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Next Review 7/6/2024

Area Medical Policy  
Lines Of Business All Lines of Business

## Inhaled Nitric Oxide (iNO)

### PURPOSE:

This policy is intended to address the medical necessity criteria of inhaled nitric oxide.

### DEFINITIONS:

**Nitric Oxide:** Nitric oxide (NO) is a lipophilic gas that is readily absorbed across pulmonary membranes in the ventilated lung after inhalation. Following absorption, iNO selectively induces pulmonary vasodilation, while leaving systematic vasculature resistance unaffected.

**Pulmonary Hypertension (PH)** occurs when blood vessels to the lungs develop an increased amount of muscle in the wall of the blood vessels. When the pressure in this artery gets too high, the arteries in the lungs can narrow and then the blood does not flow as well as it should, resulting in less oxygen in the blood. PH is defined by a mean pulmonary artery pressure  $\geq 25$  mm Hg at rest, measured during right heart catheterization.

### POLICY POSITION:

#### Indications/Inclusions:

Requests for iNO therapy services meeting **ANY** of the following criteria may be considered medically necessary:

1. As a component of the treatment of hypoxic respiratory failure *OR* when echocardiographic evidence of persistent pulmonary hypertension of the newborn (PPHN) is present in:
  - a. Neonates 34 weeks gestation or greater with
    - i. the absence of congenital diaphragmatic hernia; **and**
    - ii. when conventional therapies such as administration of high concentrations of oxygen, hyperventilation, high-frequency ventilation, the

induction of alkalosis, neuromuscular blockade, and sedation have failed or are expected to fail.

2. For post-operative management of pulmonary hypertensive crisis in infants and children with congenital heart disease.
3. As a diagnostic method of assessing pulmonary vaso-reactivity in individuals with pulmonary hypertension.

iNO therapy that does not meet the above criteria is considered experimental/investigational because safety and efficacy has not been established by peer-reviewed literature.

All requests for inhaled nitric oxide (iNO) therapy services require medical necessity review and comment by a medical director.

## **Contraindications, exclusions and/or experimental/investigational indications:**

Requests for iNO therapy services meeting **ANY** of the following criteria are considered **NOT** medically necessary, and therefore non-covered:

1. Acute bronchiolitis.
2. Acute hypoxemic respiratory failure in children (other than those who meet the medical necessity criteria above) and in adults.
3. Acute pulmonary embolism.
4. Acute respiratory distress syndrome or acute lung injury\*.
  - a. \*Including COVID-19 related ARDS
5. Bronchopulmonary dysplasia, prevention in preterm infants without hypoxic respiratory failure.
6. Lung transplantation, prevention of ischemia-reperfusion injury/acute rejection following lung transplantation.
7. Malaria, adjunctive treatment.
8. Pulmonary arterial hypertension (PAH) in adults.
9. Respiratory failure in preterm newborns (< 35 weeks gestational age) when given with conventional management as:
  - a. Early rescue within the first three days of life
  - b. After the first three days of life due to increased risk of bronchopulmonary dysplasia
  - c. Routine prophylaxis in those requiring respiratory support
10. Sickle cell disease, treatment of vaso-occlusive crises or acute chest syndrome (sickle cell vasculopathy).
11. Treatment of mycobacterium and pseudomonas aeruginosa infections in persons with cystic fibrosis.
12. Treatment of persons with congenital diaphragmatic hernia.

13. Treatment of pulmonary hypertension associated with pulmonary fibrosis.
14. Treatment of right heart failure after hemorrhagic shock and trauma pneumonectomy.
15. Treatment of traumatic brain injury.

## CODING:

Code	Description
<b>94363</b>	Pharmacologic agent administration (eg, inhaled nitric oxide, intravenous infusion of nitroprusside, dobutamine, milrinone, or other agent) including assessing hemodynamic measurements before, during, after and repeat pharmacologic agent administration, when performed (List separately in addition to code for primary procedure)
<b>94799</b>	Unlisted pulmonary service or procedure

Covered Diagnosis Codes:

ICD-10 Code	Description
I27.0	Primary pulmonary hypertension
I27.20 - I27.29	Other secondary pulmonary hypertension
P07.20 - P07.39	Disorders of newborn related to short gestation
P22.0	Respiratory distress syndrome of newborn
P28.5	Respiratory failure of newborn
P29.30 - P29.38	Persistent fetal circulation
P36.0 - P36.9	Bacterial sepsis of newborn
P84	Other problems with newborn [birth asphyxia]
P91.60 - P91.63	Hypoxic ischemic encephalopathy [HIE]
Q33.1	Accessory lobe of lung
Q33.2	Sequestration of lung
Q33.3	Agenesis of lung
Q33.4	Congenital bronchiectasis
Q33.5	Ectopic tissue in lung
Q33.6	Congenital hypoplasia and dysplasia of lung
Q33.8	Other congenital malformations of lung
Q33.9	Congenital malformation of lung, unspecified

## REFERENCES:

Abman SH, Hansmann G, Archer SL, et al; American Heart Association Council on Cardiopulmonary,

Critical Care, Perioperative and Resuscitation; Council on Clinical Cardiology; Council on Cardiovascular Disease in the Young; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Surgery and Anesthesia; and the American Thoracic Society. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.

