Extracorporeal Membrane Oxygenation for Adult Conditions

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 the 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 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) may be considered medically necessary for the management of adults with acute respiratory failure when all of the following criteria are met:  
- Respiratory failure is due to a potentially reversible etiology  
  (see below)  
AND  
- Respiratory failure is severe, as determined by 1 of the following:  
  o A standardized severity instrument such as the Murray score (see below)  
  OR  
  o One of the criteria for respiratory failure severity outlined below  
AND  
- None of the following contraindications are present:  
  o High ventilator pressure (peak inspiratory pressure >30 cm H$_2$O) or high fraction of inspired oxygen (>80%) ventilation for more than 168 hours  
  o Signs of intracranial bleeding  
  o Multisystem organ failure  
  o Prior (ie, before onset of need for ECMO) diagnosis of a terminal condition with expected survival less than 6 months  
  o A do-not-resuscitate directive  
  o Cardiac decompensation in a patient has already been declined for ventricular assist device or transplant  
  o Known neurologic devastation without potential to recover meaningful function  
  o 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
<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>optimal conventional therapy.</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracorporeal membrane oxygenation (ECMO)</td>
<td>The use of ECMO in adult patients is considered investigational when the above criteria are not met, including but not limited to:</td>
</tr>
<tr>
<td></td>
<td>• Acute and refractory cardiogenic shock</td>
</tr>
<tr>
<td></td>
<td>• As an adjunct to cardiopulmonary resuscitation</td>
</tr>
</tbody>
</table>

**Note:** Extracorporeal membrane oxygenation (ECMO) is considered investigational for most cases of cardiogenic shock. However, in individual clinical situations, ECMO may be considered beneficial or 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.

### Documentation Requirements

The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:

- Clinical documentation that the Respiratory failure of an adult patient is due to any of the following reversible causes:
  - Acute respiratory distress syndrome (ARDS)
  - Acute pulmonary edema
  - Acute chest trauma
  - Infectious and noninfectious pneumonia
  - Pulmonary hemorrhage
  - Pulmonary embolism
  - Asthma exacerbation
  - Aspiration pneumonitis
  **AND**

- Evidence of severe respiratory failure based on:
  - A standardized severity instrument such as the Murray score
  **OR**
Documentation Requirements

- One of the criteria for respiratory failure severity outlined below:
  - Uncompensated hypercapnia with a pH less than 7.2; or
  - PaO$_2$/FiO$_2$ of <100 mm Hg on fraction of inspired oxygen (FiO$_2$) >90%; or
  - Inability to maintain airway plateau pressure (Pplat) <30 cm H$_2$O despite a tidal volume of 4 to 6 mL/kg ideal body weight; or
  - Oxygenation Index >30: Oxygenation Index = FiO$_2$ x 100 x MAP/PaO$_2$ mm Hg (where FiO$_2$ x 100 = FiO$_2$ as percentage; MAP = mean airway pressure in cm H$_2$O; PaO$_2$=partial pressure of oxygen in arterial blood); or
  - CO$_2$ retention despite high Pplat (>30 cm H$_2$O)

AND

- None of the following contraindications are present:
  - High ventilator pressure (peak inspiratory pressure >30 cm H$_2$O) or high fraction of inspired oxygen (>80%) ventilation for more than 168 hours
  - Signs of intracranial bleeding
  - Multisystem organ failure
  - Prior (ie, before onset of need for ECMO) diagnosis of a terminal condition with expected survival less than 6 months
  - A do-not-resuscitate directive
  - Cardiac decompensation in a patient has already been declined for ventricular assist device or transplant
  - Known neurologic devastation without potential to recover meaningful function
  - Determination of care *futility*

Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<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)</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</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>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).
Applications and Definitions

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

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:

- 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 revised in 2012 by the European Society of Intensive Care Medicine, with endorsement from the American Thoracic Society and the Society of Critical Care Medicine, into 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 (ARDS Definition Task Force et al, 2012). 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 (CT or CXR)</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>
</tbody>
</table>

**Oxygenation**

<table>
<thead>
<tr>
<th>Level</th>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<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>
<td>$&lt; 300 \text{ mm Hg}$</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>
<td>$\leq 200 \text{ mm Hg}$</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>
<td>$\leq 100 \text{ mmHg}$</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 Lung Injury Score**

