Introduction

Extracorporeal means “outside the body.” Extracorporeal membrane oxygenation (ECMO) is a way to supply oxygen to the blood and remove carbon dioxide from it using a machine that’s similar to a heart/lung machine. For this treatment, catheters (long thin tubes) are inserted into arteries or veins. Blood flows out of the body through the catheter and goes into a machine. The machine takes out carbon dioxide from the blood and adds oxygen to it. After it’s slightly warmed, the blood is returned to the body. ECMO provides temporary help when respiratory (breathing) failure is believed to be reversible but other treatments have not yet worked. It may also be used in specific situations when the heart is suddenly unable to pump enough blood through the body. This policy describes when ECMO is considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| Extracorporeal membrane oxygenation (ECMO)  | The use of extracorporeal membrane oxygenation (ECMO) in adults may be considered medically necessary for the management of acute respiratory failure when ALL of the following criteria are met:  
  - Respiratory failure is due to a potentially reversible etiology (see below)  
  - Respiratory failure is severe, as determined by 1 of the following:  
    - A standardized severity instrument such as the Murray score (see below)  
    - One of the criteria for respiratory failure severity outlined below  
  - None of the following contraindications is present:  
    - High ventilator pressure (peak inspiratory pressure >30 cm H2O) or high fraction of inspired oxygen (FIO2) (>80%) ventilation for more than 168 hours (7 days)  
    - Signs of intracranial bleeding  
    - Multisystem organ failure  
    - Prior (ie, before onset of need for ECMO) diagnosis of a terminal condition with expected survival <6 months  
    - A do-not-resuscitate (DNR) directive  
    - Cardiac decompensation in a patient who was already declined for ventricular assist device (VAD) or transplant  
    - KNOWN neurologic devastation without potential to recover meaningful function  
    - Determination of care futility (see below)  

The use of ECMO in adults may be considered medically necessary as a bridge to heart, lung, or combined heart-lung transplantation for the management of adults with respiratory, cardiac, or combined cardiorespiratory failure refractory to optimal conventional therapy.
### Extracorporeal membrane oxygenation (ECMO)

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
</table>
| Extracorporeal membrane oxygenation (ECMO) | The use of ECMO in adult patients is considered investigational when the above criteria are not met, including but not limited to:  
- Acute and refractory cardiogenic shock  
- As an adjunct to cardiopulmonary resuscitation  
Extracorporeal membrane oxygenation (ECMO) is considered investigational for most cases of cardiogenic shock. However, in individual clinical situations, ECMO may be considered beneficial/life-saving for relatively short-term support (ie, days) for cardiogenic shock refractory to standard therapy in specific situations when shock is thought to be due to a potentially reversible condition, such as ST elevation acute myocardial infarction, acute myocarditis, peripartum cardiomyopathy, or acute rejection in a heart transplant, **AND** when there is reasonable expectation for recovery. |

### Respiratory Failure Reversibility

The reversibility of the underlying respiratory failure is best determined by the treating physicians, ideally physicians with expertise in pulmonary medicine and/or critical care. Some of the underlying causes of respiratory failure, which are commonly considered reversible, are as follows:

- Acute respiratory distress syndrome (ARDS)*
- Acute pulmonary edema
- Acute chest trauma
- Infectious and noninfectious pneumonia
- Pulmonary hemorrhage
- Pulmonary embolism
- Asthma exacerbation
Aspiration pneumonitis

*ARDS refers to a clinical condition characterized by bilateral pulmonary infiltrates and severe hypoxemia in the absence of cardiogenic pulmonary edema. A consensus definition for ARDS was first developed in 1994 at the American-European Consensus Conference (AECC) on ARDS. The AECC definition was refined in 2012 by a panel of experts convened by the European Society of Intensive Care Medicine, with endorsement from the American Thoracic Society and the Society of Critical Care Medicine. The revised definition was renamed the Berlin definition, which was validated using a patient-level meta-analysis of 4188 patients with ARDS from 4 multicenter clinical data sets and 269 patients with ARDS from 3 single-center data sets containing physiologic information. Table 1 shows the Berlin definition of ARDS.

