CLINICAL MEDICAL POLICY	
Policy Name:	Exhaled Nitric Oxide Measurement in the Management of Respiratory Disorders
Policy Number:	MP-104-MD-PA
Responsible Department(s):	Medical Management
Provider Notice/Issue Date:	11/01/2025; 11/01/2024; 11/01/2023; 11/01/2022; 12/17/2021; 11/23/2020; 12/09/2019
Effective Date:	12/01/2025; 12/01/2024; 12/01/2023; 12/01/2022; 01/17/2022; 12/21/2020; 12/09/2019
Next Annual Review:	09/2026
Revision Date:	09/16/2025; 09/18/2024; 09/20/2023; 09/21/2022; 09/15/2021; 09/16/2020
Products:	Highmark Wholecare℠ Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 6

Policy History

Date	Activity
12/01/2025	Provider Effective date
10/14/2025	PARP Approval
09/17/2025	QI/UM Committee review
09/17/2025	Annual Review: No changes to experimental/investigational stance. Updated 'Summary of Literature section.
12/01/2024	Provider Effective date
10/07/2024	PARP Approval
09/18/2024	QI/UM Committee review
09/18/2024	Annual Review: No changes to Experimental/Investigational stance. Updated 'Summary of Literature' section.
12/01/2023	Provider Effective date
10/11/2023	PARP Approval
09/20/2023	QI/UM Committee review
09/20/2023	Annual Review: No changes to E/I clinical stance. Updated 'Summary of Literature' and 'Reference Sources' sections.
12/01/2022	Provider Effective date
11/07/2022	PARP Approval
09/21/2022	QI/UM Committee review
09/21/2022	Annual Review: No changes to clinical criteria. Removed Archived Hayes information, updated 'Summary of Literature' and 'Reference Sources' sections.
01/17/2022	Provider effective date
10/27/2021	PARP Approval

09/15/2021	QI/UM Committee review
09/15/2021	Annual Review: No clinical criteria changes. Updated Summary of Literature and Reference sections. Added TAG determination information.
12/21/2020	Provider effective date
10/21/2020	PARP approval
09/16/2020	QI/UM Committee review
09/16/2020	Annual Review: No change to noncovered position; updated Summary of Literature and References
12/09/2019	Provider effective date
11/01/2019	PARP approval
09/18/2019	QI/UM Committee review
08/20/2019	Initial policy developed

Disclaimer

Highmark Wholecare℠ medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

Policy Statement

Highmark Wholecare℠ does not provide coverage under the benefits of the Company's Medicaid products for exhaled nitric oxide measurements in the management of respiratory disorders. The service is considered experimental and investigational and therefore, not medically necessary.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

Definitions

Prior Authorization Review Panel (PARP) - A panel of representatives from within the PA Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

Asthma - A chronic inflammatory disorder of airways characterized by episodes of impaired breathing caused by airflow obstruction, bronchial hyper responsiveness, and underlying inflammation.

Fractioned Exhaled Nitric Oxide (FENO) - The amount of nitric oxide present in the airways that is measurable in the exhaled air by using a (hand- held portable device) noninvasive technique utilizing chemiluminescent or electrochemical methods.

Procedures

1. Exhaled nitric oxide measurement in the treatment of asthma is considered experimental and investigational, and therefore not covered There is currently insufficient peer-reviewed medical evidence to support coverage.

2. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Wholecare℠ at any time pursuant to the terms of your provider agreement.

3. Place of Service
   The proper place of service for exhaled nitric oxide measurement is outpatient.

Governing Bodies Approval

On April 30, 2003, the FDA approved the NIOX Breath Nitric Oxide Test System®. The device is intended to be used as an aid in evaluating an asthma patient's response to anti-inflammatory therapy with the measurement of changes in the fractional exhaled nitric oxide concentration. It is to be used as an adjunct to established clinical and laboratory assessments of asthma for patients 7 years of age and older.

