Inhaled Nitric Oxide

Humana

Medical Coverage Policy

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Change Summary: Updated Description, Coverage Determination, Coverage Limitations, References

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Description

Inhaled nitric oxide (iNO) is a pulmonary vasodilator, used for the treatment of hypoxic respiratory failure associated with persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs after birth when there is increased pulmonary vascular resistance that causes right-to-left shunting of blood leading to severe hypoxemia. PPHN is often associated with pulmonary parenchymal abnormalities such as alveolar capillary dysplasia, lung hypoplasia, meconium aspiration, pneumonia and sepsis. In some neonates, there is no evidence of parenchymal disease and the cause is unknown.[6]

When nitric oxide is inhaled, pulmonary vasodilation occurs and an increase in the partial pressure of arterial oxygen results. Dilation of pulmonary vessels in well ventilated lung areas redistributes blood flow away from lung areas where

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ventilation to perfusion ratios are poor. Examples of commercially available brands of nitric oxide include, but may not be limited to, GENOSYL, INOmax and Noxivent.

iNO is most often utilized in conjunction with ventilatory support in term or near-term (at or greater than 34 weeks gestation) neonates (28 days of age or younger) to improve oxygenation and decrease the need for extracorporeal membrane oxygenation (ECMO). iNO may also be administered to infants and children for postoperative management of pulmonary hypertension. Another established use for iNO is with acute vasoreactivity testing for pulmonary arterial hypertension. It is performed during right heart catheterization procedures to determine how much the pulmonary blood vessels can relax over a period of time and help identify individuals who might respond favorably to calcium channel blockers.

Other proposed uses for iNO include, but may not be limited to, acute respiratory distress syndrome in adults, bronchopulmonary dysplasia or for treatment of pain related to sickle cell disease. **(Refer to Coverage Limitations section)**

Coverage Determination

Commercial Plan members: requests for iNO therapy greater than 14 days require review by a medical director.

Humana members may be eligible under the Plan for the use of **iNO** in conjunction with ventilatory support when the following criteria are met:

- Neonate at or greater than 34 weeks gestation; **AND**
- Failure of, contraindication or intolerance to conventional therapy (eg, high concentrations of oxygen, high frequency ventilation, hyperventilation, induction of alkalosis, neuromuscular blockade and sedation); **AND**
- Hypoxic respiratory failure associated with clinical or echocardiographic evidence of PPHN; **AND**
- Maximum duration of treatment is 14 days or until oxygen desaturation has been resolved, whichever occurs first

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Humana members may be eligible under the Plan for the use of **iNO** for postoperative management of pulmonary hypertension in infants and children with congenital heart disease.

Humana members may be eligible under the Plan for the use of **iNO** for acute vasoreactivity testing in pulmonary arterial hypertension.

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for the use of **iNO** for any indications other than those listed above including, but not limited to:

- Acute respiratory distress syndrome in an adult; **OR**
- Acute vasoreactivity testing in an individual with pulmonary veno-occlusive disease (PVOD); **OR**
- Bronchopulmonary dysplasia; **OR**
- Chronic obstructive pulmonary disease (COPD); **OR**
- Hepatopulmonary syndrome; **OR**
- Neonatal respiratory distress syndrome without PPHN; **OR**
- Neonate less than 34 weeks gestation; **OR**
- Neonate with unrepaired congenital diaphragmatic hernia (CDH); **OR**
- Prevention of primary graft dysfunction following lung transplantation; **OR**
- Treatment of pain crisis in sickle cell disease

This is considered experimental/investigational as it is not identified as widely used and generally accepted for any other proposed use as reported in nationally recognized peer-reviewed medical literature published in the English language.

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Background

Additional information about **pulmonary hypertension** may be found from the following websites:

- American Heart Association
- American Lung Association
- National Heart, Lung and Blood Institute
- National Library of Medicine

Medical Alternatives

Physician consultation is advised to make an informed decision based on an individual's health needs.

Humana may offer a disease management program for this condition. **The member may call the number on his/her identification card to ask about our programs to help manage his/her care.**

Provider Claims Codes

Any CPT, HCPCS or ICD codes listed on this medical coverage policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
93463	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)	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**

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No code(s) identified

References

1. Agency for Healthcare Research and Quality (AHRQ). Inhaled nitric oxide in preterm infants. https://www.ahrq.gov. Published October 2010. Updated October 2014. Accessed November 1, 2022.

2. American Academy of Pediatrics (AAP). American Academy of Pediatrics Committee on Fetus and Newborn. Use of inhaled nitric oxide. https://www.aap.org. Published August 2000. Updated December 2009. Accessed November 8, 2022.

3. American Academy of Pediatrics (AAP). Clinical Report. Use of inhaled nitric oxide in preterm infants. https://www.aap.org. Published January 2014. Accessed November 7, 2022.

4. American Academy of Pediatrics (AAP). Off-label use of inhaled nitric oxide after release of NIH consensus statement. https://www.aap.org. Published April 2015. Accessed November 8, 2022.

5. American Association for Respiratory Care (AARC). AARC Clinical Practice Guideline. Evidence-based clinical practice guideline: inhaled nitric oxide for neonates with acute hypoxic respiratory failure. https://www.aarc.org. Published December 2010. Accessed November 7, 2022.