### Table 1: Berlin Definition of Acute Respiratory Distress Syndrome

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing</strong></td>
<td>Within 1 week of a known clinical insult or new or worsening respiratory symptoms</td>
</tr>
<tr>
<td><strong>Chest imaging</strong></td>
<td>Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules</td>
</tr>
<tr>
<td><strong>Origin of edema</strong></td>
<td>Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factors present.</td>
</tr>
<tr>
<td><strong>Oxygenation</strong></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>$200 \text{ mm Hg} &lt; \text{PaO}_2/\text{FiO}_2 &lt; 300 \text{ mm Hg}$ with PEEP or CPAP $&gt;5 \text{ cm H}_2\text{O}$</td>
</tr>
<tr>
<td>Moderate</td>
<td>$100 \text{ mm Hg} &lt; \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mm Hg}$ with PEEP or CPAP $\geq 5 \text{ cm H}_2\text{O}$</td>
</tr>
<tr>
<td>Severe</td>
<td>$\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}$ with PEEP or CPAP $\geq 5 \text{ cm H}_2\text{O}$</td>
</tr>
</tbody>
</table>

CPAP: continuous positive airway pressure; CT: computed tomography; CXR: chest x-ray; FIO$_2$: fraction of inspired oxygen; PaO$_2$: partial pressure of oxygen in arterial blood; PEEP: peak end expiratory pressure.

**Respiratory Failure Severity**

**Murray Score**

One commonly used system for classifying the severity of respiratory failure is the Murray scoring system, which was developed for use in ARDS but has been applied to other indications. This score includes 4 subscales, each of which is scored from 0 to 4. The final score is obtained by dividing the collective score by the number of subscales used. A score of 0 indicates no lung
injury; a score of 1-2.5 indicates mild or moderate lung injury; and a score greater than 2.5 indicates severe lung injury (eg, ARDS). Table 2 shows the components of the Murray scoring system.

Table 2: Murray Lung Injury Score

<table>
<thead>
<tr>
<th>Scale</th>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray score</td>
<td>No alveolar consolidation</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation confined to 1 quadrant</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation confined to 2 quadrants</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation confined to 3 quadrants</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Alveolar consolidation in all 4 quadrants</td>
<td>4</td>
</tr>
<tr>
<td>Hypoxemia score</td>
<td>( \text{PaO}_2/\text{FiO}_2 &gt; 300 )</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>( \text{PaO}_2/\text{FiO}_2 225-299 )</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>( \text{PaO}_2/\text{FiO}_2 175-224 )</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>( \text{PaO}_2/\text{FiO}_2 100-174 )</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>( \text{PaO}_2/\text{FiO}_2 \leq 100 )</td>
<td>4</td>
</tr>
<tr>
<td>PEEP score (when ventilated)</td>
<td>PEEP ( \leq 5 \text{ cm H}_2\text{O} )</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>PEEP 6-8 \text{ cm H}_2\text{O}</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>PEEP 9-11 \text{ cm H}_2\text{O}</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>PEEP 12-14 \text{ cm H}_2\text{O}</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>PEEP ( \geq 15 \text{ cm H}_2\text{O} )</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory system compliance score</td>
<td>Compliance ( &gt;80 \text{ mL/cm H}_2\text{O} )</td>
<td>0</td>
</tr>
<tr>
<td>(when available)</td>
<td>Compliance 60-79 \text{ mL/cm H}_2\text{O}</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Compliance 40-59 \text{ mL/cm H}_2\text{O}</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Compliance 20-39 \text{ mL/cm H}_2\text{O}</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Compliance ( \leq 19 \text{ mL/cm H}_2\text{O} )</td>
<td>4</td>
</tr>
</tbody>
</table>

\( \text{FiO}_2 \): fraction of inspired oxygen; \( \text{PaO}_2 \): partial pressure of oxygen in arterial blood; PEEP: peak end expiratory pressure.

**Alternative Respiratory Failure Severity Criteria**

Respiratory failure is considered severe if the patient meets one or more of the following criteria:

- Uncompensated hypercapnea with a pH less than 7.2
- \( \text{PaO}_2/\text{FiO}_2 \) of \(<100 \text{ mm Hg} \) on fraction of inspired oxygen (FiO\textsubscript{2}) \( >90\% \)
- Inability to maintain airway plateau pressure (Pplat) \(<30 \text{ cm H}_2\text{O} \) despite a tidal volume of 4-6 mL/kg ideal body weight (IBW)
• Oxygenation Index >30: Oxygenation Index = \( \text{FiO}_2 \times 100 \times \frac{\text{MAP}}{\text{PaO}_2} \) mm Hg. \([\text{FiO}_2 \times 100 = \text{FiO}_2 \text{ as percentage; MAP = mean airway pressure in cm H}_2\text{O; PaO}_2 = \text{partial pressure of oxygen in arterial blood}]\)