The NIOX MINO® Airway Inflammation Monitor was approved by the FDA on March 3, 2008. This is a hand-held device used to measure fractional exhaled nitric oxide in human breath.

In 2015, the NIOX VERO Airway Inflammation Monitor was approved by the FDA as a replacement for the NIOX MINO device. This device cannot be used with infants or by children under age 7.

On March 14, 2008, the FDA approved the Apieron INSIGHT™ eNO System to quantitatively measure exhaled nitric oxide in expired breath as a marker of inflammation for persons with asthma. It is intended to be used in the provider office and not be used in the critical care, emergency care, or anesthesiology setting. The device may be used in patients 8 years of age and older.

The Centers for Medicare and Medicaid Services (CMS) has not published any National Coverage Determinations (NCD) or Local Coverage Determinations (LCD) for exhaled nitric oxide at the time of this medical policy review.

The Pennsylvania Department of Human Services Technology Assessment Group (TAG) workgroup meets quarterly to discuss issues revolving around new technologies and technologies or services that were previously considered to be a program exception. During this meeting, decisions are made as to whether or not certain technologies will be covered and how they will be covered. TAG's decisions are as follow:

- Option #1: Approved - Will be added to the Fee Schedule
- Option #2: Approved as Medically Effective - Will require Program Exception
- Option #3: Approved with (or denied due to) Limited/Minimal Evidence of Effectiveness - Will require Program Exception
- Option #4: Denied - Experimental/Investigational

As of January 2017, the TAG workgroup assigned exhaled nitric oxide measurement in the treatment of asthma an Option # 4, specifically for CPT code 95012.

Summary of Literature

Asthma is a chronic condition that affects approximately 300 million people worldwide, with highest prevalence in North America, Australia, and Western Europe (Sverrild et al. 2012). Asthma has had a considerable economic impact and resulted in a substantial number of missed school days. In the United States, nearly 24.8 million persons (7.7% of the population) had current asthma in 2018 (CDC, 2021).

Once an individual has been diagnosed with asthma, selecting the type of therapy and selecting the optimal dose of therapy for the individual are challenging decisions faced by clinicians. Therapies such as inhaled corticosteroids (ICS) improve lung function and asthma control, decrease daytime and nighttime symptoms, and reduce the frequency of asthma exacerbations. However, many patients do not have a substantive response to therapy, and the response of a single patient to a given dose of therapy is variable. Methods that have been developed to further assess the level of airway inflammation to guide corticosteroid responsiveness, such as inducing sputum to measure eosinophils, may not be readily available. Other measures such as airway hyper-responsiveness (AHR) and peak expiratory flow variability may provide information that is useful to clinicians but require more involved testing (Khatri, Iaccarino, Barochia, 2021).

Nitric oxide (NO) is a gas that can be measured in the exhaled breath. Measuring the fraction of this gas during a steady-state exhalation, called the fractional exhaled NO (FeNO), is a standardized and quantitative method for assessing the levels of this gas in exhaled breath (Khatri, Iaccarino, Barochia, 2021).

According to the NIOX website, measuring exhaled nitric oxide can help manage a patient's care in the following clinical situations:

- In the diagnosis of asthma and identification of patients with Th2/Type 2 allergic/eosinophilic inflammation
- To determine steroid responsiveness and optimize the dose of inhaled steroid
- To uncover nonadherence to inhaled corticosteroids
- To reduce the likelihood of exacerbations in patients at risk for future events
- To identify asthmatics who are possible candidates for treatment with a biologic

The American Thoracic Society (ATS) published clinical practice guidelines on the use of measured fractional nitric oxide concentration in exhaled breath:

- In the diagnosis of eosinophilic airway inflammation (strong recommendation, moderate quality of evidence)
- In determining the likelihood of steroid responsiveness in individuals with chronic respiratory symptoms possibly due to airway inflammation (strong recommendation, low quality of evidence)
- In measurement of exhaled nitric oxide to support the diagnosis of asthma under circumstances in which objective evidence is needed (weak recommendation with moderate quality of evidence)

ATS noted that there is no single diagnostic test for asthma, and measurement of exhaled nitric oxide cannot be considered a diagnostic for detection of all types of asthma.

