yamaya Jean, MA , Program Manager, ICER | Steven Pearson, MD, MSc , President, ICER |
| Yasmine Kayali, BA , Senior Program Coordinator, ICER | Marina Richardson, PhD, MSc , Senior Health Economist, ICER |
| Grace Lin, MD , Medical Director for Health Technology Assessment, ICER | David Rind, MD, MSc , Chief Medical Officer, ICER |
| Emily Nhan, BA , Senior Research Assistant, ICER | Mel Whittington, PhD, MS , Senior Fellow Center for the Evaluation of Value and Risk in Health (CEVR), Tufts Medical Center |

*No conflicts of interest to disclose, defined as individual health care stock ownership (including anyone in the member's household) in any company with a product under study, including comparators, at the meeting in excess of \$10,000 during the previous year, or any health care consultancy income from the manufacturer of the product or comparators being evaluated.

Appendix Table 2. Midwest CEPAC Panel Member Participants and COI Disclosures

| Participating Members of Midwest CEPAC* | |
|--|--|
| Alan J. Balch, PhD , Chief Executive Officer, Patient Advocate Foundation and the National Patient Advocate Foundation | Heather Guidone, BCPA , Program Director, Center for Endometriosis Care (CEC) |
| Bijan J. Borah, PhD , Professor of Health Services Research, Mayo Clinic College of Medicine and Science | Jill Johnson, PharmD , Professor, Department of Pharmacy Practice, University of Arkansas for Medical Sciences College of Pharmacy |
| Aaron E. Carroll, MD, MS , Professor of Pediatrics & Associate Dean for Research Mentoring, Indiana University School of Medicine | Bradley Martin, PharmD, PhD , Professor, Division of Pharmaceutical Evaluation and Policy, University of Arkansas for Medical Sciences College of Pharmacy |
| Donald Casey, MD, MPH, MBA, MACP, FAHA, DFAAPL, DFACMQ, CPE , Associate Professor of Medicine, Rush Medical College | Reem Mustafa, MD, MPH, PhD , Professor of Medicine, Division of Nephrology and Hypertension & Director, Outcomes and Implementation Research, University of Kansas Medical Center |
| Gregory Curfman, MD , Executive Editor, JAMA | Kurt Vanden Bosch, PharmD , System Formulary Manager, St. Luke’s Health System, Idaho |
| Stacie B. Dusetzina, PhD , Professor of Health Policy, Vanderbilt University School of Medicine | Stuart A. Winston, DO , Cardiologist in the Sub-Specialty of Cardiac Electrophysiology, St. Joseph Mercy Health System |
| Yngve Falck-Ytter, MD, AGAF , Professor of Medicine, Case Western Reserve University; Chief, Gastroenterology and Hepatology VA Northeast Ohio Healthcare System, Cleveland | |

*No conflicts of interest to disclose, defined as individual health care stock ownership (including anyone in the member’s household) in any company with a product under study, including comparators, at the meeting in excess of \$10,000 during the previous year, or any health care consultancy income from the manufacturer of the product or comparators being evaluated.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

| Policy Roundtable Participant | Conflict of Interest |
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| Mindy Bauer, PharmD, BCACP , Pharmacist, IPD Analytics | <i>Dr. Bauer is a full-time employee of IPD Analytics.</i> |
| Julia Feitner , Patient Expert | <i>Julia previously served as Secretary on the Board of Directors for Team PHEnominal Hope, which receives greater than 25% of its funding from health care companies.</i> |
| Katie Kroner, MSW , Vice President, Advocacy and Patient Engagement, Pulmonary Hypertension Association | <i>The Pulmonary Hypertension Association (PHA) receives greater than 25% of its funding from health care companies.</i> |
| Mckenzie McVeigh, PharmD, MS , Clinical Pharmacy Manager, MassHealth | <i>Dr. McVeigh is a full-time employee of MassHealth.</i> |
| Marc A. Simon, MD, MS , Professor of Medicine & Director of Pulmonary Vascular Disease, University of California San Francisco (UCSF) | <i>Dr. Simon has received consulting fees in excess of \$5,000 from Merck Pharmaceuticals.</i> |