Medical Policy
Inhaled Nitric Oxide

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Policy Number: 100
BCBSA Reference Number: 8.01.37
NCD/LCD: N/A

Related Policies
None

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Inhaled nitric oxide may be MEDICALLY NECESSARY as a component of treatment of hypoxic respiratory failure in neonates born at 34 or more weeks of gestation.

Other indications for inhaled nitric oxide are INVESTIGATIONAL including, but not limited to:
- 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 and children with congenital heart disease
- In lung transplantation, during and/or after graft reperfusion.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
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<tr>
<th>Outpatient</th>
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<tr>
<td>Commercial Managed Care (HMO and POS)</td>
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<td>Commercial PPO and Indemnity</td>
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<td>Medicare HMO BlueSM</td>
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CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes
There is no specific CPT code for this service.

Description
Inhaled nitric oxide (INO) has been proposed to reduce hypoxic respiratory failure in neonates and for several other applications.

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. Extracorporeal membrane oxygenation is an invasive technique that may be considered in neonates when other therapies fail. Inhaled nitric oxide (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.

Another potential application of INO is to improve oxygenation in patients with acute hypoxemic respiratory failure, including acute respiratory distress syndrome and acute lung injury. These conditions are associated with inflammation of the alveolar-capillary membrane, which leads to hypoxemia and pulmonary hypertension.

In addition, there are several potential uses 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.

INOmax, a commercially available INO product, has been approved by the U.S. Food and Drug Administration for use in term and near-term neonates with hypoxic respiratory failure along with respiratory support and other appropriate treatments.

Summary
Inhaled nitric oxide (INO), a treatment for neonates who have hypoxic respiratory failure, is intended to improve oxygenation, reduce mortality rates, and reduce the need for invasive extracorporeal membrane oxygenation (ECMO). It is also proposed as a treatment for premature infants, critically ill children, adults with respiratory failure, in the postoperative management of children undergoing repair of congenital heart disease and in lung transplantation to prevent or reduce reperfusion injury.

For individuals who are neonates and are term or near-term at birth and have hypoxic respiratory failure who receive INO, the evidence includes randomized controlled trials (RCTs) and a systematic review. Relevant outcomes are overall survival, hospitalizations, resource utilization, and treatment-related morbidity. Evidence from RCTs and a meta-analysis support the use of INO in term or near-term infants.

Pooled analyses of RCT data have found that INO leads to a significant reduction in the need for ECMO and in the combined outcome of ECMO or death. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.
For individuals who are neonates and are premature at birth and have hypoxic respiratory failure who receive INO, the evidence includes RCTs and systematic reviews. Relevant outcomes are overall survival, hospitalizations, resource utilization, and treatment-related morbidity. A large number of RCTs have evaluated INO for premature neonates, and most trials have reported no significant difference on primary end points such as mortality and bronchopulmonary dysplasia. Systematic reviews have not found better outcomes with INO than placebo or other control interventions in premature neonates. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have acute hypoxemic respiratory failure (non-neonates) who receive INO, the evidence includes RCTs and systematic reviews. Relevant outcomes are overall survival, hospitalizations, resource utilization, and treatment-related morbidity. Several systematic reviews of RCTs have not found that this significantly impacts mortality or duration of mechanical ventilation in adults or children with acute hypoxic respiratory failure. One 2015 RCT in children with acute respiratory distress syndrome found significantly better ECMO-free survival but not overall survival in children who received INO versus placebo gas. Given the large body of literature showing a lack of benefit in patients of various ages, the 2015 RCT does not provide sufficient new data to conclude that INO improves the net health outcome in this subgroup of patients. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have congenital heart disease who underwent heart surgery who receive INO, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, hospitalizations, resource utilization, and treatment-related morbidity. Evidence from a number of small RCTs and a systematic review of these trials did not find a significant benefit for INO on mortality and other health outcomes in the postoperative management of children with congenital heart disease. There is less evidence on INO for adults with congenital heart disease. One RCT found that treatment with INO did not improve postoperative outcomes in adults with congestive heart failure. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have lung transplant who receive INO, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, hospitalizations, resource utilization, and treatment-related morbidity. Several small RCTs have evaluated INO after lung transplantation and have not found statistically significant improvement in health outcomes. A systematic review of RCTs and observational studies concluded that there is insufficient evidence to support routine use of INO after lung transplant. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

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<th>Date</th>
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<tr>
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<td>New references added from BCBSA National medical policy.</td>
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<td>12/2014</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References