



## MEDICAL COVERAGE POLICY

**SERVICE:** Inhaled Nitric Oxide in Preterm Infants

**Policy Number:** 217

**Effective Date:** 09/01/2024

**Last Review:** 08/12/2024

**Next Review:** 08/12/2025

**Important note:** Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.

**SERVICE:** Inhaled Nitric Oxide Use in Preterm Infants

**PRIOR AUTHORIZATION:** Not required. This service is subject to retrospective review.

**POLICY:** Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

**Note:** Unless otherwise indicated (see below), this policy will apply to all lines of business.

**For Medicare plans,** please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). Medicare NCD or LCD specific InterQual criteria may be used when available. If there are no applicable NCD or LCD criteria, use the criteria set forth below.

**For Medicaid plans,** please confirm coverage as outlined in the [Texas Medicaid Provider Procedures Manual | TMHP](#) (TMPPM). If there are no applicable criteria to guide medical necessity decision making in the TMPPM, use the criteria set forth below.

**BSWHP may consider inhaled nitric oxide (iNO) medically necessary** when the following are met:

1. Hypoxic respiratory failure in a newborn  $\geq$  34 weeks gestation, AND
2. Diagnosis of pulmonary hypertension, AND
3. Absence of unrepaired congenital diaphragmatic hernia

Use of iNO therapy for more than 4 days is subject to medical necessity review.

All other indications for iNO are unproven or investigational, including, but not limited to, preterm infants with pulmonary disease.

### BACKGROUND:

Nitric oxide is a colorless, odorless, gas. iNO is a selective pulmonary vasodilator whose mechanism of action involves guanylyl cyclase activation leading to production of cyclic guanosine monophosphate and subsequent smooth muscle relaxation. There are several physiologic effects that make iNO an appealing therapy for infants with pulmonary hypertension: iNO can decrease pulmonary vascular resistance, improve ventilation-perfusion inequalities, and reduce right-to-left intra-cardiac shunting of blood through the foramen ovale and ductus arteriosus, all of which can contribute to improved arterial oxygenation and hemodynamic stability.



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INOMax™, a commercially available inhaled nitric oxide product, is FDA-approved for use in term and near-term neonates with hypoxic respiratory failure along with respiratory support and other appropriate treatments. INOMax™ received U.S. Food and Drug Administration (FDA) approval in 1999 for the following indication: “INOMax™, in conjunction with ventilatory support and other appropriate agents, is indicated for the treatment of term and near-term (>34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension.”

The primary clinical indication for iNO, in conjunction with ventilatory support and other medical interventions, is hypoxic respiratory failure secondary to persistent pulmonary hypertension in the neonate born at more than 34 weeks gestation. Persistent pulmonary hypertension (PPHN) may occur as a primary developmental defect or as a condition secondary to morbidities such as respiratory distress syndrome (i.e., hyaline membrane disease), meconium aspiration syndrome, pneumonia, sepsis, congenital diaphragmatic hernia, cardiac malformations and pulmonary hypoplasia.

The American Academy of Pediatrics (AAP) Clinical report (2014) recommendations for iNO for the treatment of neonates born at or near term with hypoxic respiratory failure included the following:

- The results of randomized controlled trials, traditional meta-analyses, and an individualized patient data meta-analysis study indicate that neither rescue nor routine use of iNO improves survival in preterm infants with respiratory failure (Evidence quality, A; Grade of recommendation, strong).
- The preponderance of evidence does not support treating preterm infants who have respiratory failure with iNO for the purpose of preventing/ameliorating BPD, severe intraventricular hemorrhage, or other neonatal morbidities (Evidence quality, A; Grade of recommendation, strong).
- The incidence of cerebral palsy, neurodevelopmental impairment, or cognitive impairment in preterm infants treated with iNO is similar to that of control infants (Evidence quality, A).
- The results of 1 multicenter, randomized controlled trial suggest that treatment with a high dose of iNO (20 ppm) beginning in the second postnatal week may provide a small reduction in the rate of BPD. However, these results need to be confirmed by other trials.
- An individual-patient data meta-analysis that included 96% of preterm infants enrolled in all published iNO trials found no statistically significant differences in iNO effect according to any of the patient-level characteristics, including gestational age, race, oxygenation index, postnatal age at enrollment, evidence of pulmonary hypertension, and mode of ventilation.
- There are limited data and inconsistent results regarding the effects of iNO treatment on pulmonary outcomes of preterm infants in early childhood.

