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## OVERVIEW

Current techniques for diagnosing and monitoring asthma and predicting exacerbations are suboptimal. Two new strategies, evaluation of exhaled nitric oxide (NO) and exhaled breath condensate (EBC) are proposed. These techniques are also potentially useful in the management of other conditions such as chronic obstructive pulmonary disease and chronic cough. There are commercially available devices for measuring NO in expired breath and various laboratory techniques for evaluating components of EBC.

## MEDICAL CRITERIA

Not applicable.

## PRIOR AUTHORIZATION

Not applicable.

## POLICY STATEMENT

### BlueCHiP for Medicare and Commercial

Measurement of exhaled nitric oxide and exhaled breath condensate is considered not medically necessary in the diagnosis and management of asthma and other respiratory disorders including, but not limited to, chronic obstructive pulmonary disease and chronic cough because there is insufficient evidence in the published medical literature to demonstrate its efficacy.

## COVERAGE

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## BACKGROUND

Asthma is characterized by airway inflammation that leads to airway obstruction and hyper-responsiveness, which in turn leads to characteristic clinical symptoms including wheezing, shortness of breath, cough, and chest tightness. Guidelines for the management of persistent asthma stress the importance of long-term suppression of inflammation using steroids, leukotriene inhibitors, or other anti-inflammatory drugs. Existing techniques for monitoring the status of underlying inflammation have focused on bronchoscopy, with lavage and biopsy, or analysis by induced sputum. Given the cumbersome nature of these techniques, the ongoing assessment of asthma focuses not on the status of the underlying chronic inflammation, but rather on regular assessments of respiratory parameters such as FEV-1 (forced expiratory volume in one second) and peak flow. Therefore, there has been interest in non-invasive techniques to assess the underlying pathogenic chronic inflammation as reflected by measurements of inflammatory mediators.

Two proposed strategies are the measurement of exhaled nitric oxide (NO) and the evaluation of exhaled breath condensate (EBC).

### Measurement of Exhaled Nitric Oxide

Nitric Oxide is an important endogenous messenger and inflammatory mediator that is widespread in the human body, functioning, for example, to regulate peripheral blood flow, platelet function, immune reactions, and neurotransmission and to mediate inflammation. While the role of NO in asthma pathogenesis is still

under investigation, patients with asthma have been found to have high levels of exhaled NO, which decreases with treatment with corticosteroids. In biologic tissues, NO is unstable, limiting measurement. However, in the gas phase, NO is fairly stable, permitting its measurement in exhaled air. Exhaled NO is typically measured during single breath exhalations. First, the subject inspires NO-free air via a mouthpiece until total lung capacity is achieved, followed immediately by exhalation through the mouthpiece into the measuring device.

According to a 2009 joint statement by the American Thoracic Society and the European Respiratory Society, there is a consensus that the fractional concentration of FeNO is best measured at an exhaled rate of 50 mL per second (FeNO 50 mL/s) maintained within 10% for more than 6 seconds at an oral pressure between 5 and 20 cm H<sub>2</sub>O.<sup>(1)</sup> Results are expressed as the NO concentration in parts per billion (ppb), based on the mean of 2 or 3 values.

Several devices measuring exhaled NO are commercially available in the United States. In 2003, the U.S. Food and Drug Administration (FDA) cleared for marketing the Nitric Oxide Monitoring System (NIOX<sup>®</sup>), with the indication that measurements of the fractional NO concentration in expired breath (FE-NO)] provide the physician with means of evaluating an asthma patient's response to anti-inflammatory therapy, as an adjunct to established clinical and laboratory assessments in asthma. NIOX cannot be used with infants or children approximately under the age of 4, as measurement requires patient cooperation. In March 2008, the NIOX MINO was cleared for marketing. The main differences between this new device and the NIOX are that the NIOX MINO is handheld and portable and that it is not suitable for children younger than age 7 years.

### **Measurement of Exhaled Breath Condensate**

Exhaled breath condensate consists of exhaled air passed through a condensing or cooling apparatus, resulting in an accumulation of fluid. Although EBC is primarily derived from water vapor, it also contains aerosol particles or respiratory fluid droplets, which in turn contain various nonvolatile inflammatory mediators, such as cytokines, leukotrienes, oxidants, antioxidants, and various other markers of oxidative stress. There are a variety of laboratory techniques to measure the components of EBC, including such simple techniques as pH measurement, to the more sophisticated gas chromatography/mass spectrometry or high performance liquid chromatography, depending on the component of interest.

The RTube<sup>™</sup> Exhaled Breath Condensate collection system (Respiratory Research Inc.) and the ECoScreen EBC collection system (CareFusion, Germany) are registered with the FDA as Class I devices that collect expired gas. Respiratory Research has a proprietary gas-standardized pH assay, which, when performed by the company, is considered a laboratory-developed test.

Evidence is insufficient to determine the effect of exhaled nitric oxide and exhaled breath condensate tests on health outcomes, therefore these tests are considered not medically necessary.

### **CODING**

#### **BlueCHiP for Medicare and Commercial**

The following CPT codes are considered not medically necessary:

**83987**

**95012**

### **RELATED POLICIES**

Not applicable.

### **PUBLISHED**

Provider Update, May 2015

Provider Update, June 2014

Provider Update, June 2013

Provider Update, May 2012  
Provider Update, May 2011  
Provider Update, May 2010  
Provider Update, May 2009

## REFERENCES

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2. Selby A, Clayton B, Grundy J et al. Are exhaled nitric oxide measurements using the portable NIOX MINO repeatable? *Respir Res* 2010; 11:43.
3. See KC, Christiani DC. Normal values and thresholds for the clinical interpretation of exhaled nitric oxide levels in the US general population: results from the National Health and Nutrition Examination Survey 2007-2010. *Chest* 2013; 143(1):107-16.
4. Schneider A, Schwarzbach J, Faderl B et al. FENO measurement and sputum analysis for diagnosing asthma in clinical practice. *Respir Med* 2013; 107(2):209-16.
5. Katsoulis K, Ganavias L, Michailopoulos P et al. Exhaled nitric oxide as screening tool in subjects with suspected asthma without reversibility. *Int Arch Allergy Immunol* 2013; 162(1):58-64.
6. Sverrild A, Malinovschi A, Porsbjerg C et al. Predicting airway hyperreactivity to mannitol using exhaled nitric oxide in an unselected sample of adolescents and young adults. *Respir Med* 2013; 107(1):150-2.
7. Malinovschi A, Backer V, Harving H et al. The value of exhaled nitric oxide to identify asthma in smoking patients with asthmalike symptoms. *Respir Med* 2012; 106(6):794-801.

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