Acute respiratory distress syndrome: Supportive care and oxygenation in adults. UpToDate® Web Database. Uptodate.com. Accessed 4/23/2021.

Barrington KJ, Finer N, Pennaforte T. Inhaled nitric oxide for respiratory failure in preterm infants. *Cochrane Database Syst Rev*. 2017b Jan 3;1:CD000509. PMID: PMC6464861.

Hayes Inc. Health Technology Assessment. Inhaled nitric oxide for the treatment of respiratory failure in preterm newborns. Lansdale, PA: Hayes, Inc. November 6, 2018, reviewed December 14, 2021. Accessed July 11, 2022.

Inhaled nitric oxide in adults: Biology and indications for use. UpToDate® Web Database. Uptodate.com. Accessed 4/20/2021.

Optum360® EncoderPro.com for Payers Professional. Web Database. encoderprofp.com. Accessed 4/19/2021.

Persistent pulmonary hypertension of the newborn. UpToDate® Web Database. Uptodate.com. Accessed 4/23/2021.

Wang X, Li B, Ma Y, et al. Effect of NO inhalation on ECMO use rate and mortality in infants born at or near term with respiratory failure. *Medicine (Baltimore)*. 2019 Oct;98(41):e17139. PMID: PMC6799754.

Adhikari NK, Dellinger RP, Lundin S, et al. Inhaled nitric oxide does not reduce mortality in patients with acute respiratory distress syndrome regardless of severity: systematic review and meta-analysis. *Crit Care Med*. 2014;42(2):404-412. doi:10.1097/CCM.0b013e3182a27909. Accessed July 11, 2022.

Bhat T, Neuman A, Tantary M, et al. Inhaled nitric oxide in acute pulmonary embolism: a systematic review. *Rev Cardiovasc Med*. 2015;16(1):1-8. doi:10.3909/ricm0718. Accessed July 11, 2022.

Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. *Pediatr Crit Care Med*. 2015 Jun;16(5):428-39. doi: 10.1097/PCC.0000000000000350. PMID: 25647235; PMID: PMC5253180. Accessed July 11, 2022.

Hoepfer MM, Bogaard HJ, Condliffe R, et al. Definitions and diagnosis of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62(25 Suppl):D42-D50. doi:10.1016/j.jacc.2013.10.032. Accessed July 11, 2022.

Centers for Disease Control and Prevention. Heart Disease: Pulmonary Hypertension. Reviewed December 3, 2019. Accessed July 11, 2022.

Karam O, Gebistorf F, Wetterslev J, Afshari A. The effect of inhaled nitric oxide in acute respiratory distress syndrome in children and adults: a Cochrane Systematic Review with trial sequential analysis. *Anaesthesia*. 2017;72(1):106-117. doi:10.1111/anae.13628. Accessed June 8, 2023.

Shin SS, Hwang M, Diaz-Arrastia R, Kilbaugh TJ. Inhalational Gases for Neuroprotection in Traumatic Brain Injury. *J Neurotrauma*. 2021;38(19):2634-2651. doi:10.1089/neu.2021.0053. Accessed June 8, 2023.

## POLICY HISTORY:

Date	Description of Changes
7/1/2022	Annual review. Removed "coverage policy" from title. Removed medical policy guidance section. Added policy purpose and definitions sections. Updated formatting, added diagnosis codes, and updated references.
6/28/2023	Annual Review: Corrected typos. Added criteria for vaso-reactivity testing. Added "peer-reviewed literature" to E/I statement. Added traumatic brain injury to list of E/I indications.

## POST-PAYMENT AUDIT STATEMENT:

The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by THP at any time pursuant to the terms of your provider agreement.

## DISCLAIMER:

This policy is intended to serve as a guideline only and does not constitute medical advice, any guarantee of payment, plan pre-authorization, an explanation of benefits, or a contract. This policy is intended to address medical necessity guidelines that are suitable for most individuals. Each individual's unique clinical situation may warrant individual consideration based on medical records. Individual claims may be affected by other factors, including but not necessarily limited to state and federal laws and regulations, legislative mandates, provider contract terms, and THP's professional judgment. Reimbursement for any services shall be subject to member benefits and eligibility on the date of service, medical necessity, adherence to plan policies and procedures, claims editing logic, provider contractual agreement, and applicable referral, authorization, notification, and utilization management guidelines. Unless otherwise noted within the policy, THP's policies apply to both participating and non-participating providers and facilities. THP reserves the right to review and revise these policies periodically as it deems necessary in its discretion, and it is subject to change or termination at any time by THP. THP has full and final discretionary authority for its interpretation and application. Accordingly, THP may use reasonable discretion in interpreting and applying this policy to health care services provided in any particular case.

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## All Revision Dates

7/7/2023, 9/13/2022, 5/19/2021