• \( \text{CO}_2 \) retention despite high Pplat (>30 cm H\(_2\)O)

**Assessment of ECMO Futility**

Patients undergoing ECMO treatment should be periodically reassessed for clinical improvement. ECMO should not be continued indefinitely in the following situations:

• Neurologic devastation as defined by the following:
  
  o Consensus from two attending physicians that there is no likelihood of an outcome better than “persistent vegetative state” at 6 month

  AND

  o At least one of the attending physicians is an expert in neurologic disease and/or intensive care medicine

  AND

  o Determination made following studies including CT, EEG and exam

OR

• Inability to provide aerobic metabolism, defined by the following:

  o Refractory hypotension and/or hypoxemia

  OR

  o Evidence of profound tissue ischemia based on creatine phosphokinase (CPK) or lactate levels, lactate-to-pyruvate ratio, or near-infrared spectroscopy (NIRS)

  OR

  o Presumed end-stage cardiac or lung failure without “exit” plan (ie, declined for assist device and/or transplantation)
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>33946</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; initiation, veno-venous</td>
</tr>
<tr>
<td>33947</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; initiation, veno-arterial</td>
</tr>
<tr>
<td>33948</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; daily management, each day, veno-venous</td>
</tr>
<tr>
<td>33949</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; daily management, each day, veno-arterial</td>
</tr>
<tr>
<td>33952</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of peripheral (arterial and/or venous) cannula(e), percutaneous, 6 years and older (includes fluoroscopic guidance, when performed)</td>
</tr>
<tr>
<td>33954</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of peripheral (arterial and/or venous) cannula(e), open, 6 years and older</td>
</tr>
<tr>
<td>33956</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of central cannula(e) by sternotomy or thoracotomy, 6 years and older</td>
</tr>
<tr>
<td>33958</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition peripheral (arterial and/or venous) cannula(e), percutaneous, 6 years and older (includes fluoroscopic guidance, when performed)</td>
</tr>
<tr>
<td>33962</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition peripheral (arterial and/or venous) cannula(e), open, 6 years and older (includes fluoroscopic guidance, when performed)</td>
</tr>
<tr>
<td>33964</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition central cannula(e) by sternotomy or thoracotomy, 6 years and older (includes fluoroscopic guidance, when performed)</td>
</tr>
<tr>
<td>33966</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of peripheral (arterial and/or venous) cannula(e), percutaneous, 6 years and older</td>
</tr>
<tr>
<td>33984</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of peripheral (arterial and/or venous) cannula(e), open, 6 years and older</td>
</tr>
<tr>
<td>33986</td>
<td>Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of central cannula(e) by sternotomy or thoracotomy, 6 years and older</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>33987</td>
<td>Arterial exposure with creation of graft conduit (eg, chimney graft) to facilitate arterial perfusion for ECMO/ECLS (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>33988</td>
<td>Insertion of left heart vent by thoracic incision (eg, sternotomy, thoracotomy) for ECMO/ECLS</td>
</tr>
<tr>
<td>33989</td>
<td>Removal of left heart vent by thoracic incision (eg, sternotomy, thoracotomy) for ECMO/ECLS</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

### Related Information

#### Applications and Definitions

Adults are considered patients older than age 18. This policy addresses the use of long-term (ie, over 6 hours) extracorporeal cardiopulmonary support. It does not address the use of extracorporeal support, including ECMO, during surgical procedures.

#### Evidence Review

### Description

Extracorporeal membrane oxygenation (ECMO) provides circulation and physiologic gas exchange outside the body for temporary cardiorespiratory support in cases of severe respiratory and cardiorespiratory failure. ECMO uses a pump and a membrane oxygenator to supply oxygen to the blood and remove carbon dioxide from it.
Background

Extracorporeal Membrane Oxygenation

ECMO has generally been used in clinical situations in which there is respiratory or cardiac failure, or both, and conventional therapies have failed to support the function of the heart and lungs. Without the support of ECMO, death would likely be imminent. Potential indications for ECMO in adults include: acute, potentially reversible respiratory failure due to a variety of causes; as a bridge to lung transplantation; in potentially reversible cardiogenic shock; and as an adjunct to cardiopulmonary resuscitation (ECMO-assisted cardiopulmonary resuscitation [ECPR]).

