

# Clinical Policy: Fractional Exhaled Nitric Oxide

Reference Number: PA.CP.MP.103

Last Review Date: 06/3/2021

Effective Date: 09/2018

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)<sup>®</sup> 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.<sup>1</sup> Conventional, objective methods to assess asthma include spirometry/peak flow and degree of airway hyper-responsiveness.<sup>2</sup> These methods are often used as measures of asthma control in addition to patient symptoms, clinical questionnaires, and use of rescue medications.<sup>2,3</sup> Newer methods of diagnosing and assessing control of asthma include the use of biomarkers of airway inflammation such as FeNO and induced sputum analysis.<sup>4</sup>

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.<sup>5</sup> Increased levels of FeNO are associated with eosinophilic inflammation, severe asthma, and inhaled glucocorticoid-naïve asthma.<sup>4</sup> 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.<sup>3</sup> However, there are no established guidelines for adjusting FeNO values according to these factors,<sup>3</sup> potentially making the test less accurate for certain populations.

There are currently three types of FeNO tests approved by the FDA<sup>5</sup> 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.<sup>3,4,6</sup> 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.<sup>2,4,7-9</sup>

Among the studies that found a benefit to the use of FeNO testing,<sup>6,10-13</sup> there was little agreement regarding FeNO cutoff values which would indicate asthma diagnosis or control.<sup>3,5</sup> Although the ATS has recommended specific FeNO cutoff values to serve as guidelines for the diagnosis and treatment of asthma,<sup>14</sup> these standardized values have not been consistently used in the research to date on FeNO testing.<sup>3-5</sup> 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.<sup>4</sup>

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.<sup>15</sup> Furthermore, a systematic review and meta-analysis evaluating the diagnostic accuracy of FeNO in asthmatic children found that FeNO has only moderate diagnostic performance.<sup>16</sup>

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**

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<b>CPT® Codes</b>	<b>Description</b>
95012	Nitric Oxide expired gas determination

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

<b>ICD-10-CM Code</b>	<b>Description</b>
n/a	

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

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