One commonly used system for classifying the severity of respiratory failure is the Murray Lung Injury Score, which was developed for use in ARDS but has been applied to other indications. This score includes 4 scales, each of which is scored from 0 to 4. A final score is obtained by dividing the collective score by the number of scales used. A score of 0 indicates no lung injury; a score of 1 to 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>
</tbody>
</table>
Alternative Respiratory Failure Severity Criteria

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

- Uncompensated hypercapnia with a pH less than 7.2; or
- PaO₂/FiO₂ of <100 mm Hg on fraction of inspired oxygen (FiO₂) >90%; or
- Inability to maintain airway plateau pressure (Pplat) <30 cm H₂O despite a tidal volume of 4 to 6 mL/kg ideal body weight; or
- Oxygenation Index >30: Oxygenation Index = FiO₂ x 100 x MAP/PaO₂ mm Hg (where FiO₂ x 100 = FiO₂ as percentage; MAP = mean airway pressure in cm H₂O; PaO₂=partial pressure of oxygen in arterial blood); or
- CO₂ retention despite high Pplat (>30 cm H₂O)

Assessment of ECMO Futility

Patients undergoing ECMO treatment should be periodically reassessed for clinical improvement. ECMO should not be continued indefinitely if the following criteria are met:
• Neurologic devastation as defined by the following:
  o Consensus from 2 attending physicians that there is no likelihood of an outcome better than “persistent vegetative state” at 6 months

  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 computed tomography, electroencephalography, 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

• Presumed end-stage cardiac or lung failure without “exit” plan (ie, declined for assist device and/or transplantation)

Evidence Review

Description

Extracorporeal membrane oxygenation (ECMO) provides extracorporeal circulation and physiologic gas exchange for temporary cardiorespiratory support in cases of severe respiratory and cardiorespiratory failure. ECMO has generally been used in clinical situations in which there is respiratory or cardiac failure, or both, in which death would be imminent unless medical interventions can immediately reverse the underlying disease process, or physiologic functions
can be supported long enough that normal reparative processes or treatment can occur (eg, resolution of acute respiratory distress syndrome, treatment of infection) or other life-saving intervention can be delivered (eg, provision of a lung transplant). Potential indications for ECMO in the adults include acute, potentially reversible respiratory failure due to a variety of causes; as a bridge to lung transplant; in potentially reversible cardiogenic shock; and as an adjunct to cardiopulmonary resuscitation (ECMO-assisted cardiopulmonary resuscitation [ECPR]).

**Background**

*Extracorporeal Membrane Oxygenation*

Extracorporeal membrane oxygenation (ECMO) provides extracorporeal circulation and physiologic gas exchange for temporary cardiorespiratory support in cases of severe respiratory and cardiorespiratory failure. ECMO devices use an extracorporeal circuit, combining a pump and a membrane oxygenator, to undertake oxygenation of and removal of carbon dioxide from the blood.

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 and meconium aspiration syndrome. Interest has developed in the use of ECMO for cardiorespiratory support for adult conditions. Early studies of the use of ECMO for cardiorespiratory conditions, particularly severe acute respiratory distress syndrome (ARDS), included a randomized controlled trial conducted in the United Kingdom in the 1970s that showed poor survival and high complications 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 renewed. For example, during the 2009-2010 H1N1 influenza pandemic, the occurrence of influenza-related ARDS in relatively young healthy people prompted an interest of ECMO for adults.

ECMO has generally been used in clinical situations of respiratory or cardiac failure, or both. In these situations, death is imminent unless medical interventions immediately reverse the underlying disease process, physiologic functions can be supported until normal reparative processes, treatment can occur (eg, resolution of ARDS, treatment of infection), or other life-saving interventions can be delivered (eg, provision of a lung transplant).
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 (eg, H1N1 influenza infection leading to ARDS and 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 pneumonia, and a variety of other pulmonary disorders.

- **Bridge to lung transplant.** Lung transplant is used to manage chronic respiratory failure, most frequently in the setting of advanced chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, cystic fibrosis, emphysema due to α1-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. Also, patients who have undergone a transplant may require retransplantation due to graft dysfunction of the primary transplant.

- **Acute-onset cardiogenic or obstructive shock.** Acute-onset cardiogenic or obstructive shock 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.** ECMO-assisted cardiopulmonary resuscitation can be used as an adjunct to cardiopulmonary resuscitation 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 (venovenous) or VA (venoarterial). VA ECMO has the potential to provide cardiac and ventilatory support.