ECMO has been investigated as an intervention since the late 1960s. ECMO has been widely used in the pediatric population, particularly in neonates with pulmonary hypertension, meconium aspiration syndrome, and congenital diaphragmatic hernia. Interest has developed in the use of ECMO for cardiorespiratory support for adult conditions. Early studies of the use of ECMO for adult respiratory and cardiorespiratory conditions, particularly severe acute respiratory distress syndrome (ARDS), included 1 RCT conducted in the United Kingdom in the 1970s that showed poor survival and high complication rates due to the anticoagulation required for the ECMO circuit.¹

With improvements in ECMO circuit technology and methods of supportive care, interest in the use of ECMO in adults has resurged. For example, during the 2009-2010 H1N1 influenza pandemic, the occurrence of influenza-related ARDS in relatively young, healthy people prompted an interest in ECMO for adults.

Disease-Specific Indications for ECMO

Venoarterial (VA) and venovenous (VV) ECMO have been investigated for a wide range of adult conditions that can lead to respiratory or cardiorespiratory failure, some of which overlap clinical categories. For example, H1N1 influenza infection can lead to ARDS as well as cardiovascular collapse, which makes categorization difficult. However, in general, indications for ECMO can be categorized as follows:

- **Acute respiratory failure due to potentially reversible causes.** Acute respiratory failure refers to the failure of either oxygenation, removal of carbon dioxide, or both, and may be due to a wide range of causes. ARDS has been defined by consensus in the Berlin definition, which includes criteria for the timing of symptoms, imaging findings, exclusion of other
causes, and degree of oxygenation. In ARDS cases, ECMO is most often used as a bridge to recovery. Specific potentially reversible or treatable indications for ECMO may include ARDS, acute pneumonias, and a variety of other pulmonary disorders.

- **Bridge to lung transplant.** Lung transplantation is used to manage chronic respiratory failure. Most frequently, this could be due to advanced chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis, cystic fibrosis, emphysema due to α-1-antitrypsin deficiency, and idiopathic pulmonary arterial hypertension. In the end stages of these diseases, patients may require additional respiratory support while awaiting an appropriate lung donor. In addition, patients who have undergone a transplant may require retransplantation due to problems with the initial transplant.

- **Acute-onset cardiogenic or obstructive shock.** This is defined as shock that is due to cardiac pump failure or vascular obstruction, refractory to inotropes and/or other mechanical circulatory support. Examples include postcardiotomy syndrome (ie, failure to wean from bypass), acute coronary syndrome, myocarditis, cardiomyopathy, massive pulmonary embolism, and prolonged arrhythmias.

- **ECMO-assisted cardiopulmonary resuscitation (E-CPR).** ECMO can be used as an adjunct to CPR in patients who do not respond to initial resuscitation measures.

**Technology Description**

The basic components of ECMO include a pump, an oxygenator (sometimes referred to as a “membrane lung”), and some form of vascular access. Based on the vascular access type, ECMO can be described as venovenous (VV) or venoarterial (VA). VA ECMO has the potential to provide cardiac and ventilatory support.

**Venovenous ECMO**

**Technique**

In venovenous extracorporeal membrane oxygenation (VV ECMO), the ECMO oxygenator is in series with the native lungs, and the ECMO circuit provides respiratory support. Venous blood is withdrawn through a large-bore intravenous line; oxygen is added and CO\(_2\) removed, and oxygenated blood is returned to the venous circulation near the right atrium.
Indications

VV ECMO provides only respiratory support, and therefore it is used to provide adequate gas exchange when there are abnormalities in the lung parenchyma, airways, or chest wall. Right ventricular (RV) dysfunction due to pulmonary hypertension caused by parenchymal lung disease may sometimes be effectively treated by VV ECMO. However, acute or chronic obstruction of the pulmonary vasculature (e.g., saddle pulmonary embolism) may require VA ECMO. There also may be cases in which VA ECMO is required to treat severe RV dysfunction due to pulmonary hypertension caused by severe parenchymal lung disease. In adults, VV ECMO is generally used when all other reasonable avenues of respiratory support have been exhausted, including mechanical ventilation with lung protective strategies, pharmacologic therapy, and prone positioning.

Venoarterial ECMO

Technique

In venoarterial extracorporeal membrane oxygenation (VA ECMO), the ECMO oxygenator is in parallel with the native lungs and the ECMO circuit provides both cardiac and respiratory support. In VA ECMO, venous blood is withdrawn, oxygen is added, and CO₂ is removed similar to VV ECMO, but blood is returned to the arterial circulation. Cannulation for VA ECMO can be done peripherally, with withdrawal of blood from a cannula in the femoral or internal jugular vein and return of blood through a cannula in the femoral or subclavian artery. Alternatively, it can be done centrally, with withdrawal of blood directly from a cannula in the right atrium and return of blood through a cannula in the aorta. VA ECMO typically requires a high blood flow extracorporeal circuit.

