

08.01.32 Stem Cell Therapy for Lung Disease



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Related Policies

None

Summary

Description

Lung disease remains a significant cause of morbidity and mortality worldwide in which currently there is no cure. The use of stem cell products including mesenchymal stem cells (MSCs) (mesenchymal stromal cells) from bone marrow (BM), adipose tissue (fat), myocytes (muscle) or peripheral blood, alone or in combination with platelet-derived products (e.g. platelet-rich plasma, lysate) are being investigated in the treatment of lung disease including but not limited to chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), acute respiratory distress syndrome (ARDS), pulmonary hypertension, and bronchopulmonary dysplasia.

Summary of Evidence

For individuals who have lung disease (i.e., acute respiratory distress syndrome (ARDS), bronchopulmonary dysplasia (BPD), chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), pulmonary hypertension) the evidence includes 1 systematic review of 17 randomized controlled trials (RCTs) for ARDS and 1 RCT for COPD. There were no studies identified for BPD, IPF, or pulmonary hypertension. Relevant outcomes are overall survival, test validity, symptoms, morbid events, and treatment-related morbidity. The systematic review of RCTs for ARDS found that stem cell therapy of various sources and doses significantly reduced mortality and did not increase adverse events at various short-term time-points. However, interpretation of these findings is limited by lack of long-term data from studies on ARDS unrelated to COVID-19, small sample sizes, and the absence of an established standard for optimum product source and dose. The COPD RCT concluded that MSCs may be beneficial for those with moderate to severe COPD. Additional large studies with longer follow-up are necessary to confirm the safety and efficacy profile of MSCs in the treatment of lung disease to establish the best strategy for MSC administration, including concomitant medication, dosage, and frequency. The evidence is insufficient to determine the technology results in an improvement in the net health outcomes.

Additional Information

None

OBJECTIVE

The objective of this evidence review is to evaluate whether stem cell therapy improves the net health outcome in individuals with lung disease.

PRIOR APPROVAL

- Prior approval is **ONLY** required for codes 38240 and 38241 when used for Hematopoietic Stem Cell Transplantation Autologous and Allogeneic* see [07.01.11](#)
- When these codes and all other [codes](#) in this medical policy are used for stem cell therapy they do **NOT** require prior approval.

POLICY

The use of stem cell products including mesenchymal stem cells (MSC) therapy from bone marrow, adipose tissue, or peripheral blood, alone or in combination with platelet-derived products (e.g., platelet-rich plasma, lysate) is considered **investigational** for the treatment of lung disease, including but not limited to the following because the evidence is insufficient to determine the technology results in an improvement in the net health outcomes:

- Acute respiratory distress syndrome (ARDS)
- Bronchopulmonary dysplasia (BDP)
- Chronic obstructive pulmonary disease (COPD)
- Idiopathic pulmonary fibrosis (IPF)
- Pulmonary hypertension

POLICY GUIDELINES

Coding

See the [Codes](#) table for details.

BACKGROUND

Mesenchymal stem cells (MSCs) are multipotent stromal cells that can differentiate into a variety of cell types, including osteoblasts (bone cells), chondrocytes (cartilage cells), myocytes (muscle cells) and adipocytes (fat cells that give rise to marrow adipose tissue). Mesenchymal stem cells (MSCs) have immunomodulatory properties and secrete cytokines. MSCs remain in a quiescent (non-proliferative) state during most of their lifetime, pending stimulation by the signals triggered by tissue renewal, damage, and remodeling processes. Because of their multi-lineage potential, immunomodulatory properties, and ability to secrete anti-inflammatory molecules, MSCs may have the potential to treat various chronic autoimmune, inflammatory, and degenerative diseases. MSCs have been isolated from various sites, including dermis, amniotic fluid, adipose tissue, endometrium, dental tissue, synovial fluid, placenta and umbilical cord tissue, however, bone marrow derived MSCs are considered the preferred source for bone repair and regeneration as there is better chondrogenic differentiation potential and have been identified as currently the primary source of procurement.

