

Policy: MP174

Section: Medical Benefit Policy

Subject: Exhaled Nitric Oxide for Asthma Management

I. Policy: Exhaled Nitric Oxide for Asthma Management

II. Purpose/Objective:

To provide a policy of coverage regarding Exhaled Nitric Oxide for Asthma Management

III. Responsibility:

- A. Medical Directors
- B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

- a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
- b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
- c. in accordance with current standards of good medical treatment practiced by the general medical community.
- d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
- e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

- (i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
- (ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.
- (iii) The service or benefit will assist the Member to achieve or maintain maximum functional

capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for members of the same age.

DESCRIPTION:

Nitric Oxide (NO) is an important endogenous regulatory molecule widely distributed throughout the body that is a messenger in many different biological processes. In biological tissue, nitric oxide is highly reactive making a determination of the amount of NO very difficult. However, in the gas phase nitric oxide is relatively stable, permitting its measurement in exhaled air. Of greatest clinical interest is the role of NO as an inflammatory mediator, particularly in the management of eosinophilic asthma to determine the likelihood of steroid responsiveness in individuals with chronic symptoms suggestive of airway inflammation

INDICATIONS:

The measurement of exhaled nitric oxide may be considered medically necessary for the management of when all of the following criteria are met:

- Utilization is limited to Pulmonary or Allergy/Immunology specialists; and
- Diagnosis of eosinophilic asthma has been established or highly suspected

EXCLUSIONS:

The use of exhaled nitric oxide outside of the indications outlined in this policy is considered **experimental, investigational or unproven**, and therefore **NOT COVERED**. The Geisinger Technology Assessment Committee evaluated this technology and concluded that there is insufficient evidence in the peer-reviewed published medical literature to establish the effectiveness of this test on health outcomes for use outside of the indications outlined in this document, when compared to established tests or technologies.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

CODING ASSOCIATED WITH: Exhaled Nitric Oxide for Asthma Management

The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.

95012 Nitric oxide expired gas determination

Current Procedural Terminology (CPT®) © American Medical Association: Chicago, IL

LINE OF BUSINESS:

Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:

Geisinger Clinic Technology Assessment Committee, Exhaled Nitric Oxide for Asthma Management. January 11, 2006.

Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR. Use of Exhaled Nitric Oxide Measurements to Guide Treatment in Chronic Asthma. NEJM 26 May 2005;352:2163-2173.

Thomas PS, Gibson PG, Wang H, Shah S, Henry RL. The relationship of exhaled nitric oxide to airway inflammation and responsiveness in children. J Asthma. 2005 May;42(4):291-5.

Gill M, Walker S, Khan A, Green SM, Kim L, Gray S, Krauss B. Exhaled nitric oxide levels during acute asthma exacerbation. Acad Emerg Med. 2005 Jul;12(7):579-86.

Pijnenburg MW, Bakker EM, Lever S, Hop WC, De Jongste JC. High fractional concentration of nitric oxide in exhaled air despite steroid treatment in asthmatic children. Clin Exp Allergy. 2005 Jul;35(7):920-5.

Pijnenburg MW, Bakker EM, Hop WC, De Jongste JC. Titrating Steroids on Exhaled Nitric Oxide in Asthmatic Children: a Randomized Controlled Trial. *Am J Respir Crit Care Med*. 2005 Jun 23; 172(7):831-6.

Prasad A, Langford B, Stradling JR, Ho LP. Exhaled nitric oxide as a screening tool for asthma in school children. *Respir Med*. 2005 May 7; (1):167-73.

Berkman N, Avital A, Breuer R, Bardach E, Springer C, Godfrey S. Exhaled nitric oxide in the diagnosis of asthma: comparison with bronchial provocation tests. *Thorax*. 2005 May;60(5):383-8.

Pijnenburg MW, Hoffhuis W, Hop WC, De Jongste JC. Exhaled nitric oxide predicts asthma relapse in children with clinical asthma remission. *Thorax*. 2005 Mar;60(3):215-8.

Nordvall SL, Janson C, Kalm-Stephens P, Foucard T, Toren K, Alving K. Exhaled nitric oxide in a population-based study of asthma and allergy in schoolchildren. *Allergy*. 2005 Apr;60(4):469-75.

Zacharasiewicz A, Wilson N, Lex C, Erin EM, Li AM, Hansel T, Khan M, Bush A. Clinical use of noninvasive measurements of airway inflammation in steroid reduction in children. *Am J Respir Crit Care Med*. 2005 May 15;171(10):1077-82.

Saito J, Inoue K, Sugawara A, Yoshikawa M, Watanabe K, Ishida T, Ohtsuka Y, Munakata M. Exhaled nitric oxide as a marker of airway inflammation for an epidemiologic study in schoolchildren. *J Allergy Clin Immunol*. 2004 Sep;114(3):512-6.

Winifred S. Hayes. Hayes Directory (online). Nitric Oxide Breath Analysis for the Diagnosis and Management of Asthma. Winifred S. Hayes (online). Current as of August 28, 2007.

Smith A.D., Cowan J.O., Filsell, S. McLachlan C, Monti-sheehan G, Jackson P, and Taylor D.R. Diagnosing Asthma: Comparisons between exhaled nitric oxide measurements and conventional tests. *Am J Respir Crit Care Med*. 2004; 169:473-478.

Szeftler SJ, Mitchell H, Sorkness CA, et al. Management of asthma based on exhaled nitric oxide in addition to guideline-based treatment for inner-city adolescents and young adults: a randomized controlled trial. *Lancet* 2008;372:1065-1072.

Boot JD, de Ridder L, de Kam ML, Calderon C, Mascelli MA, Diamant Z. Comparison of exhaled nitric oxide measurements between NIOX MINO((R)) electrochemical and Ecomedics chemiluminescence analyzer. *Respir Med*. 2008 Aug 9. [Epub ahead of print]

Fortuna AM, Feixas T, González M, Casan P. Diagnostic utility of inflammatory biomarkers in asthma: exhaled nitric oxide and induced sputum eosinophil count. *Respir Med*. 2007 Nov;101(11):2416-21. Epub 2007 Aug 21.

Ramser M, Hammer J, Amacher A, Trachsel D. The value of exhaled nitric oxide in predicting bronchial hyperresponsiveness in children. *J Asthma*. 2008;45(3):191-195.

ECRI Institute HTAIS Hotline Service (Online). Exhaled Nitric Oxide for Diagnosing and Monitoring Asthma. Current as of March 28, 2008.

Petsky HL, Cates CJ, Li AM, et al. Tailored interventions based on exhaled nitric oxide versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev*. 2009;(4):CD006340.

Rodway GW, Choi J, Hoffman LA, Sethi JM. Exhaled nitric oxide in the diagnosis and management of asthma: Clinical implications. *Chron Respir Dis*. 2009;6(1):19-29.

U.S Department of Health and Human Services. Monitoring Exhaled Nitric Oxide Does Not Help Manage Asthma. NIH News. September, 2008.

<http://www.nih.gov/news/health/sep2008/niaid-18.htm>

Thomas PS, Lowe AJ, Samarasinghe P, et al. Exhaled condensate in pediatric asthma: promising new advance or pouring cold water on a lot of hot air? a systematic review. *Pediatr Pulmonol*. 2013;48(5):419-442

Arga M, Bakirtas A, Topal E, et al. Can exhaled nitric oxide be a surrogate marker of bronchial hyperresponsiveness to adenosine 5'-monophosphate in steroid-naive asthmatic children? *Clin Exp Allergy*. 2015;45(4):758-66.

Peirsman EJ, Carvelli TJ, Hage PY, et al. Exhaled nitric oxide in childhood allergic asthma management a randomised controlled trial. *Pediatr Pulmonol.* 2014;49(7):624-31

Pike K, Selby A, Price S, et al. Exhaled nitric oxide monitoring does not reduce exacerbation frequency or inhaled corticosteroid dose in paediatric asthma: a randomised controlled trial. *Clin Respir J.* 2013;7(2):204-13

Boon M, Meyts I, Proesmans M, et al. Diagnostic accuracy of nitric oxide measurements to detect primary ciliary dyskinesia. *Eur J Clin Invest.* 2014;44(5):477-485

Honkoop PJ, Loijmans RJ, Termeer EH, et al. Symptom- and fraction of exhaled nitric oxide-driven strategies for asthma control: A cluster-randomized trial in primary care. *J Allergy Clin Immunol.* 2015;135(3):682-8.