Indications

VA ECMO provides both cardiac and respiratory support. It is used in situations of significant cardiac dysfunction that is refractory to other therapies. It is also used when significant respiratory involvement is suspected or demonstrated, such as in treatment-resistant cardiogenic shock, pulmonary embolism, or primary parenchymal lung disease severe enough to compromise right heart function.
Extracorporeal Carbon Dioxide Removal

In addition to complete ECMO systems, there are ventilation support devices that provide oxygenation and removal of CO₂ without the use of a pump system or interventional lung assist devices (eg, iLA® Membrane Ventilator; Novalung GmbH). At present, none of these systems has Food and Drug Administration approval for use in the United States. These technologies are not the focus of this evidence review, but are described briefly because there is overlap in patient populations treated with extracorporeal carbon dioxide removal (ECCO₂R) and those treated with ECMO, and some studies have reported on both technologies.

Unlike VA and VV ECMO, which use large-bore catheters and generally require high flow rates of blood through the ECMO circuits, other systems use pumpless systems to remove CO₂. These pumpless devices achieve ECCO₂R via a thin double-lumen central venous catheter and relatively low extracorporeal blood flow. They have been investigated as a means to allow low tidal volume ventilator strategies, which may have benefit in ARDS and other conditions where lung compliance is affected. Although ECMO systems can effect CO₂ removal, dedicated ECCO₂R systems are differentiated by simpler mechanics and the fact that they do not require dedicated staff.³

Medical Management During ECMO

During ECMO, patients require supportive care and treatment for their underlying medical condition, including ventilator management, fluid management, systemic anticoagulation to prevent circuit clotting, nutritional management, and appropriate antimicrobials. Maintenance of the ECMO circuit requires frequent (ie, multiple times in 24 hours) monitoring by medical and nursing staff and evaluation at least once per 24 hours by a perfusion expert.

Because of the need for systemic anticoagulation, ECMO may be associated with significant complications. These may include hemorrhage, limb ischemia, compartment syndrome, cannula thrombosis, and limb amputation. Patients are also at risk of progression of their underlying disease process.

Summary of Evidence

For adults who undergo extracorporeal membrane oxygenation (ECMO) to treat their acute respiratory failure, the evidence includes 1 moderately sized randomized controlled trial, nonrandomized comparative studies, and multiple case series. Relevant outcomes are overall
survival, change in disease status, morbid events, and treatment-related mortality and morbidity. The most direct evidence about the efficacy of ECMO in adult respiratory failure comes from the CESAR trial. The CESAR trial had limitations, including nonstandardized management in the control group and unequal intensity of treatment between the treatment and the control groups. But for the trial’s primary outcome of disability-free survival at 6 months, there was a large effect size, with an absolute risk reduction in mortality of 16.25% (95% CI, 1.75% to 30.67%). Recent nonrandomized comparative studies generally report improvements in outcomes with ECMO. The available evidence supports the conclusion that outcomes are improved for adults with acute respiratory failure, particularly those who meet the criteria outlined in the CESAR trial. However, questions remain about the generalizability of findings from the CESAR trial and nonrandomized study results to other patient populations, and further clinical trials in more specific patient populations are needed. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For adult lung transplant candidates who receive ECMO as a bridge to pulmonary transplant, the evidence includes 2 large nonrandomized comparator studies and small case series. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related mortality and morbidity. One of the large comparator studies found that patients receiving ECMO had 3-year survival rates similar to patients receiving no support, and significantly better survival rates than patients receiving invasive mechanical support. Single-arm series have reported rates of successful bridge to transplant on the order of 70% to 80%. Clinical input supported the use of ECMO in adult lung transplant candidates as a bridge to pulmonary transplant. Given the lack of other treatment options for this population, the suggestive clinical evidence, and the support from clinical input, ECMO may be considered medically necessary for this patient population. The evidence is sufficient to determine the effects of the technology on health outcomes.