**Venovenous ECMO**

**Technique**

In 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 CO₂ removed, and oxygenated blood is returned to the venous circulation near the right atrium. Venous access for VV ECMO can be configured through 2 single lumen catheters (typically in the right internal jugular and femoral veins), or through 1 dual-lumen catheter in the right internal jugular vein. In the femorojugular approach, a single large multiperforated drainage cannula is inserted in the femoral vein and advanced to the cavo-atrial junction, and the return cannula is inserted into the superior vena cava via the right internal jugular vein. Alternatively, in the bi-femoral-jugular approach, drainage cannulae are placed in the superior vena cava and the inferior vena cava via the jugular and femoral veins, and a femoral return cannula is advanced to the right atrium. In the dual-lumen catheter approach, a single bicaval cannula is inserted via the right jugular vein and positioned to allow drainage from the inferior vena cava and superior vena cava and return via the right atrium.

**Indications**

VV ECMO provides only respiratory support and therefore it is used for conditions in which there is a progressive loss in the ability to provide adequate gas exchange due to abnormalities in the lung parenchyma, airways, or chest wall. Right ventricular dysfunction due to pulmonary hypertension caused by parenchymal lung disease can sometimes be effectively treated by VV ECMO. However, acute or chronic obstruction of the pulmonary vasculature (e.g., saddle pulmonary embolism) might require VA ECMO, as might cases in which right ventricular dysfunction due to pulmonary hypertension caused by severe parenchymal lung disease is severe enough. 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 VA ECMO, the ECMO oxygenator operates 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 CO$_2$ 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. Thus, it is used in situations of significant cardiac dysfunction refractory to other therapies, when significant respiratory involvement is suspected or demonstrated, such as treatment-resistant cardiogenic shock, pulmonary embolism, or primary parenchymal lung disease severe enough to compromise right heart function. Echocardiography should be used before ECMO is considered or started to identify severe left ventricular dysfunction that might necessitate the use of VA ECMO. The use of peripheral VA ECMO in the presence of adequate cardiac function may cause severe hypoxia in the upper part of the body (brain and heart) in the setting of a severe pulmonary shunt.

Extracorporeal Carbon Dioxide Removal

Also, to complete ECMO systems, there are ventilation support devices that provide oxygenation and removal of CO$_2$ 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 U. S. Food and Drug Administration (FDA) approval for use in the United States. These technologies are not the focus of this policy but are briefly described because there is overlap in patient populations treated with extracorporeal carbon dioxide removal 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 through the ECMO circuits, other systems use pumpless systems to remove CO$_2$. These pumpless devices achieve extracorporeal carbon dioxide removal 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 CO$_2$ removal, dedicated extracorporeal carbon dioxide 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, and 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.

ECMO may be associated with significant complications, which can be related to the vascular access needed for systemic anticoagulation, including hemorrhage, limb ischemia, compartment syndrome, cannula thrombosis, and limb amputation. Patients are also at risk of progression of their underlying disease.

**Outcome Measures**

Outcomes should include short- and long-term mortality, along with measures of significant morbidity (eg, intracranial hemorrhage, thrombosis, vascular access site hemorrhage, limb ischemia) and short- and long-term disability and quality-of-life measures.

**Summary of Evidence**

For adults with acute respiratory failure who receive ECMO, the evidence includes randomized controlled trials, systematic reviews, nonrandomized comparative studies, and case series. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related mortality and morbidity. The most direct evidence on the efficacy of ECMO in adult respiratory failure comes from the CESAR trial. Although this trial had limitations, including nonstandardized management of the control group and unequal intensity of treatment between treatment and control groups, for the trial’s primary outcome (disability-free survival at 6 months), there was a large effect size, with an absolute risk reduction in mortality of 16.25%. Recent nonrandomized comparative studies have generally reported 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 patient selection criteria 
outlined in the CESAR trial. However, questions remain about the generalizability of findings to 
other patient populations, and additional clinical trials in more specific patient populations are 
needed. The evidence is sufficient to determine 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 lung transplantation, 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 the successful bridge to transplant on the order of 70% to 80%. Given the lack 
of other treatment options for this population and the suggestive clinical evidence ECMO may 
be an appropriate therapy for this patient population, the evidence is sufficient to determine the 
effects of the technology on health outcomes.

