**Subject: Inhaled Nitric Oxide**

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**DESCRIPTION:**

Inhaled nitric oxide (INO) is a natural vasodilator and has been studied for a variety of types of respiratory failure. Most commonly, it is used as an initial treatment for neonates with hypoxic respiratory failure to improve oxygenation and reduce the need for invasive extracorporeal membrane oxygenation (ECMO). It is also proposed as a treatment for premature infants, critically ill children and adults with respiratory failure, as well as in the postoperative management of children undergoing repair of congenital heart disease and patients after lung transplantation to prevent or reduce reperfusion injury.

Hypoxic respiratory failure may result from respiratory distress syndrome, persistent pulmonary hypertension, meconium aspiration, pneumonia, or sepsis. Its treatment typically includes oxygen support, mechanical ventilation, induction of alkalosis, neuromuscular blockade, or sedation. INO is both a vasodilator and a mediator in many physiologic and pathologic processes. INO has also been proposed for use in preterm infants less than 34 weeks of gestation.

There are several potential uses for INO in surgery. One is the proposed use of INO to manage pulmonary hypertension after cardiac surgery in infants and children with congenital heart disease. In congenital heart disease patients, increased pulmonary blood flow can cause pulmonary hypertension. Cardiac surgery can restore the pulmonary vasculature to normal, but there is the potential for complications, including postoperative pulmonary hypertension, which can prevent weaning from ventilation and is associated with substantial morbidity and mortality. Another potential surgical application is use of INO in lung transplantation to prevent or reduce reperfusion injury.

Inhaled nitric oxide (INO) appears to be of greatest benefit in individuals for whom primary or secondary pulmonary hypertension is a component of hypoxic respiratory failure. The benefit of INO appears limited in term or near-term infants whose hypoxic respiratory failure is due to diaphragmatic hernia.
POSITION STATEMENT:
Inhaled nitric oxide meets the definition of medical necessity as a component of treatment for hypoxic respiratory failure in neonates born at more than 34 weeks of gestation.

Inhaled nitric oxide meets the definition of medical necessity for management of post-operative pulmonary hypertension in infants and children following heart or lung surgery (Exception: lung transplantation, see below).

Inhaled nitric oxide meets the definition of medical necessity as a method of assessing pulmonary vasoreactivity in children and adults with pulmonary hypertension.

Inhaled nitric oxide is considered experimental or investigational for all other indications, including but not limited to the conditions below, as data in published medical literature are inadequate to permit scientific conclusions on long-term and net health outcomes:

- Treatment of premature neonates born at less than or equal to 34 weeks of gestation with hypoxic respiratory failure
- Treatment of adults and children with acute hypoxemic respiratory failure
- Postoperative use in adults with congenital heart disease
- In lung transplantation, during and/or after graft reperfusion

BILLING/CODING INFORMATION:
There is no specific CPT or HCPCS code to report inhaled nitric oxide.

REIMBURSEMENT INFORMATION:
Refer to section entitled POSITION STATEMENT.

PROGRAM EXCEPTIONS:
Federal Employee Program (FEP): Follow FEP guidelines.
State Account Organization (SAO): Follow SAO guidelines.
Medicare Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:
Congenital diaphragmatic hernia (CDH): Herniation (bulging, looping) of the abdominal or retroperitoneal structures into the thorax, present at birth.

Hypoxic respiratory failure: A condition of under-oxygenation; an inadequate level of tissue oxygenation for cellular metabolism. Symptoms include dyspnea and tachypnea.

Hypoxemia: abnormally low arterial oxygen levels.

Meconium: A fetus or newborn’s first feces (a dark green mucous material); typically passed in the uterus during early pregnancy and again in the first few days after birth.
**Meconium aspiration syndrome (MAS):** Inhalation of meconium by the fetus or newborn, which may block the newborn’s airways right after birth. It can cause respiratory difficulty due to inflammation in the lungs after birth.

**Pulmonary hypertension:** High blood pressure in the arteries to the lungs. The blood vessels that carry blood from the heart to the lungs become hard and narrow, causing the heart to work harder to pump the blood. Over time, the heart weakens and cannot do its job, resulting in heart failure.

**Neonatal respiratory distress syndrome (RDS):** Condition of the newborn marked by dyspnea with cyanosis, often caused by a lack of surfactant in the lungs, or by genetic problems with lung development.

**RELATED GUIDELINES:**
None applicable.

**OTHER:**
GeNOsyl™ MV-1000
INOmax®

**REFERENCES:**


15. ClinicalTrials.gov. NCT02652429: Long-Term Extension Study of Inhaled Nitric Oxide (iNO) for PAH. Bellerophon Pulse Technologies (August 2017).


COMMITTEE APPROVAL:
This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy & Coverage Committee on 09/26/19.

GUIDELINE UPDATE INFORMATION:

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<tr>
<th>Date</th>
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<tbody>
<tr>
<td>04/15/01</td>
<td>New Medical Coverage Guideline.</td>
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<tr>
<td>09/27/01</td>
<td>Medical Coverage Guideline reviewed.</td>
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<tr>
<td>01/01/02</td>
<td>HCPCS changes.</td>
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<tr>
<td>10/15/03</td>
<td>Scheduled review; no change in coverage statement.</td>
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<tr>
<td>01/15/06</td>
<td>Revision - additional reference added.</td>
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<tr>
<td>04/01/07</td>
<td>2nd Quarter HCPCS coding update; deleted S1025.</td>
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<tr>
<td>12/15/17</td>
<td>Medical Coverage Guideline returned to active status. Revised MCG title, description section, position statement, program exceptions, and definitions. Updated references.</td>
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<tr>
<td>10/15/18</td>
<td>Unscheduled review. Revised position statement; added coverage for post-operative pulmonary hypertension and assessment of pulmonary vasoreactivity. Updated references.</td>
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<tr>
<td>10/15/19</td>
<td>Scheduled review. Maintained position statement, revised index terms, and updated references.</td>
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