For adults who have acute cardiac failure and receive ECMO, the evidence includes case series and case reports. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related mortality and morbidity. Case series in patients who failed to wean off bypass after cardiotomy have reported rates of successful decannulation from ECMO on the order of 60%. Case series in populations affected by other causes of acute cardiac failure report rates of survival to discharge of 40% to 60%. Complication rates are high. Evidence comparing ECMO with other medical therapy options is lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

For adults who have cardiac arrest and receive ECMO-assisted cardiopulmonary resuscitation (ECPR), the evidence includes a meta-analysis, nonrandomized comparative studies, and case
series. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related mortality and morbidity. The meta-analysis looked at which patients would benefit most from ECPR, and reported that patients who had initial shockable cardiac rhythms, shorter low-flow duration, higher arterial pH, and lower serum lactate concentrations experienced more favorable outcomes. The most direct evidence comes from an observational study comparing ECPR to standard CPR, using propensity score matching. It reported higher rates of survival to discharge with ECPR, with minimal neurologic impairment. Other nonrandomized studies report higher survival in ECPR groups. However, the benefit associated with ECPR is uncertain given the potential for bias in nonrandomized studies. Additionally, factors related to the implementation of ECPR procedures in practice need to be better delineated. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

Current on-going and unpublished trials that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01470703</td>
<td>Extracorporeal Membrane Oxygenation(ECMO) for Severe Acute Respiratory</td>
<td>331</td>
<td>Feb 2018</td>
</tr>
<tr>
<td></td>
<td>Distress Syndrome (ARDS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01605409</td>
<td>Emergency Cardiopulmonary Bypass After Cardiac Arrest With Ongoing</td>
<td>40</td>
<td>May 2018</td>
</tr>
<tr>
<td></td>
<td>Cardiopulmonary Resuscitation - a Pilot Randomized Trial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01511666</td>
<td>Hyperinvasive Approach to Out-of Hospital Cardiac Arrest Using Mechanical</td>
<td>170</td>
<td>May 2018</td>
</tr>
<tr>
<td></td>
<td>Chest Compression Device, Prehospital Intraarrest Cooling, Extracorporeal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Life Support and Early Invasive Assessment Compared to Standard of Care.</td>
<td></td>
<td></td>
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<td>NCT01685112</td>
<td>Comparison of ECMO Use and Conventional Treatment in Adults With Septic Shock</td>
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<td>NCT01186614</td>
<td>Refractory Out-Of-Hospital Cardiac Arrest Treated With Mechanical CPR, Hypothermia, ECMO and Early Reperfusion</td>
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<tr>
<td>NCT01990456</td>
<td>Strategies for Optimal Lung Ventilation in ECMO for ARDS: The SOLVE ARDS Study</td>
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**Clinical Input Received from Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may provide appropriate reviewers who collaborate with and make recommendations during this process, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests while this policy was under review in 2015, input was received from 2 academic medical centers, one of which provided 3 responses, and 3 physician specialty societies, 1 of which provided 2 responses and 1 of which provided 2 responses and a consensus letter. There was consensus that ECMO is medically necessary for adults with severe and potentially reversible respiratory failure. There was consensus that ECMO is medically necessary for adults as a bridge to heart, lung, or heart-lung transplant. There was no consensus that ECMO is medically necessary for adults with refractory cardiac failure. There was consensus that ECMO is investigational as an adjunct to cardiopulmonary resuscitation.

**Practice Guidelines and Position Statements**

**The Extracorporeal Life Support Organization (ELSO)**

The Extracorporeal Life Support Organization (ELSO) provides education, training, and guidelines related to the use of ECMO, along with supporting research and maintaining an ECMO patient registry. In addition to general guidelines that describe ECMO, ELSO has published specific
recommendations in 2013 related to the use of ECMO in adult respiratory failure, adult cardiac failure, and in adult ECMO-assisted cardiopulmonary resuscitation (ECPR), which are outlined in Table 4. 