**MANDATES:** None

### **CODES:**

**Important note:**

*Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented,*



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but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

CPT Codes	94799 – Under Pulmonary Diagnostic Testing and Therapies
CPT Not Covered	
ICD-10 codes	I27.0 - Primary pulmonary hypertension I27.2 - Secondary pulmonary hypertension P07.37 - P07.39 - Preterm newborn 34-36 complete weeks P28.5 - Respiratory failure of newborn P29.30 - Pulmonary hypertension of newborn P29.38 - Other persistent fetal circulation
ICD10 Not covered	P27.x - Chronic respiratory disease originating in the perinatal period

## POLICY HISTORY:

Status	Date	Action
New	09/24/2015	New policy
Reviewed	09/29/2016	No changes in coverage
Reviewed	09/19/2017	No changes
Reviewed	08/14/2018	No changes
Reviewed	10/31/2019	No changes
Reviewed	11/19/2020	No changes
Reviewed	12/23/2021	Updated language. No change in coverage
Reviewed	12/29/2022	No changes
Reviewed	12/29/2023	No policy changes. Added CPT Code 94799 and reformatted existing criteria. Other formatting changes and added hyperlinks to TMPPM, beginning and ending note sections updated to align with CMS requirements and business entity changes.
Reviewed	08/12/2024	No changes

## REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. American Academy of Pediatrics. Committee on Fetus and Newborn. Use of Inhaled Nitric Oxide. Recommendations. Pediatrics Vol 106, No.2, August 2000. Available at: [pediatrics.aappublications.org/content/pediatrics/106/2/344.full](https://pediatrics.aappublications.org/content/pediatrics/106/2/344.full).



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accessed 9/11/2017.

2. American Academy of Pediatrics. Committee on Fetus and Newborn. Use of inhaled nitric oxide in preterm infants. Pediatrics 2014;133:1 165-170.
3. American Association for Respiratory Care (AARC). Evidence-based clinical practice guideline: inhaled nitric oxide for neonates with acute hypoxic respiratory failure. 2010. Accessed 9/8/17. Available at URL address: <http://www.rcjournal.com/cpgs/index.cfm>
4. Cole FS, Alleyne C, Barks JD, et al. NIH Consensus Development Conference statement: inhaled nitric-oxide therapy for premature infants. Pediatrics. 2011;127(2):363–369
5. Kinsella JP, Cutter GR, Steinhorn RH, Nelin LD, Walsh WF, Finer NN, Abman SH. Noninvasive inhaled nitric oxide does not prevent bronchopulmonary dysplasia in premature newborns. J Pediatr. 2014 Dec;165(6):1104-1108.
6. Kinsella JP, Steinhorn RH, Krishnan US, Feinstein JA, Adatia I, Austin ED, Rosenzweig EB, Everett AD, Fineman JR, Hanna BD, Hopper RK, Humpl T, Ivy DD, Keller RL, Mullen MP, Raj JU, Wessel DL, Abman SH. Recommendations for the Use of Inhaled Nitric Oxide Therapy in Premature Newborns with Severe Pulmonary Hypertension.. J Pediatr. 2016 Mar;170:312-4. doi: 10.1016/j.jpeds.2015.11.050. Epub 2015 Dec 15. PMID: 26703869
7. Jiang Q, Gao X, Liu C, Chen D, Lin X, Xia S, Zhuang D, Yang C, Zhu W, Liu L, Chen C, Sun B. Early inhaled nitric oxide in preterm infants <34 weeks with evolving bronchopulmonary dysplasia. J Perinatol. 2016 Jul 21. doi: 10.1038/jp.2016.112. PMID: 27442155
8. American Academy of Pediatrics. Maduekwe E, DeCristofaro JD., Neoreviews, March 2017, Volume 18/Issue 3 section on Inhaled Nitric Oxide. Available at [http://neoreviews.aappublications.org/content/18/3/e173?utm\\_source=TrendMD&utm\\_medium=TrendMD&utm\\_campaign=NeoRev\\_TrendMD\\_0](http://neoreviews.aappublications.org/content/18/3/e173?utm_source=TrendMD&utm_medium=TrendMD&utm_campaign=NeoRev_TrendMD_0). Accessed 9/11/2017.
9. Carey WA, Weaver AL, Mara KC, Clark RH. Inhaled Nitric Oxide in Extremely Premature Neonates with Respiratory Distress Syndrome. Pediatrics March 2018, 141 (3) e20173108; DOI: <https://doi.org/10.1542/peds.2017-3108>
10. Lakshminrusimha S, Kinsella JP, Abman SH, et al. Just Say No to iNO in Preterms—Really? J Pediatr 2020 Mar;218:243-252. doi: 10.1016/j.jpeds.2019.10.063. Epub 2019 Dec 4. PMID: 31810629
11. Barrington KJ, Finer N, Pennaforte T. Inhaled nitric oxide for respiratory failure in preterm infants. Cochrane Database Syst Rev. 2017;1:CD000509
12. Hayes Review, annual review March 17, 2021
13. Hayes Review, December 14, 2021

#### Note:

Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid plans are offered through Scott and White Health Plan in the Central Managed Care Service Area (MRSA) and STAR and CHIP plans are offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSA.