

Clinical Policy: Fractional Exhaled Nitric Oxide

Reference Number: CP.MP.103

Last Review Date: 09/2022

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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 health plans affiliated with Centene Corporation[®] 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}

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

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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

A recent meta-analysis of pooled randomized controlled trial (RCT) data by Fielding, et al. concluded that the role of repeated FeNO measurements in predicting asthma outcomes in children is uncertain, as large changes in FeNO were associated with small changes in the risk of asthma exacerbation and indicators of asthma control.²³ A different meta-analysis by Fielding, et al. of the same seven pooled RCTs suggested that asthma treatment guided by FeNO may improve outcomes in non-obese children not treated with leukotriene receptor antagonists.²⁴ However, the treatment protocols in the included RCTs varied in their management protocols based on FeNO levels, and included only data from trials that found positive results from FeNO management.

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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| CPT® Codes | Description |
|------------|--|
| 95012 | Nitric Oxide expired gas determination |

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

| ICD-10-CM Code | Description |
|----------------|-------------|
| N/A | |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|-------|---------------|
| Policy created | 12/15 | 01/16 |
| Changed FeNO to investigational from not medically necessary. References reviewed and updated, along with background information. | 12/16 | 01/17 |
| References reviewed and updated. | 12/17 | 01/18 |
| References reviewed and updated. | 12/18 | 12/18 |
| References reviewed and updated. | 11/19 | 11/19 |
| Added that testing FeNO is investigational for all other conditions, in addition to asthma, with supporting sources. | 12/19 | 12/19 |
| Background updated. Replaced all instances of “member” with “member/enrollee.” References reviewed and updated. | 11/20 | 11/20 |

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Important reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or

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Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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