Table 4: Extracorporeal Life Support Organization Indications for ECMO in Adults

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Indications</th>
<th>Contraindications</th>
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</table>
| **Adult respiratory failure**  | 1. In hypoxic respiratory failure due to any cause (primary or secondary) ECLS should be considered when the risk of mortality is ≥50%, and is indicated when the risk of mortality is ≥80%.  
   a. 50% mortality risk is associated with a \( \text{PaO}_2/\text{FiO}_2 < 150 \) on \( \text{FiO}_2 > 90\% \) and/or Murray score 2-3  
   b. 80% mortality risk is associated with a \( \text{PaO}_2/\text{FiO}_2 < 100 \) on \( \text{FiO}_2 > 90\% \) and/or Murray score 3-4, despite optimal care for ≥6 h  
   2. \( \text{CO}_2 \) retention on mechanical ventilation, despite high Pplat (> 30 cm H\(_2\)O)  
   3. Severe air leak syndromes  
   4. Need for intubation in a patient on lung transplant list  
   5. Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)  | Relative contraindications:  
1. Mechanical ventilation at high settings (\( \text{FiO}_2 > 0.9, \text{Pplat} > 30 \)) for ≥7 d  
2. Major pharmacologic immunosuppression (absolute neutrophil count < 400/mm\(^3\))  
3. CNS hemorrhage that is recent or expanding  
4. Nonrecoverable comorbidity such as major CNS damage or terminal malignancy  
5. Age: no specific age contraindication but consider increasing risk with increasing age  |
| **Adult cardiac failure**      | Indications for ECLS in adult cardiac failure is cardiogenic shock, defined by the following:  
1. Inadequate tissue perfusion manifested as hypotension and low cardiac output, despite adequate intravascular volume.  
2. Shock persists despite volume administration, inotropes and vasoconstrictors, and intra-aortic balloon counterpulsation, if appropriate.  
3. Typical causes: acute myocardial infarction, | Absolute contraindications:  
1. Unrecoverable heart and not a candidate for transplant or VAD.  
2. Advanced age.  
3. Chronic organ dysfunction (emphysema, cirrhosis, renal failure).  
4. Compliance (financial, cognitive, psychiatric, or social limitations).  
5. Prolonged CPR without adequate tissue |
### Conditions, Indications, Contraindications

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<thead>
<tr>
<th>Conditions</th>
<th>Indications</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>myocarditis, peripartum cardiomyopathy, decompensated chronic heart failure, postcardiotomy shock.</td>
<td>perfusion. Relative contraindications: 1. Contraindication for anticoagulation. 2. Advanced age (Note: advanced age appears in both relative and absolute contraindication lists). 3. Obesity.</td>
<td>1. All contraindications to ECMO use (eg, gestational age &lt;34 wks.) 2. Do-not-resuscitate orders</td>
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<td>4. Septic shock is an indication in some centers.</td>
<td>AHA guidelines for CPR recommend consideration of ECMO to aid CPR in patients who have an easily reversible event, have had excellent CPR</td>
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</table>

AHA: American Hospital Association; CNS: central nervous system; CPR: cardiopulmonary resuscitation; ECLS: extracorporeal lung support; ECMO: extracorporeal membrane oxygenation; ECPR: extracorporeal membrane oxygenation-assisted cardiopulmonary resuscitation; FIO2: fraction of inspired oxygen; PaO2: partial pressure of oxygen in arterial blood; Pplat: airway plateau pressure; PE: pulmonary embolus; VAD: ventricular assist device.

### International ECMO Network

In 2014, the International ECMO Network, with endorsement by ELSO, published a position paper detailing institutional, staffing, and reporting requirements for facilities providing ECMO, with recommendations including but not limited to the following:

- Organization of ECMO programs on a regional or national level is needed to provide the best, safest and most efficient care possible to the population.
- Local, regional or interregional networks of hospitals with a mobile ECMO team should ideally be created around each ECMO center.
- Staff training and continuing education, as well as regular audits evaluating program performance, should be routinely organized to assure quality.

### National Institute for Health and Care Excellence (NICE)

In 2014, NICE issued guidance on the use of ECMO for acute heart failure in adults, which made the following recommendations:
The evidence on the efficacy of extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults is adequate but there is uncertainty about which patients are likely to benefit from this procedure, and the evidence on safety shows a high incidence of serious complications. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

In 2011, NICE issued guidance on the use of extracorporeal membrane oxygenation for severe acute respiratory failure in adults, which made the following recommendations⁸²:

Evidence on the safety of extracorporeal membrane oxygenation (ECMO) for severe acute respiratory failure in adults is adequate but shows that there is a risk of serious side effects. Evidence on its efficacy is inadequate to draw firm conclusions: data from the recent CESAR (Conventional ventilation or extracorporeal membrane oxygenation for severe adult respiratory failure) trial were difficult to interpret because different management strategies were applied among many different hospitals in the control group and a single centre was used for the ECMO treatment group. Therefore this procedure should only be used with special arrangements for clinical governance, consent and research.

**American Heart Association (AHA)**

In 2015, the AHA issued updated guidelines on cardiopulmonary resuscitation (CPR) and emergency cardiovascular care, which included a new systematic review of the evidence for ECPR and recommendations about the use of ECPR for adults with in- or out-of-hospital cardiac arrest.⁵⁴

The guidelines make the following recommendations related to ECPR:

There is insufficient evidence to recommend the routine use of ECPR for patients with cardiac arrest. In settings where it can be rapidly implemented, ECPR may be considered for select cardiac arrest patients for whom the suspected etiology of the cardiac arrest is potentially reversible during a limited period of mechanical cardiorespiratory support” (Class IIb, level of evidence C—limited data).

