MEDICAL POLICY STATEMENT
INDIANA MEDICAID

Policy Name		Policy Number	Date Effective
Inhaled Nitric Oxide for Neonates		MM-1047	02/01/2021-10/31/2021
Policy Type			
MEDICAL	Administrative	Pharmacy	Reimbursement

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A. Subject

Inhaled Nitric Oxide for Neonates

B. Background

Nitric oxide (NO) is a lipophilic gas that is naturally produced in numerous cells in the body and is readily absorbed across pulmonary membranes in the ventilated lung after inhalation. When administered via inhalation, it is a potent endogenous vasodilator that induces relaxation of vascular and bronchial smooth muscle and vasodilatation of blood vessels. Inhaled nitric oxide (INO) has been used in conjunction with ventilator support as a treatment of hypoxic respiratory failure associated with persistent pulmonary hypertension of the newborn (PPHN), in term or near-term (greater than 34 weeks gestation) neonates to improve oxygenation and decrease the need for extracorporeal membrane oxygenation (ECMO).

C. Definitions

- **Extracorporeal membrane oxygenation (ECMO)** - is temporary support of heart and lung function by partial cardiopulmonary bypass (up to 75% of cardiac output). It is used for patients who have reversible cardiopulmonary failure from pulmonary, cardiac or other disease.
- **Nitric oxide** - Nitric oxide (NO), also called nitrogen monoxide, colorless lipophilic gas that is formed by the oxidation of nitrogen. Nitric oxide performs important chemical signaling functions in humans and other animals and has various applications in medicine.
- **Persistent pulmonary hypertension of the newborn (PPHN)** - is a serious disorder in which the blood flow and the amount of oxygen in the bloodstream is limited due to constriction of the arteries of the lungs after delivery.
- **Hypoxic respiratory failure** - is a serious condition that develops when the lungs can't get enough oxygen into the blood to reach the tissues of the body.
- **Oxygen Index** - Oxygenation index is used to assess severity of hypoxic respiratory failure (HRF) and persistent pulmonary hypertension of the newborn (PPHN). The OI is calculated as the mean airway pressure divided by the partial pressure of arterial oxygen times 100.

D. Policy

I. CareSource will review medical necessity guidelines based on the clinical documentation that is submitted prior to payment of claims.

II. CareSource considers the initiation of iNO therapy as medically necessary for ONE of the following indications (A,B,C):

A. Indicator:

1. Hypoxic respiratory failure; and
2. Neonates ≥ 34 weeks gestational age at birth; and
3. Echocardiographic evidence of PPHN <u>without</u> congenital heart disease that is a ductal dependent lesion(s) ; and one of the following:

a. Conventional therapies (such as mechanical ventilation, administration of high concentrations of oxygen (80-100%), high frequency oscillatory ventilation (HFOV), induction of alkalosis, neuromuscular blockade and sedation) have failed or are expected to fail; or
b. Diagnosis of congenital diaphragmatic hernia (when iNO is used as a bridge to surgical repair).

B. Indicator:
1. Post-operative management of neonates ≥ 34 weeks gestational age at birth including ONE of the following conditions:
a. Pulmonary hypertension following repair of congenital heart disease; or
b. Pulmonary hypertensive crisis following pediatric heart or lung surgery.

C. Indicator:
1. Management of pulmonary hypertension during heart catheterization to determine pulmonary vasoreactivity.

III. iNO administration must be initiated with alternative vasodilator therapies with the intent to wean iNO (e.g. sildenafil or others).

IV. For continued iNO therapy, documentation must be obtained every 48 hours with evidence of re-evaluation for iNO therapy.
A. Conditions for continuation of iNO therapy beyond 48 hours require one of the following:
1. Patient continues to require iNO due to a continued O2 requirement of 80 - 100% FiO2; or
2. A weaning protocol has been initiated after a 4-6 hour period of stability, indicated by a decreasing O2 requirement.

V. If there is a lack of positive response and inability to wean on 20ppm after 48 hrs, discontinuation of iNO therapy should be considered.
A. Documentation of reasons to continue therapy must be submitted.

VI. CareSource considers the use of iNO not medically necessary for the following indications:
A. Preterm infants < 34 weeks gestation at birth.
B. Acute bronchiolitis.
C. Bronchopulmonary dysplasia (BPD).
D. Echocardiogram demonstrating congenital heart disease with ductal dependent lesion(s).

