



Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	Submission Date: 01/01/2022
Policy Number: PA.CP.MP.103	Effective Date: 09/01/18 Revision Date: 12/22/2021
Policy Name: Fractional Exhaled Nitric Oxide	HC Approval Date:
Type of Submission – Check all that apply: <input type="checkbox"/> New Policy <input type="checkbox"/> Revised Policy* <input checked="" type="checkbox"/> Retiring Policy– <i>This option indicates the retirement of an active policy. If there is no indicated replacement, then “NONE” will be listed as the New/Replacement Policy.</i> <input type="checkbox"/> Annual Review – No Revisions <input type="checkbox"/> Statewide PDL - <i>Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.</i>	
*All revisions to the policy <u>must</u> be highlighted using track changes throughout the document. Please provide any changes or clarifying information for the policy below: Background updated. Replaced all instances of “member” with “member/enrollee.” References reviewed and updated. Policy being retired effective 1/1/2022 with no replacement indicated.	

CLINICAL POLICY
Fractional Exhaled Nitric Oxide



Name of Authorized Individual (Please type or print): Carla Huitt, MD MPH	Signature of Authorized Individual:
---	--

Clinical Policy: Fractional Exhaled Nitric Oxide

Reference Number: PA.CP.MP.103

Last Review Date: 06/3/2021

Effective Date: ~~09/2018~~01/01/2022

[Coding Implications](#)

[Revision Log](#)

Description

Fractional exhaled nitric oxide (FeNO) measurement is a noninvasive and simple test thought to reflect eosinophilic airway inflammation. While measurement of FeNO is standardized, there are currently no reference guidelines available to aid practitioners in appropriately applying test results in practice.

Policy/Criteria

It is the policy of PA Health & Wellness (PHW)[®] that testing for fractionated exhaled nitric oxide (FeNO) is **investigational** for diagnosing and guiding the treatment of asthma, **as well as all other conditions**, as there is insufficient evidence proving it more than or as effective as existing standards of care.

Background

There are multiple methods for diagnosing and assessing control of asthma and, according to the American Thoracic Society (ATS), no single test is an adequate indicator of asthma control.¹ Conventional, objective methods to assess asthma include spirometry/peak flow and degree of airway hyper-responsiveness.² These methods are often used as measures of asthma control in addition to patient symptoms, clinical questionnaires, and use of rescue medications.^{2,3} Newer methods of diagnosing and assessing control of asthma include the use of biomarkers of airway inflammation such as FeNO and induced sputum analysis.⁴

FeNO describes the levels of exhaled nitric oxide (NO) in the breath and NO is a mediator involved in lung inflammation that is largely formed in the lower airways.⁵ Increased levels of FeNO are associated with eosinophilic inflammation, severe asthma, and inhaled glucocorticoid-naïve asthma.⁴ Although there are some correlations between FeNO and characteristics related to asthma, there is large variability in FeNO levels between individuals. Other factors that may affect FeNO include atopy, sex, age, and cigarette smoking.³ However, there are no established guidelines for adjusting FeNO values according to these factors,³ potentially making the test less accurate for certain populations.

There are currently three types of FeNO tests approved by the FDA⁵ and there is a large body of literature on FeNO testing for the diagnosis and management of asthma. Overall, the evidence is mixed for using FeNO as an adjunct to the diagnosis or management of asthma. Multiple studies have shown that FeNO can serve as an indicator of glucocorticoid response.^{3,4,6} However, large studies, randomized control trials and a meta-review have found no clinical benefit to the use of FeNO testing over other methods of assessing or managing asthma.^{2,4,7-9}

CLINICAL POLICY
Fractional Exhaled Nitric Oxide



Among the studies that found a benefit to the use of FeNO testing,^{6,10-13} there was little agreement regarding FeNO cutoff values which would indicate asthma diagnosis or control.^{3,5} Although the ATS has recommended specific FeNO cutoff values to serve as guidelines for the diagnosis and treatment of asthma,¹⁴ these standardized values have not been consistently used in the research to date on FeNO testing.³⁻⁵ An additional drawback to FeNO testing for the diagnosis or management of asthma is that it is most indicative of inflammation caused by eosinophils, which characterizes only one subtype of asthma.⁴

A 2016 Cochrane Review evaluating the use of FeNO in guiding treatment for adults with asthma concluded that, while management guided by FeNO levels results in reduced exacerbations, it cannot be advocated universally since it does not affect day-to-day clinical symptoms, end-of-study FeNO levels, or inhaled corticosteroid dose.¹⁵ Furthermore, a systematic review and meta-analysis evaluating the diagnostic accuracy of FeNO in asthmatic children found that FeNO has only moderate diagnostic performance.¹⁶

Given the equivocal results of research on the accuracy and usefulness of FeNO testing for the diagnosis and management of asthma, the lack of standardized cutoff values, and the need for further study, FeNO testing for the diagnosis and/or management of asthma is considered experimental, investigational, or unproven.