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
Regulatory Status

The regulatory status of ECMO devices is complex. Historically, the U.S. Food and Drug Administration (FDA) evaluated the components of an ECMO circuit separately, and the ECMO oxygenator has been considered the primary component of the circuit.

ECMO Oxygenator

The ECMO oxygenator (membrane lung, FDA product code: BYS), defined as a device used to provide to a patient for extracorporeal blood oxygenation for more than 24 hours, has been classified as a class III device but cleared for marketing by FDA through the preamendment 510(k) process (for devices legally marketed in the United States before May 28, 1976, which are considered “grandfathered” devices not requiring a 510(k) approval).

In 1977, the Membrane Lung (William Harvey Life Products), for long-term respiratory support, was cleared for marketing by FDA through the 510(k) process.

In 1979, FDA reclassified the membrane lung as a class III device, but that designation has since been reversed (see Regulatory Changes section).

ECMO procedures can also be performed using cardiopulmonary bypass (CPB) circuit devices on an off-label basis. Multiple CPB oxygenators have been cleared for marketing by FDA through the 510(k) process (FDA product code: DTZ).

Other ECMO Components

FDA also regulates other components of the ECMO circuit through the 510(k) process, including the arterial filter (FDA product code DTM), the roller pump (FDA product code DWB), the tubing (FDA product code DWE), the reservoir (FDA product code DTN), and the centrifugal pump (FDA product code KFM).

Several dual-lumen catheters have approval for use during extracorporeal life support (eg, Kendall Veno-Venous Dual-Lumen Infant ECMO Catheter; Origen Dual Lumen Cannulas; Avalon Elite Bi-Caval Dual Lumen Catheter).
Regulatory Changes

FDA has convened several advisory committees to discuss the classification of the ECMO oxygenator and other components. On January 8, 2013, FDA issued a proposed order to make the class III (premarket approval) ECMO devices class II (special controls) subject to 510(k) premarket notification. On September 12, 2013, the FDA reviewed the classification of the membrane lung for long-term pulmonary support specifically for pediatric cardiopulmonary and failure-to-wean from cardiac bypass patient population. The committee approved the FDA’s proposed premarket regulatory classification strategy for extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support to reclassify from class III to class II for conditions in which an acute (reversible) condition prevents the patient’s own body from providing the physiologic gas exchange needed to sustain life in conditions where imminent death is threatened by respiratory failure (eg, meconium aspiration, congenital diaphragmatic hernia, pulmonary hypertension) in neonates and infants, or cardiorespiratory failure (resulting in the inability to separate from cardiopulmonary bypass following cardiac surgery) in pediatric patients. The committee agreed with the proposed reclassification of ECMO devices from class III to class II for conditions where imminent death is threatened by cardiopulmonary failure in neonates and infants or where cardiopulmonary failure results in the inability to separate from cardiopulmonary bypass following cardiac surgery. As of February 12, 2016, the proposed order was approved.4

On May 7, 2014, the FDA convened an advisory committee to discuss the classification of the ECMO oxygenator for adult pulmonary and cardiopulmonary indications and to discuss the overall classification of the ECMO components. FDA’s Center for Devices and Radiological Health proposed a classification regulation to change the title of the regulation from “Membrane Lung for Long-Term Pulmonary Support” to “Extracorporeal Circuit and Accessories for Long-Term Pulmonary/Cardiopulmonary Support,” move the regulation from an anesthesia device regulation to a cardiovascular device regulation, and to define “long-term” as extracorporeal support longer than 6 hours. These proposals were approved as of February 12, 2016.

References


36. Schechter MA, Ganapathi AM, Englum BR, et al. Spontaneously breathing extracorporeal membrane oxygenation support provides the optimal bridge to lung transplantation. Transplantation. Dec 2016;100(12):2699-2704. PMID 26910331


### History

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<td>03/10/15</td>
<td>New Policy. Policy created with literature review through July 28, 2014, and review of clinical input. ECMO for adults considered medically necessary for acute respiratory failure meeting criteria outlined in policy guidelines and as a bridge to heart, lung, and heart-lung transplant, and investigational for other indications.</td>
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Email AppealsDepartmentinquines@Premera.com

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
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