Harvesting the mesenchymal stem cells is performed by withdrawing bone marrow (BM), adipose tissue (fat), peripheral blood, or MSCs from another site. The harvested cells are isolated and concentrated, and along with platelet-rich plasma, and the MSCs are then reintroduced into the body and enter the pulmonary vasculature (vessels of the lungs) where cells are trapped in the microcirculation (i.e., the “pulmonary trap”). Alternatively, nebulized stem cells are reintroduced through the airways in individuals who have undergone an adipose (fat tissue) treatment. Recent studies have demonstrated that mesenchymal stem cells modulate the immune response and may reduce lung injury.

Acute Respiratory Distress Syndrome (ARDS)

Acute respiratory distress syndrome (ARDS) is a major cause of respiratory failure and is often associated with multiple organ failure. Clinical disorders such as pneumonia, sepsis, aspiration of gastric contents, and major trauma can precipitate ARDS. The pathogenesis of ARDS involves lung endothelial injury, alveolar epithelial injury, and the accumulation of protein-rich fluid and cellular debris in the alveolar space. Even with current advances in lung-protective ventilation and fluid management, mortality rate remains high. A clinical diagnosis of ARDS is associated with large financial burdens due to long hospitalization and ICU stays, a poor survival rate, and an increased use of health services after hospital discharge. Most patients who survive an episode of ARDS will sustain some degree of permanent physical disability as well as reduction in their quality of life. To decrease the occurrence of these life-changing consequences, alternative therapeutic options are needed that can reduce lung injury while facilitating and enhancing lung repair. Mesenchymal stem cells (MSCs) are being investigated as a treatment modality for ARDS.

Bronchopulmonary Dysplasia (BPD)

According to the American Lung Association, Bronchopulmonary dysplasia (BPD) is a form of chronic lung/ respiratory disease that affects newborns, most often those who are born prematurely and need oxygen therapy. Newborns' lungs are particularly vulnerable, high amounts of inhaled oxygen and pressure may overstretch the alveoli, causing inflammation and damage to the inside lining of the airways, the alveoli, and the blood vessels around them. In the lungs, BPD causes damage to the current and developing alveoli. Additionally, the tiny blood vessels surrounding the alveoli may be affected, making the passage of blood through the lungs more difficult. The lower the number of working alveoli, the longer the infant may need to remain on a ventilator, which can cause further damage to the child's lungs. In the long run, increased pressure inside the blood vessels in the lungs and between the heart and lungs can cause pulmonary hypertension. In severe cases, heart failure can occur. Newborns who suffer from BPD may also experience trouble feeding, leading to delayed development.

BPD remains a major contributor to mortality and morbidity in infants born prematurely, and current strategies to prevent this disease have been only moderately successful. BPD is a multifactorial disease where none of the current treatment strategies has effectively decreased complications in BPD survivors. Over the past years, the interest in using mesenchymal stem cell (MSC)-based therapies to treat BPD has increased especially in response to findings in pre-clinical studies demonstrating positive benefits (Augustine et al and Nitikin et al).

Pulmonary Hypertension

Pulmonary hypertension is a type of high blood pressure that affects the arteries in the lungs and the right side of the heart. With pulmonary hypertension the tiny arteries in the lungs called pulmonary arterioles and capillaries become narrowed, blocked, or destroyed which makes it harder for blood to flow through the lungs and raises pressure within the lungs' arteries. As the pressure builds, the heart's lower chamber (right ventricle) must work harder to pump blood through the lungs which eventually causes the heart muscle to weaken and fail. Pulmonary hypertension cannot be cured, and treatment can help lessen symptoms and improve quality of life. Current treatment of pulmonary hypertension includes medications, oxygen therapy, and surgery (atrial septostomy or transplantation). Stem cell therapies are being investigated in the treatment of pulmonary hypertension.

Pulmonary hypertension is classified into five groups depending on the cause:

- Pulmonary arterial hypertension
- Pulmonary hypertension caused by left-sided heart disease
- Pulmonary hypertension caused by lung disease
 - Chronic obstructive pulmonary disease (COPD), such as emphysema
 - Pulmonary fibrosis
 - Sleep apnea and other sleep disorders
 - Long term exposure to high altitudes
- Pulmonary hypertension caused by chronic blood clots
- Pulmonary hypertension associated with other conditions that have unclear reasons why the pulmonary hypertension occurs

Chronic Obstructive Pulmonary Disease (COPD)

Chronic obstructive pulmonary disease (COPD) is a progressive lung disorder that occurs as result of prolonged cigarette smoking, second-hand smoke, and polluted air or working conditions. COPD is the most prevalent form of chronic lung disease. The symptoms of COPD include shortness of breath (dyspnea), cough, and sputum production, exercise intolerance and reduced quality of life (QOL). These signs and symptoms are brought about by chronic inflammation of the airways, which restricts breathing. When fibrotic tissues contract, the lumen is narrowed, compromising lung function. As histological studies confirm, airway fibrosis and luminal narrowing are major features that lead to airflow limitation in COPD.

Chronic obstructive pulmonary disease (COPD) is a serious global health issue, with a prevalence of 9-10% of adults aged 40 and older, and the prevalence of the disease is only expected to rise. Currently COPD accounts for 27% of tobacco related deaths and is anticipated to become the fourth leading cause of death worldwide by 2030. COPD affects approximately 600 million individuals roughly 5% of the world's population. Despite modern medicine and technological advancements, there is no known cure for COPD.

The difficulty in treating COPD and other lung diseases rests in the trouble of stimulating alveolar wall formation. Treatment has been limited by two things: a lack of understanding of the pathophysiology of these disease processes on a molecular level and a lack of pharmaceutical development that would affect

these molecular mechanisms. Treatment is focused primarily on addressing the symptoms of the disease rather than healing or slowing the progression of the disease itself.

There are few options available outside bronchodilators and corticosteroids. Although lung transplants are performed as an alternative option, there is currently a severe shortage of donor lungs, leaving many patients to die on waiting lists prior to transplantation. Lung transplantation is also a very invasive form of treatment with a 5-year mortality rate of approximately 50% and is also associated with lifelong immunosuppression. Stem cell therapy using mesenchymal stem cells (mesenchymal stromal cells) is being utilized and studied in the treatment of COPD.

Idiopathic Pulmonary Fibrosis (IPF)

Idiopathic pulmonary fibrosis (IPF) is a type of interstitial lung disease, which causes progressive scarring, leading to the lung tissue thickening and stiffening. In particular, it affects the interstitium, or the area between the alveoli where gas exchange takes place in the lungs, and the blood vessels. The scar tissue reduces lung capacity and restricts gas exchange, resulting in less oxygen being transferred to the blood.

The exact mechanism through which IPF can cause pulmonary hypertension is not well understood, but it is through which IPF can cause pulmonary hypertension is not well understood, but it is thought that the scarring restricts blood vessels, impeding blood flow and making it more difficult for the heart to pump blood through the lungs. Another theory is that the damage response and resulting scar tissue reactivates pathways involved in lung development and triggers vascular remodeling. This can change the shape of the blood vessels, such as causing them to narrow and restrict blood flow.

IPF is a debilitating and fatal condition, and while current therapies can help to improve survival and quality of life, there is no known cure. However, research into promising approaches like stem cell therapy is ongoing. Mesenchymal stem cells (MSCs) are now being investigated to treat IPF due to their ability to potentially reduce inflammation in the lungs. Damage caused by inflammation can lead to scarring in the lungs, so reducing lung inflammation may be able to lessen further scarring.

Regulatory Status

The only stem cell-based products that are FDA-approved for use in the United States consist of blood-forming stem cells (hematopoietic progenitor cells) derived from cord blood. These products are approved for limited use in patients with disorders that affect the body system that is involved in the production of blood (called the “hematopoietic” system).