Anderson WJ, Short PM, Williamson PA, et al. Inhaled corticosteroid dose response using domiciliary exhaled nitric oxide in persistent asthma: the FENOtype trial. *Chest.* 2012;142(6):1553-1561.

LaForce C, Brooks E, Herje N, et al. Impact of exhaled nitric oxide measurements on treatment decisions in an asthma specialty clinic. *Ann Allergy Asthma Immunol.* 2014;113(6):619-23.

Syk J, Malinovschi A, Johansson G, et al. Anti-inflammatory Treatment of Atopic Asthma Guided by Exhaled Nitric Oxide: A Randomized, Controlled Trial. *J Allergy Clin Immunol Pract.* 2013;1(6):639-648.

Petsky HL, Li AM, Au CT, et al. Management based on exhaled nitric oxide levels adjusted for atopy reduces asthma exacerbations in children: A dual centre randomized controlled trial. *Pediatr Pulmonol.* 2015;50(6):535-43.

Schneider A, Faderl B, Schwarzbach J, et al. Prognostic value of bronchial provocation and FENO measurement for asthma diagnosis--results of a delayed type of diagnostic study. *Respir Med.* 2014;108(1):34-40.

Geisinger Technology Assessment Triage Group. Review of current literature. Jan. 2013

Geisinger Technology Assessment Committee. Measurement of Exhaled FeNO. April 2017.

Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. *Cochrane Database of Systematic Reviews* 2016a, Issue 11. Art. No.: CD011439. DOI: 10.1002/14651858.CD011439.pub2

Petsky HL, Kew KM, Turner C, Chang AB. Exhaled nitric oxide levels to guide treatment for adults with asthma. *Cochrane Database of Systematic Reviews* 2016b, Issue 9. Art. No.: CD011440. DOI: 10.1002/14651858.CD011440.pub2.

Lee QU. Fractional exhaled nitric oxide-guided algorithm for children with asthma. *Pediatr Pulmonol.* 2015;50(9):932-933

Lu M, Wu B, Che D, Qiao R, Gu H. FeNO and asthma treatment in children: a systematic review and meta-analysis. *Medicine.* 2015; 94(4): e347.

ECRI Institute. Fractional Exhaled Nitric Oxide Measurement for Diagnosing and Monitoring Inflammatory Airway Diseases. Hotline Response April 2016

Agency for Healthcare Research and Quality (AHRQ). Evidence-based Practice Center Systematic review Protocol. Fractional Exhaled Nitric oxide Clinical Utility in Asthma Management. Sept. 2016

Essat M, Harnan S, et al. Fractional exhaled nitric oxide for the management of asthma in adults: a systematic review. *Eur Resp J* 2016 doi:10.1183/13993003.01882-2015

Bjerner L, Alving K, et al. Current evidence and future research needs for FeNO measurement in respiratory disease. *Resp Med* 2014;108:830-841.

Donohue JF, Jain N. Exhaled nitric oxide to predict corticosteroid responsiveness and reduce asthma exacerbation rates. *Resp Med* 2013;107:943-952.

Wang Z, Pianosi PT, Keogh KA, et al. The Diagnostic Accuracy of Fractional Exhaled Nitric Oxide Testing in Asthma: A Systematic Review and Meta-analyses. *Mayo Clin Proc.* 2017 e-published ahead of print:1-8

Harnan SE, Essat M, Gomersall T, et al. Exhaled nitric oxide in the diagnosis of asthma in adults: a systematic review. *Clin Exp Allergy.* 2017;47(3):410-429

Karrasch S, Linde K, Rucker G, et al. Accuracy of FENO for diagnosing asthma: a systematic review. Thorax. 2017;72(2):109-116.

Global Strategy for Asthma Management and Prevention (GINA). 2018

This policy will be revised as necessary and reviewed no less than annually.

Devised: 02/06/06

Revised: 2/09(Add'l section added); 5/17 (added coverage criteria)

Reviewed: 2/07, 2/08, 2/10 (refs), 3/11, 3/12, 3/13, 3/14; 3/15, 3/16, 3/17, 5/18, 5/19