E. Conditions of Coverage

F. Related Policies/Rules

G. Review/Revision History

	DATE	ACTION
Date Issued	09/16/2020	New policy
Date Revised		
Date Effective	02/01/2021	
Date Archived	10/31/2021	This Policy is no longer active and has been archived. Please note that there could be other Policies that may have some of the same rules incorporated and CareSource reserves the right to follow CMS/State/NCCI guidelines without a formal documented Policy

H. References

1. American Academy of Pediatrics (AAP). Committee on Fetus and Newborn. Use of inhaled nitric oxide. Pediatrics. 2000 (reaffirmed in 2010); 106 (2 Pt 1):344-345. Retrieved June 24, 2020 from www.pediatrics.aappublications.org.
2. American Thoracic Society. "What is ECMO?" Patient Education/Patient information Series. Am J Respir Crit Care Med Vol. 193, P9-P10, 2016. Retrieved June 17, 2020 from www.thoracic.org.
3. Barrington KJ, Finer N, Pennaforte T. Inhaled nitric oxide for respiratory failure in preterm infants. Cochrane Database Syst Rev. 2017 Jan 3; 1:CD000509. doi: 10.1002/14651858. Retrieved June 24, 2020 from www.ncbi.nlm.nih.gov.
4. Barrington KJ, Finer N, Pennaforte T, Altit G and Cochrane Neonatal Group. Nitric oxide for respiratory failure in infants born at or near term. Cochrane Database Syst Rev. 2017 Jan; 2017(1): CD000399.
5. Carey WA, et al. Inhaled Nitric oxide in Extremely Premature Neonates with Respiratory Distress Syndrome. Pediatrics. 2018. 141(3). Retrieved June 24, 2020 from www.pediatrics.aappublications.org.
6. Chandrasekharan P, et al. Early Use of Inhaled Nitric Oxide in Preterm Infants: Is there a Rationale for Selective Approach? Am J Perinatol. 2017 Apr; 34(5): 428–440.
7. DiBlas RM, Myers TR and Hess DR. Evidence-based Clinical Practice Guideline: Inhaled Nitric Oxide for Neonates with Acute Hypoxic Respiratory Failure. Respir Care 2010 Dec; 55(12):1717-45.
8. Dowell, JC, et al. Association of Response to Inhaled Nitric Oxide and Duration of Mechanical Ventilation in Pediatric Acute Respiratory Distress Syndrome. Pediatr Crit Care Med. 2017 Nov; 18(11): 1019–1026.
9. Hsiao, HF, et al. The Off-Label Use of Inhaled Nitric Oxide as a Rescue Therapy in Neonates with Refractory Hypoxemic Respiratory Failure: Therapeutic Response and Risk Factors for Mortality. J Clin. Med. 2019 Aug; 8(8): 1113.
10. Karam O, et al. 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 Jan; 72(1):106-117. Retrieved June 24, 2020 from www.onlinelibrary.wiley.com.
11. Keszler M. Guidelines for Rational and Cost-Effective Use of iNO Therapy in Term and Preterm Infants. J Clin. Neonatol [serial online] 2012 [cited 2020 Jun 30]; 1:59-

12. Kinsella JP, et al. Recommendations for the Use of Inhaled Nitric Oxide Therapy in Premature Newborns with Severe Pulmonary Hypertension, J Pediatr. 2016 Mar; 170:312-4. Retrieved June 24, 2020 from www.pediatrics.aappublications.org.
13. Martin R. Prevention and treatment of respiratory distress syndrome in preterm infants. (May 2020). Joseph A Garcia-Prats (Ed.), UpToDate. Retrieved June 24,2020 from www.uptodate.com.
14. Mayo Clinic. Nitric Oxide (Inhalation Route), Drugs and Supplements. (Feb. 01,2020). Retrieved June 24, 2020 from www.mayoclinic.org.
15. National Heart, Lung and Blood Institute. Respiratory Failure. 2020. Retrieved June17, 2020 from www.nhlbi.nih.gov.
16. Nelin LD and Potenziano JL. Inhaled nitric oxide for neonates with persistent pulmonary hypertension of the newborn in the CINRGI study: time to treatmentresponse. BMC Pediatrics. 2019. 19(17). Retrieved July 8, 2020 from www.bmcpediatr.biomedcentral.com.
17. Persistent pulmonary hypertension of the newborn (PPHN). (Oct 2019). Merck Manual-Consumer Edition. Retrieved June 17, 2020 from www.merckmanuals.com.
18. The Neonatal Inhaled Nitric Oxide Study Group. Inhaled Nitric Oxide in Full-Term and Nearly Full-Term Infants with Hypoxic Respiratory Failure. N Engl J Med 1997;336:597-604.

The Medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.

Independent medical review – 6/29/2020

IN-Med-P-277278 Issue Date 09/16/2020 OMPP approved 11/20/2020