In April 2019, the FDA issued a statement regarding their ongoing efforts to protect patients from stem cell clinics who mislead patients with unapproved and harmful medical products. This statement included the following: Stem cell products hold significant potential to improve human health. However, that potential will never be fully realized if careful scientific work and thoughtful clinical investigation supporting the safety and efficacy of these products are not conducted. The FDA is committed to helping advance the safe and effective development of novel stem cell products. We look forward to working with those who share our goal of bringing safe and effective products to market to benefit individuals in need.

In August 2017, the FDA announced increased enforcement of regulations and oversight of stem cell clinics. The FDA will continue to help with the development and licensing of new stem cell therapies where the scientific evidence supports the product’s safety and effectiveness.

RATIONALE

This evidence review was created in January 2019 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through February 2026.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Stem Cell Therapy in Individuals with Lung Disease

Clinical Context and Therapy Purpose

The purpose of stem cell therapy is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with lung disease (i.e., acute respiratory distress syndrome (ARDS), bronchopulmonary dysplasia (BPD), chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), pulmonary hypertension).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with lung disease (i.e., acute respiratory distress syndrome (ARDS), bronchopulmonary dysplasia (BPD), chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), pulmonary hypertension).

Interventions

The therapy being considered is stem cell therapy.

Comparators

Comparators of interest include conservative management rehabilitation protocols or surgical intervention.

Outcomes

The general outcomes of interest are overall survival, symptoms, change in disease status, morbid events, functional outcomes, QOL, and treatment-related morbidity. Follow-up at 3, 6, and 12 months is of interest for stem cell therapy to monitor relevant outcomes. Longer-term follow-up is also of interest.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence

Acute Respiratory Distress Syndrome (ARDS)

Systematic Review

Fang et al (2024) conducted a systematic review and meta-analysis of RCTs that evaluated the efficacy and safety of mesenchymal stem cell therapy for acute respiratory distress syndrome. Reviewers searched 3 databases (PubMed, Embase, Cochrane) through June 23, 2024 and identified 17 RCTs (N=796) published from 2014 through 2024. The majority of RCT participants were male (63%), with COVID-19 as the ARDS' etiology. The stem cell therapy products were from diverse sources (e.g., adipose tissue, bone marrow, umbilical cord, and placenta) and used dosages ranging from 1×10^6 /kg to 10×10^6 /kg. Placebo was the comparator in the majority of RCTs. Outcomes were measured at short-term and non-uniform time points. Analyses indicated that stem cell therapy significantly reduced mortality (RR = 0.79; 95% confidence interval (CI): 0.64, 0.97; P=0.02; I²=0%) and did not increase adverse events (RR = 1.04; 95% CI: 0.90, 1.19; P=0.59; I²=0%). However, interpretation of these findings is limited by lack of long-term data from studies on ARDS unrelated to COVID-19, small sample sizes, and the absence of an established standard for optimum product source and dose.

Bronchopulmonary Dysplasia (BPD)

There were no randomized or systematic reviews identified that evaluated the durability of the long term health outcomes in individuals with bronchopulmonary dysplasia (BPS) being treated with MSCs.

Chronic Obstructive Pulmonary Disease (COPD)

Randomized Controlled Trial

Weiss et al. (2013) published a placebo-controlled, randomized trial to assess the safety and evaluate the potential efficacy of systemic mesenchymal stem cells in those with moderate to severe chronic obstructive pulmonary disease (COPD). There was 62 individuals who received either allogenic MSCs or control. Infections were received 4 times monthly and followed for 2 years. All of the individuals completed the protocol and 74% finished the full follow-up for 2 years. The end points included, "comprehensive safety evaluation, pulmonary function testing (PFT), and quality-of-life (QOL) indicators including questionnaires, 6MWT, and assessments of systemic inflammation". No statistically significant differences were reported in QOL, PFTs, total number of adverse events, COPD exacerbations, disease worsening in those who received MSCs. Allogenic MSCs may be beneficial for those with moderate to severe COPD but ultimately further clinical investigation is warranted because the MSC treatment and dosing schedule

was empirically data based from additional MSC trials for other diseases and may not be optimal for COPD. Additionally, it is unknown if MSCs are effective in reducing the complete pathophysiology contributing to the clinical manifestations of COPD.