For adults with acute cardiac failure who receive ECMO, the ev 
idence includes meta-
analyses, 
observational studies, 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 with postcardiotomy failure to wean off bypass 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 have reported 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 in cardiac arrest who receive ECPR, the evidence includes systematic reviews, 
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 addressed 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 with standard cardiopulmonary 
resuscitation, using propensity score matching. It reported higher rates of survival to discharge, 
with minimal neurologic impairment with ECPR. Other nonrandomized studies have reported 
better survival in ECPR groups. However, the benefit associated with using ECPR is uncertain 
given the potential for bias in nonrandomized studies. Additionally, factors related to the
implementation of ECPR procedures in practice need better delineation. The evidence is insufficient to determine the effects of the technology on health outcomes.

## Ongoing and Unpublished Clinical Trials

Current ongoing 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><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01470703</td>
<td>Extracorporeal Membrane Oxygenation(ECMO) for Severe Acute Respiratory Distress Syndrome (ARDS)</td>
<td>331</td>
<td>Feb 2018 (ongoing)</td>
</tr>
<tr>
<td>NCT01605409</td>
<td>Emergency Cardiopulmonary Bypass After Cardiac Arrest With Ongoing Cardiopulmonary Resuscitation – a Pilot Randomized Trial</td>
<td>40</td>
<td>May 2018</td>
</tr>
<tr>
<td>NCT01511666</td>
<td>Hyperinvasive Approach to Out-of Hospital Cardiac Arrest Using Mechanical Chest Compression Device, Prehospital Intraarrest Cooling, Extracorporeal Life Support and Early Invasive Assessment Compared to Standard of Care. “Prague OHCA Study”</td>
<td>170</td>
<td>May 2018</td>
</tr>
<tr>
<td>NCT01992237</td>
<td>Pilot Study of Measuring Energy Expenditure in ECMO Patients Under Consideration of Type of Ventilation and to Approximate Cardiac Output</td>
<td>40</td>
<td>Jun 2018</td>
</tr>
<tr>
<td>NCT02870946</td>
<td>The Effect of Simultaneous Renal Replacement Therapy on Extracorporeal Membrane Oxygenation Support for Cardiogenic Shock Patients</td>
<td>262</td>
<td>Dec 2018</td>
</tr>
<tr>
<td>NCT03210818</td>
<td>Effects of Adjustment of Blood Flow of Venoarterial Extracorporeal Membrane Oxygenation Life Support on Microcirculation</td>
<td>50</td>
<td>Mar 2019</td>
</tr>
<tr>
<td>NCT02527031</td>
<td>A Comparative Study Between a Pre-hospital and an In-hospital Circulatory Support Strategy (Extracorporeal Membrane Oxygenation) in Refractory Cardiac Arrest</td>
<td>210</td>
<td>Mar 2019</td>
</tr>
<tr>
<td>NCT02754193</td>
<td>Effects of Induced Moderate Hypothermia on Mortality in Cardiogenic Shock Patients Rescued by Venoarterial Extra</td>
<td>334</td>
<td>Sep 2019</td>
</tr>
</tbody>
</table>
### NCT No. | Trial Name | Planned Enrollment | Completion Date
---|---|---|---
NCT02301819 | Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock | 120 | Sep 2019

**Unpublished**

NCT01990456 | Strategies for Optimal Lung Ventilation in ECMO for ARDS: The SOLVE ARDS Study | 20 | Dec 2015 (unknown)

NCT: national clinical trial

---

**Clinical Input Received from Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, 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 input was received from 3 physician specialty societies, 1 of which provided 2 responses and 1 of which provided 2 responses and a consensus letter, and 2 academic medical centers, 1 of which provided 3 responses, while this policy was under review in 2015. There was a consensus that extracorporeal membrane oxygenation (ECMO) is medically necessary for adults with respiratory failure that is severe and potentially reversible. There was a 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 a consensus that ECMO is investigational as an adjunct to cardiopulmonary resuscitation.

---

**Practice Guidelines and Position Statements**

*The Extracorporeal Life Support Organization*

The Extracorporeal Life Support Organization provides education, training, and guidelines related to the use of extracorporeal membrane oxygenation (EMCO), along with supporting research and an ECMO patient registry. In addition to general guidelines that describe ECMO, Extracorporeal Life Support Organization has published specific recommendations in 2013.
related to use of ECMO in adult respiratory failure, adult cardiac failure, and in adult ECMO-assisted cardiopulmonary resuscitation (ECPR), which are outlined in Table 4.\textsuperscript{77-79} 

### Table 4: Guidelines for Use of ECMO in Adults

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Indications</th>
<th>Contraindications</th>
<th>Relative contraindications</th>
</tr>
</thead>
</table>
| **Adult respiratory failure**\textsuperscript{77} | 1. In hypoxic respiratory failure due to any cause (primary or secondary) ECLS should be considered when the risk of mortality is $\geq50\%$, and is indicated when the risk of mortality is $\geq80\%$.  
   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 $\geq6$ 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) | Absolute contraindications:  
1. Mechanical ventilation at high settings ($\text{FiO}_2 > 0.9$, Pplat $> 30$) for $\geq 7$ d  
2. Major pharmacologic immunosuppression (absolute neutrophil count $< 400/(\text{mm}^3)$)  
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**\textsuperscript{78} | 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, myocarditis, peripartum cardiomyopathy, decompensated chronic heart failure, postcardiotomy shock. | 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 perfusion.  
Relative contraindications: |
<table>
<thead>
<tr>
<th>Conditions</th>
<th>Indications</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Contraindication for anticoagulation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Advanced age (Note: advanced age appears in both relative and absolute contraindication lists).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Obesity.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Septic shock is an indication in some centers.</td>
<td></td>
<td></td>
</tr>
<tr>
<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>
<td></td>
<td></td>
</tr>
<tr>
<td>1. All contraindications to ECMO use (eg, gestational age &lt;34 wk) should apply to ECPR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Do-not-resuscitate orders</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**International ECMO Network**

The International ECMO Network (2014), with endorsement by Extracorporeal Life Support Organization, (2014) published a position paper detailing institutional, staffing, and reporting requirements for facilities providing ECMO.80

**National Institute for Health and Care Excellence**

The National Institute for Health and Care Excellence (2014) issued guidance on the use of ECMO for acute heart failure in adults, which made the following recommendations81:

- 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.

Previously, in 2011, the Institute issued guidance on the use of ECMO 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.

**American Heart Association**

The American Heart Association (2015) issued its updated guidelines on cardiopulmonary resuscitation and emergency cardiovascular care, which included a new systematic review of the evidence for ECPR and recommendations on the use of ECPR for adults with in- or out-of-hospital cardiac arrest.\(^5\) The guidelines made 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. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Regulatory Status**

The regulatory status of ECMO devices is complex. Historically, FDA evaluated the components of an ECMO circuit separately, with the ECMO oxygenator 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 a patient with 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 circuit devices on an off-label basis. Multiple cardiopulmonary bypass 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 reclassify ECMO devices from class III to class II (special controls) subject to 510(k) premarket notification. On September 12, 2013, 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. FDA approved a 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 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. FDA also 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. Considered was a reclassification of the regulation from “Membrane Lung for Long-Term Pulmonary Support” to “Extracorporeal Circuit and Accessories for Long-Term Pulmonary/Cardiopulmonary Support,” moving the regulation from an anesthesia device regulation to cardiovascular device regulation and defining “long-term” as extracorporeal support longer than 6 hours. These proposals were approved as of February 12, 2016.

References


37. 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

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<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>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2018 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
- Provides free aids and services to people with disabilities to communicate effectively with you, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5952. TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue SW, Room S09F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Call 800-722-1471 (TTY: 800-842-5357).

 Arabic (Arabic):

يحيى هذا الإشعار معلومات هامة، إذ يحيى هذه المعلومات معلومات مهمة يقصدهم طلبي أو العملية التي تتيح الحصول عليها من خلال compagny Premera Blue Cross. قد تكون هناك تأثير مهمة

Oromo (Cushite):


Francais (French):


Appelez le 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):


Illoko (Ilocano):

Daytoy a Pakdaar ket nagaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket nagaon iti napateg nga impormasion maipanggep iti aplikasyon yowo coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a pelta iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramideng nga adda sangbay dagiti partikular a naituding nga adda tabaay tapo mapagatilaidyoy ti coverage ti salun-atyo wenno tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong ti bukadyo a pagasasao nga awan ti bayadanyo. Turmawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.

Chiamare 800-722-1471 (TTY: 800-842-5357).
Premera Blue Cross has important information you need to know.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important information about your coverage.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This information may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This information may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This information may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.

Premera Blue Cross

This notice may contain important dates.

Premera Blue Cross

This notification may contain important dates.