Easy Choice Health Plan, Inc.

Exactus Pharmacy Solutions, Inc.

Harmony Health Plan of Illinois, Inc.

Missouri Care, Incorporated

WellCare Health Insurance of Arizona, Inc., operating in Hawai’i as ‘Ohana Health Plan, Inc.

WellCare of Kentucky, Inc.

WellCare Health Plans of Kentucky, Inc.

WellCare Health Plans of New Jersey, Inc.

WellCare of Connecticut, Inc.

WellCare of Florida, Inc., operating in Florida as Staywell

WellCare of Georgia, Inc.

WellCare of Louisiana, Inc.

WellCare of New York, Inc.

WellCare of South Carolina, Inc.

WellCare of Texas, Inc.

WellCare Prescription Insurance, Inc.

Windsor Health Plan, Inc.

Exhaled Nitric Oxide and Breath Condensate pH Measurement for Respiratory Disorders

Policy Number: HS-186

Original Effective Date: 8/19/2010

Revised Date(s): 8/2/2011; 8/2/2012; 8/1/2013; 8/7/2014; 3/5/2015; 9/17/2015

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

Clinical Coverage Guideline

Original Effective Date: 8/19/2010 - Revised: 8/2/2011, 8/2/2012, 8/1/2013, 8/7/2014, 3/5/2015, 9/17/2015
Chemiluminescence analyzers measure the concentration of nitric oxide (NO) in exhaled breath as a marker of airway inflammation. Specifically, the NIOX system uses a chemiluminescence gas analyzer than can measure low concentrations of NO. The device is calibrated between 0 and 200 parts per billion (ppb) for exhaled NO measurements, with an accuracy of ±2.5 ppb or 5% (at 200 ppb). The ideal operating environment for NIOX includes an ambient temperature of 15° to 30°C, relative humidity of 30% to 7%, and atmospheric pressure of 860 hPa to 1060 hPa. The NIOX system can be used in an online and offline fashion. The patient exhales through a mouthpiece that is connected to the analyzer. A flow control system maintains exhalation at 50 mL per second, regardless of how forcefully a patient exhales. A visual display guides the patient to maintain an appropriate range of pressure while exhaling. According to the manufacturer, NIOX is suitable for children and adults, ≥ 4 years of age.¹

Evidence from the reviewed studies indicates that exhaled NO demonstrates moderate to good accuracy in diagnosing asthma and may be useful in predicting and monitoring inflammatory responses indicative of asthma exacerbation before and during anti-inflammatory treatment. There is also some evidence suggesting that exhaled NO may be useful for treatment management by dose titration to achieve optimal asthma control. However, the overall strength of the available evidence was moderate, with limitations in study design, small sample size, heterogeneous patient populations, variable methodological and treatment protocols, different outcome measures, and wide variations in threshold values of exhaled NO. There were no studies that evaluated whether exhaled NO resulted in improved long-term health outcomes, including effects on long-term asthma control, or improved quality of life. Additional studies are needed to clarify the role of exhaled NO breath testing in clinical practice.²³

Nitric oxide (NO) is now recognized as a biological mediator in animals and humans. NO is produced by the human lung and is present in the exhaled breath. It has been implicated in the pathophysiology of lung diseases, including asthma. The measurement of exhaled NO has been standardized for clinical use. Numerous studies have provided evidence regarding the applications of NO measurements in clinical practice, together with the performance characteristics and the strengths and the weaknesses of the test. Based on this evidence, this Clinical Practice Guideline is designed to guide clinicians as to how exhaled NO measurements should be used and interpreted.⁴

American Thoracic Society

Advances in technology and standardization have made FE\textsubscript{NO} measurement simple, permitting its use as a biomarker that adds a new dimension to the traditional clinical tools in the assessment and management of airways diseases.⁴ The ATS guidelines for interpretation of FE\textsubscript{NO} measurements are meant to enhance their clinical utility, but more work is still needed to better define the use of FENO in different clinical settings. The ATS recommends the following with respect to FE\textsubscript{NO}:

- The use of FE\textsubscript{NO} in the diagnosis of eosinophilic airway inflammation (strong recommendation, moderate quality of evidence).
- The use of FE\textsubscript{NO} in determining the likelihood of steroid responsiveness in individuals with chronic respiratory symptoms possibly due to airway inflammation (strong recommendation, low quality of evidence).
- FE\textsubscript{NO} may be used to support the diagnosis of asthma in situations in which objective evidence is needed (weak recommendation, moderate quality of evidence).
- Suggestion for the use of cut points rather than reference values when interpreting FE\textsubscript{NO} levels (weak recommendation, low quality of evidence).
• The accounting for age as a factor affecting $\text{FE}_{\text{NO}}$ in children younger than 12 years of age (strong recommendation, high quality of evidence).
• That low $\text{FE}_{\text{NO}}$ less than 25 ppb (, 20 ppb in children) be used to indicate that eosinophilic inflammation and responsiveness to corticosteroids are less likely (strong recommendation, moderate quality of evidence).
• That $\text{FE}_{\text{NO}}$ greater than 50 ppb (, 35 ppb in children) be used to indicate that eosinophilic inflammation and, in symptomatic patients, responsiveness to corticosteroids are likely (strong recommendation, moderate quality of evidence).
• That $\text{FE}_{\text{NO}}$ values between 25 ppb and 50 ppb (20–35 ppb in children) should be interpreted cautiously and with reference to the clinical context (strong recommendation, low quality of evidence).
• Accounting for persistent and/or high allergen exposure as a factor associated with higher levels of $\text{FE}_{\text{NO}}$ (strong recommendation, moderate quality of evidence).
• The use of $\text{FE}_{\text{NO}}$ in monitoring airway inflammation in patients with asthma (strong recommendation, low quality of evidence).
• Using the following values to determine a significant increase in $\text{FE}_{\text{NO}}$: greater than 20% for values over 50 ppb or more than 10 ppb for values lower than 50 ppb from one visit to the next (weak recommendation, low quality of evidence).
• Using a reduction of at least 20% in $\text{FE}_{\text{NO}}$ for values over 50 ppb or more than 10 ppb for values lower than 50 ppb as the cut point to indicate a significant response to anti-inflammatory therapy (weak recommendation, low quality of evidence).

National Specialty Organizations

The American College of Allergy, Asthma, and Immunology (ACAAI) notes in ACAAI published practice parameters that more novel measures of asthma control are being researched and developed. Measures include markers for asthma and airway inflammation, (e.g., sputum eosinophils, bronchial hyperresponsiveness, exhaled NO). The measures are currently being evaluated as markers of asthma control.3,5

Upon review of current evidence for clinical applications of exhaled NO, the American Thoracic Society (ATS) reviewed the available evidence concerning clinical applications of exhaled NO measurements and made two recommendations. First, based on low-quality evidence, measurement of fractional exhaled NO (FENO) was strongly recommended for monitoring airway inflammation in asthmatic patients. Based on moderate-quality evidence, the ATS weakly recommended that measurement of FENO be used to support the diagnosis of asthma under circumstances in which objective evidence is needed. With regard to the latter recommendation, the ATS emphasizes that FENO detects eosinophilic airway inflammation, which is often but not always the cause of asthma; therefore, there is no single diagnostic test for asthma and measurement of FENO cannot be considered a diagnostic test for detection of all types of asthma.3,6,7

Review of available evidence led to the Canadian Thoracic Society (CTS) recommendation that exhaled NO should not be utilized as an adjunct to or replacement for usual methods for guidance of asthma treatment, including adjustment of anti-inflammatory treatment in adults or children. In addition, insufficient evidence was found to develop a recommendation regarding the use of exhaled NO instead of or in addition to usual methods for guidance of asthma treatment in preschool children.3,8