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2020, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	Description
95012	Nitric Oxide expired gas determination

ICD-10-CM Diagnosis Codes that Support Coverage Criteria – Not Applicable

ICD-10-CM Code	Description
n/a	

Reviews, Revisions, and Approvals	Date	Approval Date
Policy created	09/18	
References reviewed and updated.	12/18	

Formatted Table

Reviews, Revisions, and Approvals	Date	Approval Date
References reviewed and updated. Added that testing FeNO is investigational for all other conditions, in addition to asthma, with supporting sources.	06/2020	
Background updated. Replaced all instances of “member” with “member/enrollee.” References reviewed and updated.	6/3/2021	
Policy being retired effective 1/1/2022 with no replacement indicated.	12/22/2021	

Formatted Table

Formatted: Right: 0.44", Tab stops: Not at 0.5"

References

1. Reddel HK, Taylor DR, Bateman ED, et al. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations; standardizing endpoints for clinical asthma trials and clinical practice. *Am J Respir Crit Care Med.* 2009; 180: 602-615. doi: 10.1164/rccm.200801-060ST
2. Petsky HL, Cates CJ, Lasserson TJ, et al. A systematic review and meta-analysis: tailoring asthma treatment on eosinophilic markers (exhaled nitric oxide or sputum eosinophils). *Thorax.* 2012; 67: 199-208. doi:10.1136/thx.2010.135574
3. Dweik RA. Exhaled nitric oxide analysis and applications. UpToDate. Barnes PJ (Ed.). Accessed Nov. 12, 2020.
4. Wadsworth SJ, Sin DD, Dorscheid DR. Clinical update on the use of biomarkers of airway inflammation in the management of asthma. *J Asthma Allergy.* 2011; 4: 77-86. <http://dx.doi.org/10.2147/JAA.S15081>
5. Hayes Medical Technology Directory: Nitric oxide breath analysis for the diagnosis of asthma. Hayes. Published Oct. 6, 2016. Reviewed Jan. 2, 2020.
6. Hayes Medical Technology Directory: Nitric oxide breath analysis for the management of asthma. Hayes. Published September 29, 2016. Reviewed Dec. 23, 2020.
7. Donohue JF, Jain N. Exhaled nitric oxide to predict corticosteroid responsiveness and reduce asthma exacerbation rates. *Respiratory Med.* 2013; 107: 943-952.
8. Calhoun WJ, Ameredes BT, King TS, et al. Comparison of physician-, biomarker-, and symptom-based strategies for adjustment of inhaled corticosteroid therapy in adults with asthma: the BASALT randomized controlled trial. *JAMA.* 2012; 10; 987-997. doi: 10.1001/2012.jama.10893
9. Szeffler SJ, Mitchell H, Sorkness CA, et al. Adding exhaled nitric oxide to guideline-based asthma treatment in inner-city adolescents and young adults: a randomized controlled trial. *Lancet.* 2008; 372(9643): 1065-1072. doi: 10.1016/S0140-6736(08)61448-8
10. Shaw DE, Berry MA, Thomas M, et al. The use of exhaled nitric oxide to guide asthma management. *Am J Respir Crit Care Med.* 2007; 176(3): 231-237. doi: 10.1164/rccm.200610-1427OC
11. Sippel JM, Holden WE, Tilles SA, et al. Exhaled nitric oxide levels correlate with measures of disease control in asthma. *J Allergy Clin Immunol.* 2000; 106: 645-50. doi:10.1067/mai.2000.109618
12. Dupont LJ, Demedts MG, Verleden M. Prospective evaluation of the validity of exhaled nitric oxide for the diagnosis of asthma. *Chest.* 2003; 123(3): 751-756. doi:10.1378/chest.123.3.751

CLINICAL POLICY
Fractional Exhaled Nitric Oxide



13. Smith AD, Cowan JO, Filsell S, et al. Diagnosing asthma comparisons between exhaled nitric oxide measurements and conventional tests. *Am J Respir Crit Care Med.* 2004; 169: 473-478. doi: 10.1164/rccm.200310-1376OC
14. Powell H, Murphy VE, Taylor DR, et al. Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial. *Lancet.* 2011; 378(9795): 983-990. [http://dx.doi.org/10.1016/S0140-6736\(11\)60971-9](http://dx.doi.org/10.1016/S0140-6736(11)60971-9).
15. Dweik RA, Boggs RB, Erzurum SC, et al. An official ATS clinical practice guideline: Interpretation of exhaled nitric oxide levels (FeNO) for clinical applications. *Am J Respir Crit Care Med.* 2011; 184: 602-615. doi: 10.1164/rccm.912011ST
16. Petsky HL, Kew KM, Turner C, Change AB. Exhaled nitric oxide levels to guide treatment for adults with asthma. *Cochrane Database Syst Rev.* 2016 Sep 1;9: CD011440.
17. Tang S, Xie Y, Yuan C, Sun X, Cui Y. Fractional exhaled nitric oxide for diagnosis of childhood asthma: a systematic review and meta-analysis. *Clin Rev Allergy Immunol.* 2016 Jul 21.
18. Global Initiative for Asthma. 2020 GINA Report, Global Strategy for Asthma Management and Prevention. Accessed 11/12/20.
19. Global Initiative for Chronic Obstructive Lung Disease. 2020 Report, Pocket guide to COPD diagnosis, management and prevention: a guide for health care professionals. Accessed 11/12/20.
20. Qaseem A, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med.* 2011 Aug 2;155(3):179-91.
21. Horváth I, Barnes PJ, Loukides S, et al. A European Respiratory Society technical standard: exhaled biomarkers in lung disease. *Eur Respir J.* 2017;49(4).
22. Barnes PJ, Dweik RA, Gelb AF, et al. Exhaled nitric oxide in pulmonary diseases: a comprehensive review. *Chest.* 2010 Sep;138(3):682-92.
23. Fielding S, Pijnenburg M, de Jongste J, et al. Change in FEV1 and Feno Measurements as Predictors of Future Asthma Outcomes in Children. *Chest* 155(2) p. 331-334. Feb 2019.
24. Fielding S, Jijenburg M, de Jongste J, et al. Does treatment guided by exhaled nitric oxide fraction improve outcomes in subgroups of children with asthma? *Eur. Resp. J* 55(5). May 2020.