6. American College of Cardiology (ACC). ACCF/AHA 2009 expert consensus document on pulmonary hypertension. https://www.acc.org. Published April 28, 2009. Accessed November 3, 2022.

7. American Heart Association (AHA). Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. https://www.heart.org. Published November 24, 2015. Accessed November 3, 2022.

8. ClinicalKey. Drug Monograph. Nitric oxide. https://www.clinicalkey.com. Updated January 16, 2020. Accessed November 21, 2022.

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9. ClinicalKey. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults. Update of the CHEST guideline and expert panel report. *Chest.* 2019;155(3):565-586. https://www.clinicalkey.com. Accessed October 26, 2021.

10. ClinicalKey. Nativi-Nicolau J, Ryan JJ, Fang JC. Hemodynamics in heart failure. In: Felker GM, Mann DL. *Heart Failure: A Companion to Braunwald's Heart Disease*. 4th ed. Elsevier; 2020:467-486.e2. https://www.clinicalkey.com. Accessed November 8, 2022.

11. ClinicalKey. Novelli E, Gladwin M, Lakshmanan K. Sickle cell disease. In: Kellerman RD, Rakel DP. *Conn's Current Therapy 2022*. Elsevier; 2020:476-490. https://www.clinicalkey.com. Accessed November 14, 2022.

12. ECRI Institute. Hotline Response (ARCHIVED). Inhaled nitric oxide for treating pulmonary hypertension or acute respiratory distress syndrome in adults. https://www.ecri.org. Published March 8, 2005. Updated October 15, 2015. Accessed October 31, 2022.

13. ECRI Institute. Hotline Response (ARCHIVED). Inhaled prostacyclins as alternatives to nitric oxide for treating pulmonary hypertension in neonates and children. https://www.ecri.org. Published April 15, 2015. Accessed October 31, 2022.

14. ECRI Institute. Hotline Response (ARCHIVED). Nitric oxide for treating pulmonary hypertension in pediatric cardiac patients. https://www.ecri.org. Published April 4, 2012. Updated July 9, 2013. Accessed October 31, 2022.

15. ECRI Institute. Product Brief (ARCHIVED). INOmax inhaled nitric oxide (Mallinckrodt/INO Therapeutics LLC) for treating pulmonary hypertension in neonates. https://www.ecri.org. Published February 27, 2017. Accessed October 31, 2022.

16. Hayes, Inc. Clinical Research Response (ARCHIVED). Inhaled nitric oxide versus inhaled Veletri (Epoprostenol) for the management of acute pulmonary arterial hypertension. https://evidence.hayesinc.com. Published May 22, 2018. Accessed October 21, 2021.

See the **DISCLAIMER.** All Humana member health plan contracts are **NOT** the same. All legislation/regulations on this subject may not be included. This document is for informational purposes only.

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17. Hayes, Inc. Health Technology Assessment. Inhaled nitric oxide for the treatment of respiratory failure in preterm newborns. https://evidence.hayesinc.com. Published November 6, 2018. Updated December 14, 2021. Accessed October 31, 2022.

18. Hayes, Inc. Health Technology Brief (ARCHIVED). Inhaled nitric oxide for acute respiratory distress syndrome (ARDS) in adults. https://evidence.hayesinc.com. Published March 31, 2014. Updated March 2, 2016. Accessed October 31, 2022.

19. Hayes, Inc. Medical Technology Directory (ARCHIVED). Inhaled nitric oxide for the treatment of persistent pulmonary hypertension in term and near-term newborns. https://evidence.hayesinc.com. Published January 15, 2009. Updated January 22, 2013. Accessed October 31, 2022.

20. IBM Micromedex. Nitric oxide. https://www.micromedexsolutions.com. Updated November 19, 2021. Accessed November 16, 2022.

21. UpToDate, Inc. Acute respiratory distress syndrome: supportive care and oxygenation in adults. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

22. UpToDate, Inc. Bronchopulmonary dysplasia: prevention. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

23. UpToDate, Inc. Congenital diaphragmatic hernia in the neonate. https://www.uptodate.com. Updated October 2022. Accessed November 2, 2022.

24. UpToDate, Inc. Hepatopulmonary syndrome in adults: natural history, treatment, and outcomes. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

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25. UpToDate, Inc. Inhaled nitric oxide in adults: biology and indications for use. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

26. UpToDate, Inc. Management of respiratory distress syndrome in preterm infants. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

27. UpToDate, Inc. Meconium aspiration syndrome: prevention and management. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

28. UpToDate, Inc. Persistent pulmonary hypertension of the newborn: management and outcome. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

29. UpToDate, Inc. Primary lung graft dysfunction. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

30. UpToDate, Inc. Pulmonary hypertension due to lung disease and/or hypoxemia (group 3 pulmonary hypertension): treatment and prognosis. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

31. UpToDate, Inc. Pulmonary hypertension in children: classification, evaluation, and diagnosis. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

32. UpToDate, Inc. Pulmonary hypertension in children: management and prognosis. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

33. UpToDate, Inc. Treatment and prognosis of pulmonary veno-occlusive disease/pulmonary capillary hemangiomatosis in adults. https://www.uptodate.com. Updated September 2022. Accessed November 1, 2022.

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34. UpToDate, Inc. Treatment of pulmonary arterial hypertension (group 1) in adults: pulmonary hypertension-specific therapy. https://www.uptodate.com. Updated September 2022. Accessed November 8, 2022.

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