The Global Initiative for Asthma (GINA) states that exhaled NO and carbon monoxide (CO) levels have been suggested as noninvasive markers of airway inflammation in asthma. In those with asthma and not prescribed steroids compared with those without asthma, the levels of exhaled NO and CO are elevated, yet these findings are not specific for asthma. Due to the cost and unavailability of tests for measurement of exhaled NO, GINA recommends that primary care be focused on controlling the clinical features of disease, including abnormalities of lung function (GINA, 2012).3,5

Asthma management guidelines from the Scottish Intercollegiate Guidelines Network (SIGN) specify that exhaled NO can be used for noninvasive detection of eosinophilic airway inflammation but FENO is not a sensitive or specific marker for the presence of asthma. SIGN concludes that there is insufficient evidence to support a role for FENO or sputum cytological analysis in the diagnosis of asthma in children. However, these tests may have a role in the assessment of disease severity or treatment response.3,10
Indications for Use

NIOX VERO® measures Nitric Oxide (NO) in human breath. Nitric Oxide is frequently increased in some inflammatory processes such as asthma. The fractional NO concentration in expired breath (FeNO), can be measured by NIOX VERO according to guidelines for NO measurement established by the American Thoracic Society. Measurement of FeNO by NIOX VERO is a quantitative, non-invasive, simple and safe method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti-inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels. NIOX VERO is suitable for children, approximately 7 - 17 years, and adults 18 years and older.

FeNO measurements provide the physician with means of evaluating an asthma patient's response to anti-inflammatory therapy, as an adjunct to the established clinical and laboratory assessments in asthma. The NIOX VERO is intended for prescription use and should only be used as directed in the NIOX VERO User Manual by trained healthcare professionals. NIOX VERO cannot be used with infants or by children approximately under the age of 7, as measurement requires patient cooperation. NIOX VERO should not be used in critical care, emergency care or in anesthesiology.

POSITION STATEMENT

Applicable To:
- ☑ Medicaid – Florida
- ☑ Medicaid – Georgia

Measurement of exhaled nitric oxide **is considered medically necessary and a covered benefit** in the diagnosis and monitoring of asthma and other respiratory disorders.

Applicable To:
- ☑ Medicaid – All Markets, excluding Florida and Georgia
- ☑ Medicare – All Markets

Measurement of exhaled nitric oxide **is considered experimental and investigational and NOT a covered benefit** in the diagnosis and monitoring of asthma and other respiratory disorders.

Measurement of exhaled breath condensate pH **is considered experimental and investigational and NOT a covered benefit** in the diagnosis and monitoring of asthma and other respiratory disorders.

Experimental, investigational or unproven and not covered when used to report measurement of exhaled nitric oxide or exhaled breath condensate.

CODING

**Covered CPT® Code**

95012 Nitric oxide expired gas determination (Georgia Medicaid only)

**Non-Covered CPT® Codes**

83987 pH; exhaled breath condensate

94799 Unlisted pulmonary service or procedure when billed to report exhaled nitric oxide measurement

95012 Nitric oxide expired gas determination

**HCPCS Level II Code** – No applicable codes.

**ICD-9-CM Procedure Code** – No applicable codes.
EXHALED NITRIC OXIDE AND BREATH CONDENSATE pH MEASUREMENT FOR RESPIRATORY DISORDERS

ICD-10-PCS Codes – No applicable codes.

Non-Covered ICD-9-CM Diagnosis Code – Not a covered benefit for all diagnosis including:
493.00-493.92 Asthma

Non-Covered Draft ICD-10-CM Diagnosis Code - Not a covered benefit for all diagnosis including:
J45.20 – J45.998 Asthma; mild, moderate, severe, unspecified, other


REFERENCES


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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<td>Approved by MPC. Included manufacturer information.</td>
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<td>3/5/2015</td>
<td>Approved by MPC. Expanded coverage for the Florida market.</td>
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<td>12/1/2011</td>
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