Idiopathic Pulmonary Fibrosis (IPF)

There were no randomized or systematic reviews identified that evaluated the durability of the long term health outcomes in individuals with idiopathic pulmonary fibrosis (IPF) being treated with MSCs.

Pulmonary Hypertension

There were no randomized or systematic reviews identified that evaluated the durability of the long term health outcomes in individuals with pulmonary hypertension being treated with MSCs.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Lung Association (ALA)

In 2016, (last updated November 2024) the American Lung Association provided a statement on Stem Cell Therapy (Advisory) for lung disease that included the following information:

“The use of stem cells for treating lung diseases has great appeal. As we learn more about the therapeutic potential of stem cells and other cell therapies in clinical trials of non-lung diseases, we hope to be able to move toward further consideration of these approaches in lung diseases.

However, as yet, there is very little known about the short and long-term effects of administering any type of stem cell therapy to patients with lung diseases. Until we know more, we are strongly concerned that the treatment could cause adverse effects and could worsen the patient's condition.

You may come across information on the internet or other sources about stem cells being administered to patients with lung diseases, such as emphysema, pulmonary hypertension, or pulmonary fibrosis. We caution all patients to carefully consider the claims of benefit being made by many of these programs as they have not been substantiated or reviewed by experts in the field or any regulatory agency. We understand that patients may be attracted to these therapies because they have severe, irreversible disease and are under great stress. Although we understand this motivation, we still advise against the use of these unproven and often expensive therapies.

Because of the potential for harm, the lack of any proven benefit, and the high fees that many of these programs charge, we caution you not to participate in these or any other unauthorized or unapproved stem cell administrations, unless independent credible, reliable, and objective sources of information are available to substantiate the information and claims being made.

Additionally, the Food and Drug Administration recently issued draft guidelines clarifying that stem cells are considered drugs and need to be reviewed through a rigorous approval process before being used in patients.

At present, there are only a small number of approved clinical trials in the United States and Canada investigating cell therapy approaches for lung diseases. These can be found on the website of the National Institutes of Health at clinicaltrials.gov. We are hopeful there will be more in the future.

The American Lung Association has recently signed onto a [statement](#) along with a number of respiratory and thoracic societies, outlining the potential dangers and risks in using unregulated stem cell treatments for respiratory diseases.”

American Thoracic Society (ATS)

- A. In 2017, the ATS issued public health/information series regarding unproven stem cell treatments for lung disease that included the following information:
- **“Are stem cell treatments an option for lung disease?”**
 - In theory, yes in the future. In many lung diseases, cells that make up the respiratory system are either lost or do not function properly. A stem cell treatment that restores lung cell function might be able to reverse or even cure some lung diseases. As of now, there are no proven stem cell treatments for any lung disease.
 - **“What is an unproven stem cell treatment?”**
 - Unproven stem cell treatments are those that have not yet been adequately or fully tested for safety and effectiveness (how well they work). The best way to test potential stem cell therapies is through clinical research trials that have to follow certain rules. These rules are set by national regulatory agencies such as the FDA (Food and Drug Administration) to make sure that the treatments are tested following proper scientific methods without any conflict of interest.”
 - **“Who offers unproven stem cell treatments?”**
 - Unfortunately, there are hundreds of clinics and other groups offering unproven stem cell treatments in the United States. A frequent method that they use to treat lung disease involves removing cells from the person’s fat or bone marrow and given the cells back to the person through his or her bloodstream. These approaches have not been proven to work and are not FDA regulated or approved as accepted treatments for any type of lung disease. This means that the necessary clinical research trials to make sure that these treatments are safe and effective have not been done. Unfortunately, this does not prevent them from being offered despite unknown risk or benefit.”
 - **“Do unproven stem cell treatments work for lung disease?”**
 - There have been promising studies in animal models of lung diseases. Yet, there is no reliable evidence that stem cell treatments are effective for any lung disease. To date, there have been some legitimate clinical trials, approve and regulated by the FDA or by appropriate regulatory agencies in other countries. These have been done for a number of lung diseases including COPD, acute respiratory distress syndrome, idiopathic pulmonary fibrosis and pulmonary hypertension. These studies have used several different types of stem cells including mesenchymal stromal cells and endothelial progenitor cells. Initial results suggest that the stem cells used appear to be safe over a short-term period. However, further follow-up is necessary to ensure long term safety. Importantly, none of these studies have shown any beneficial effect in any lung disease tested so far.”

- **“Could unproven stem cell treatments be harmful?”**
 - Yes, these treatments can be potentially harmful. Potential risks include cell embolism (stem cells clotting in the lungs) and the cells causing abnormal growth including tumors. In addition, a number of clinics are giving treatment in ways that do not meet normal standards of sterility (to prevent infection) and safety.”
- **“What do pulmonologists say about unproven stem cell treatments?”**
 - Pulmonologists (lung specialists) familiar with the issues of unproven stem cell therapies for lung diseases are opposed to this approach. However, many lung specialists are not yet familiar with the field. The American Thoracic Society (ATS) Stem Cell Working Group as well as other professional societies have developed educational resources for doctors as well as for patients and their families. All involved are strongly encouraged to read these resources to learn more about stem cells and their use. Patients and doctors should take time to learn all they can about the issues surrounding unproven stem cell therapies.”
- **“What do lung disease foundations and patient’s advocacy groups say about unproven stem cell treatments?”**
 - A growing number of national and international respiratory disease societies and patient advocacy groups have taken strong positions against unproven stem cell therapies. This is also true for the leading stem cell scientific societies who do not support use of unproven stem cell therapies at this time. All these groups are trying to educate patients, families, caregivers, and health care professionals about the potential dangers of unproven stem cell treatments. In the U.S., these foundations include the Alpha-1 Foundation, American Lung Association (ALA), COPD Foundation, Cystic Fibrosis Foundation, Pulmonary Fibrosis Foundation, and the Pulmonary Hypertension Association. None of these groups believes there is enough known about stem cell therapies to use them in lung disease without more research.”

B. In 2016 the American Thoracic Society issued a statement on unproven stem cell interventions for lung disease which included the following information:

“A central component of the mission of medical societies is to translate new scientific information into patient education. The undersigned lung, respiratory, and thoracic societies, and patient advocacy groups strongly believe that patients and their families along with the general public should have at their disposal unbiased and scientifically sound information on new potential therapeutic options including stem cell-based treatments.

Continuing advances in stem cell biology have created justified excitement at the prospect of personalized stem cell-based therapies through the use of clinically relevant cell populations. We recognize the enormous potential of stem cells for disease management including acute and chronic ailments of the respiratory system. As we learn more about the therapeutic potential of stem cells and other cell therapies in clinical trials of non-lung diseases and in initial trials in lung diseases, we hope to move towards further consideration and potential implementation of these approaches. However, as with all medical interventions, patient safety must be the top priority of any prospective stem cell-based therapy or treatment. As yet, there is very little known about the short- and long-term effects in terms of safety and efficacy of administering any type of stem cell-based therapy to patients with lung diseases. Until we know more, we must be strongly concerned that the treatment could cause adverse effects and could worsen the patient's condition rather than improve it.

At present, there are only a small number of peer reviewed and appropriately regulated approved clinical trials in the United States, Canada, the European Union, Brazil, Asia and Australia investigating cell therapy approaches for lung diseases.

Thus, we are particularly wary of the ever-increasing examples of direct-to-consumer advertising of untested, unapproved, and potentially dangerous “stem-cell” treatments that take place in several countries. One may come across information on the internet or other sources about stem cells being administered to patients with lung diseases such as emphysema, pulmonary hypertension, cystic fibrosis, or pulmonary fibrosis in several locations worldwide including the United States. We fully acknowledge that patients with severe irreversible lung diseases are under extreme physical and emotional distress that provide the motivation to resort to expensive unproven treatments. Nevertheless, we strongly caution all patients that the claims of benefit being made by many of these programs have not been substantiated nor have they been reviewed by experts in the field or any regulatory agency. These programs are usually characterized by:

- Exorbitant fees
- Misrepresentation of risks and benefits
- Overreliance on, and advertisement of, patient testimony
- Poor patient follow-up
- Absence of regulatory oversight and objective clinical evidence for claimed benefits

Therefore, they differ substantially from therapies approved by legitimate regulatory agencies, from well-designed, controlled, and appropriately regulated clinical trials, and from regulated compassionate use of innovative cell therapies. Because of the potential for harm and the lack of any proven benefit, we strongly caution patients not to participate in these or any other comparable unauthorized or unapproved stem cell interventions, unless independent credible, reliable, and objective sources of information are available to substantiate the information and claims being made. To better educate the lung scientific community about the complex issues of stem cell medical tourism, we propose the inclusion of relevant sessions, whenever possible, in future national and international conferences related to lung biology and disease. Representatives of regulatory agencies, patient advocacy groups, and bioethics and health policy scholars should be included as speakers and discussants. We also urge patient advocacy groups and foundations to work together with their national lung, respiratory, and thoracic societies, their local chapters, and with regulatory agencies on the issues of stem cell medical tourism and unproven stem cell interventions. Open channels of communication between these organizations and dissemination of reliable, evidence-based information through patient networks including social media, will ensure that lung disease patients make informed and safe decisions regarding cell-based treatments.”

COPD Foundation

In 2015 the COPD Foundation has issued the following position related to Stem Cell Therapy:

- “Autologous stem cell therapy is not currently recommended for the treatment of COPD. The COPD Foundation does not recommend the use of autologous stem cell therapy in the treatment of COPD or other lung disease until there is more rigorous scientific and medical proof of its effectiveness. Instead, the COPD Foundation encourages individuals to participate in clinical trials that test the development and potential benefit of this technique.”

Pulmonary Hypertension Association (PHA)

In 2009 the PHA issued the following statement in the “The Facts on Stem Cell Therapy & PH”:

- “It is understandable that many patients may be willing to undergo cell therapy even though the risks and benefits still remain to be determined.

- However, it is important for patients to understand that there is no solid evidence to support the clinical use of cell therapy for PAH at this time, among the possible outcomes are that cell therapy might, in some patients, actually make the disease worse, instead of better. It should be only provided as part of a research study that will address the key issues of effectiveness and safety. Practitioners who may charge large amounts of money to administer unproven treatments raise serious ethical concerns among the PH community.”

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
	38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
	38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
	38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer
	38230	Bone marrow harvesting for transplantation; allogeneic
	38232	Bone marrow harvesting for transplantation; autologous
	38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
	38241	Hematopoietic progenitor cell (HPC); autologous transplantation
	0232T	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed
HCPCS		
	No code(s)	
Type of Service	Therapy	
Place of Service	Outpatient/ Inpatient	

POLICY HISTORY

Date	Reason	Action
March 2026	Annual Review	Policy Renewed
March 2025	Annual Review	Policy Revised
March 2024	Annual Review	Policy Renewed
March 2023	Annual Review	Policy Revised
January 2022	Annual Review	Policy Renewed
January 2021	Annual Review	Policy Revised
January 2020	Annual Review	Policy Renewed
January 2019		New Policy

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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