'Ohana Health Plan, a plan offered by WellCare Health Insurance of Arizona

WellCare (Alabama, Arizona, Arkansas, California, Connecticut, Florida, Georgia, Illinois, Indiana, Louisiana, Maine, Michigan, Mississippi, Missouri, New Hampshire, New Jersey, New York, North Carolina, Ohio, South Carolina, Tennessee, Texas, Washington)

WellCare Prescription Insurance

WellCare TexanPlus (Houston & Dallas markets)

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; 1/12/2017; 5/3/2018, 6/6/2019

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

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this CCG. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the CCG 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. All links are current at time of approval by the Medical Policy Committee (MPC). Lines of business (LOB) are subject to change without notice; current LOBs can be found at www.wellcare.com – select the Provider tab, then "Tools" and "Clinical Guidelines".

BACKGROUND

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.

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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 FENO 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 FENO 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 FENO:

- The use of FENO in the diagnosis of eosinophilic airway inflammation (strong recommendation, moderate quality of evidence).
- The use of FENO in determining the likelihood of steroid responsiveness in individuals with chronic respiratory symptoms possibly due to airway inflammation (strong recommendation, low quality of evidence).
- FENO 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 FENO levels (weak recommendation, low quality of evidence).
- The accounting for age as a factor affecting FENO in children younger than 12 years of age (strong recommendation, high quality of evidence).
- That low FENO 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 FENO 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 FENO 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 FENO (strong recommendation, moderate quality of evidence).
- The use of FENO in monitoring airway inflammation in patients with asthma (strong recommendation, low quality of evidence).
- Using the following values to determine a significant increase in FENO: 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 FENO 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

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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). 3,9

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 Use11

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:

☑ Medicare – All Markets (excluding KY)

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Exclusions

Other than diagnosis and monitoring of Asthma and eosinophilia airway inflammation, the use of NO in other conditions such as COPD (or Chronic Obstructive Pulmonary Disease), Pulmonary Hypertension and Cystic Fibrosis is considered to be experimental and investigational. An exception is the use of FENO in determining the likelihood of steroid responsiveness in individuals with chronic respiratory symptoms possibly due to airway inflammation (such as chronic bronchitis and COPD).

Per the American Thoracic Society Guidelines: In summary, the use of FENO in COPD and pulmonary hypertension and the use of nasal NO in diagnosis and monitoring of other respiratory disorders (e.g., allergic rhinitis, sinusitis, nasal polyposis, CF) are potentially of interest, but more re- search is needed before we know how clinically useful these tests can be for these disorders.[7]

Coverage

Measurement of exhaled nitric oxide **is considered medically necessary and a covered benefit** when the member meets one of the following criteria: [7]

- Member has a diagnosis of eosinophilic airway inflammation; **OR,**
- Member has chronic respiratory symptoms possibly due to airway inflammation and requires testing to determine the likelihood of steroid responsiveness; **OR,**
- Member requires further testing to support the diagnosis of asthma in situations in which objective evidence is needed; **OR,**
- Member receives FeNo testing to monitoring airway inflammation and has a diagnosis of asthma.

CODING

Covered CPT®* Code

95012 Nitric oxide expired gas determination

Non-Covered CPT®* Codes

83987 pH; exhaled breath condensate
94799 Unlisted pulmonary service or procedure when billed to report exhaled nitric oxide measurement

HCPCS Level II Codes – No applicable codes

ICD-10-PCS Codes – No applicable codes

Covered ICD-10-CM Diagnosis Codes

J4520 Mild intermittent asthma, uncomplicated
J4521 Mild intermittent asthma, with (acute) exacerbation
J4522 Mild intermittent asthma, with status asthmaticus
J4530 Mild persistent asthma, uncomplicated
J4531 Mild persistent asthma, with (acute) exacerbation
J4532 Mild persistent asthma, with status asthmaticus
J4540 Moderate persistent asthma, uncomplicated
J4541 Moderate persistent asthma, with (acute) exacerbation
J4542 Moderate persistent asthma, with status asthmaticus
J4550 Severe persistent asthma, uncomplicated
J4551 Severe persistent asthma, with (acute) exacerbation
J4552 Severe persistent asthma, with status asthmaticus
J45901 Unspecified asthma, with (acute) exacerbation
J45902 Unspecified asthma, with status asthmaticus
J45909 Unspecified asthma, uncomplicated
J45990 Exercise induced bronchospasm

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J45991 Cough variant asthma
J45998 Other asthma

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal / state laws.

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MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

Date	Action
6/6/2019	• Approved by MPC. No changes.
5/3/2018	• Approved by MPC. Updated coverage; applies to Medicare only.
1/12/2017	• Approved by MPC. Included language from AHCA (Florida).
9/17/2015	• Approved by MPC. Included manufacturer information.
3/5/2015	• Approved by MPC. Expanded coverage for the Florida market.
8/7/2014	• Approved by MPC. Expanded coverage for the Georgia market.
4/3/2014, 2/6/2014, 8/1/2013, 8/2/2015	• Approved by MPC. No changes.
12/1/2011	• New template design approved by MPC.
8/2/2011	• Approved by MPC. No changes.

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