The Canadian Thoracic Society issued recommendation on the use of exhaled nitric oxide. These recommendations include that exhaled nitric oxide should not be used as a routine or adjunct measurement or as a replacement for standard assessment methodologies. This recommendation is based on the lack of scientific evidence.

Rationale
A Cochrane evaluation was published on exhaled nitric oxide levels used to guide treatment for children with asthma. In this review, nine randomized controlled trials comparing adjustment of asthma medications based on exhaled nitric oxide levels compared to those not using exhaled nitric oxide as in patient management based on clinical symptoms or asthma guidelines (or both) involving children. The studies ranged from 6 to 12 months, and there were a total of 1,426 children with 1,329, ranging from 10 to 14 years of age, who completed the studies. The exhaled nitric oxide cut-off values used by the different studies as a basis for decreasing or increasing medicines varied. It was reported that the use of exhaled nitric oxide level was beneficial in reducing the number of children who had least one exacerbation during the study. No difference was noted between the control group and the trial group in other measures of asthma severity that impact on day-to-day clinical symptoms or inhaled corticosteroid dose. The authors concluded that using exhaled nitric oxide levels to adjust asthma therapy may reduce the number of asthma attacks, but there was no impact on the day-to-day symptoms.

A systematic review of the use of fractional exhaled nitric oxide as a determinant for the clinical course of asthma demonstrated the prognostic value of measurement of FeNO as a surrogate biomarker for type 2 inflammation in the airways. High FeNO levels measured at the time of asthma diagnosis may reflect ongoing airway inflammation and indicate a poorer prognosis, with long-term impairment of lung function and increased exacerbation risk and loss of control. In order to determine individual disease characteristics and optimize treatment, a combination of the FeNO assessment with other biomarkers could be useful (Ulrik, Lange, Hilberg, 2021).

Coding Requirements

Non-covered Procedure Code
T*his procedure code will not be reimbursed without Medical Director approval.*

CPT Code	Description
95012	Nitric oxide expired gas determination

Reimbursement
Participating facilities will be reimbursed per their Highmark Wholecare℠ contract.

Reference Sources

Pennsylvania Department of Human Services. Technology Assessment Group (TAG) Coverage Decisions. Managed Care Operations Memorandum: OPS # 01/2017-003, Option #4. Accessed on August 22, 2022.

U.S. Department of Health and Human Services. Monitoring exhaled nitric oxide does not help manage asthma. NIH News. September 2008. Accessed on August 20, 2019.

Sverrild A, Porbjerg C, Backer V. The use of inhaled mannitol in the diagnosis and management of asthma. Expert Opin Pharmacother. 2012. Accessed on August 20, 2019.

Zitt M. Clinical applications of exhaled nitric oxide for the diagnosis and management of asthma: a consensus report. Clin Ther. 2005. Accessed on August 20, 2019.

Canadian Thoracic Society. Canadian Thoracic Society 2012 guidelines update: diagnosis and management of asthma in preschoolers, children and adults.

Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide the treatment for children with asthma. Cochrane Database of Systematic Review 08 November 2016. Accessed on August 22, 2019.

Ulrik CS, Lange P, Hilberg O. Fractional exhaled nitric oxide as a determinant for the clinical course of asthma: a systematic review. Eur Clin Respir J. February 24, 2021. Accessed on August 10, 2021.

Khatri SB, Iaccarino JM, Barochia A, et al. American Journal of Respiratory and Critical Care Medicine. Volume 204, Issue 10. September 2021. Accessed on August 22, 2022.

Centers for Disease Control and Prevention (CDC). Morbidity and Mortality Weekly Report (MMWR): Asthma Surveillance — United States, 2006–2018. September 17, 2021. Accessed on August 25, 2023.