



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 10/03/05
LAST REVIEW DATE: 07/31/18
LAST CRITERIA REVISION DATE: 01/10/12
ARCHIVE DATE:

MEASUREMENT OF EXHALED NITRIC OXIDE AND EXHALED BREATH CONDENSATE

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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MEASUREMENT OF EXHALED NITRIC OXIDE AND EXHALED BREATH CONDENSATE (cont.)

Description:

Measurement of exhaled nitric oxide (NO) has been investigated as a tool in the management of respiratory disorders, including asthma. Suggested uses in the management of asthma include assessing response to anti-inflammatory treatment, monitoring compliance with treatment and predicting exacerbations. Measurement of exhaled NO has also been investigated in the management of chronic obstructive pulmonary disease and chronic cough.

Exhaled breath condensate (EBC) pH indicates the acidity and alkalinity of water vapor created by the lungs. Evaluation of EBC components has also been investigated as a tool in the management of respiratory disorders, including asthma.

Criteria:

- Measurement of exhaled nitric oxide (NO) in the diagnosis and management of respiratory disorders is considered ***experimental or investigational*** based upon insufficient scientific evidence to permit conclusions concerning the effect on health outcomes.

These respiratory disorders include, *but are not limited to*:

- Asthma
- Chronic cough
- Chronic obstructive pulmonary disease

- Measurement of exhaled breath condensate (EBC) in the diagnosis and management of respiratory disorders is considered ***experimental or investigational*** based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
4. Insufficient evidence to support improvement outside the investigational setting.

These respiratory disorders include, *but are not limited to*:

- Asthma
- Chronic cough
- Chronic obstructive pulmonary disease



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Resources:

Literature reviewed 07/31/18. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

1. 2.01.61 BCBS Association Medical Policy Reference Manual. Measurement of Exhaled Nitric Oxide and Exhaled Breath Condensate in the Diagnosis and Management of Respiratory Disorders. Re-issue date 06/14/2018, issue date 10/09/2003.
2. Agency for Healthcare Research and Quality. The Clinical Utility of Fractional Exhaled Nitric Oxide (FeNO) in Asthma Management. 12/01/2017 (Comparative Effectiveness Review Number 197).
3. American Academy of Allergy Asthma & Immunology. AAAAI/ACAAI Joint Statement of Support of the ATS Clinical Practice Guideline: Interpretation of Exhaled Nitric Oxide for Clinical Applications. 02/01/2012.
4. American Thoracic Society, Dweik R, Boggs P, Erzurum S, CG I. An Official ATS Clinical Practice Guideline: Interpretation of Exhaled Nitric Oxide Levels (FENO) for Clinical Applications. May 2011.
5. BCBS Association Technology Assessment Program. Exhaled Nitric Oxide Monitoring as a Guide to Treatment Decisions in Chronic Asthma. 10/28/2005.
6. Borrill Z, Starkey C, Vestbo J, Singh D. Reproducibility of exhaled breath condensate pH in chronic obstructive pulmonary disease. *Eur Respir J*. 2005 Feb 2005;25(2):269-274.
7. California Technology Assessment Forum BSoCF. Exhaled Nitric Oxide Monitoring as a Guide to Treatment Decisions in Chronic Asthma. 02/15/2006.
8. Circassia Pharmaceuticals, Decision Driver Analytics, Massanari M, Brooks EA, Rickard KA. Investigation of the cost-effectiveness of FeNO measurement as a screening tool to direct omalizumab responsiveness in difficult-to-treat asthma patients. *Value in Health*. 2017;20.
9. Circassia Pharmaceuticals, Decision Driver Analytics, Massanari M, Brooks EA, Rickard KA, Roman AA. Cost-effectiveness of using FeNO in the management of asthma. *Value in Health*. 2017;20.

MEASUREMENT OF EXHALED NITRIC OXIDE AND EXHALED BREATH CONDENSATE (cont.)

Resources: (cont.)

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11. Donohue JF, Jain N. Exhaled nitric oxide to predict corticosteroid responsiveness and reduce asthma exacerbation rates. *Respir Med.*
12. Hanania NA, Wenzel S, Rosen K, et al. Exploring the effects of omalizumab in allergic asthma: an analysis of biomarkers in the EXTRA study. *Am J Respir Crit Care Med.* Apr 15 2013;187(8):804-811.
13. J. Konradsen, B. Nordlund, C. Pedroletti K, Alving GH. Exhaled nitric oxide in children with severe asthma. *European Respiratory Society.* 2012.
14. Lester D, Mohammad A, Leach EE, Hernandez PI, Walker EA. An investigation of asthma care best practices in a community health center. *J Health Care Poor Underserved.* Aug 2012;23(3 Suppl):255-264.
15. Mahr TA. Inflammometry in pediatric asthma: A review of fractional exhaled nitric oxide in clinical practice. *Allergy Asthma Proc.* 2013.
16. Malinowski A, Alving K, Kalm-Stephens P, Janson C, Nordvall L. Increased exhaled nitric oxide predicts new-onset rhinitis and persistent rhinitis in adolescents without allergic symptoms. *Clin Exp Allergy.* Mar 2012;42(3):433-440.
17. Mattes J, Murphy VE, Powell H, Gibson PG. Prenatal origins of bronchiolitis: protective effect of optimised asthma management during pregnancy. *Thorax.* Apr 2014;69(4):383-384.
18. McNicholl DM, Stevenson M, McGarvey LP, Heaney LG. The utility of fractional exhaled nitric oxide suppression in the identification of nonadherence in difficult asthma. *Am J Respir Crit Care Med.* Dec 1 2012;186(11):1102-1108.
19. National Heart Lung and Blood Institute. Guidelines for the Diagnosis and Management of Asthma. 2007.
20. National Institute for Health and Care Excellence (NICE) Guideline. Asthma: diagnosis, monitoring and chronic asthma management. 11/29/2017.
21. National Institutes of Health Clinical Center. Exhaled Breath Condensate as a Measure of Airway Inflammation in Children With Asthma. Accessed 09/28/05.



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Resources: (cont.)

22. Perez-de-Llano LA, Carballada F, Castro Anon O, et al. Exhaled nitric oxide predicts control in patients with difficult-to-treat asthma. *Eur Respir J*. Jun 2010;35(6):1221-1227.
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24. Rosias PP, Dompeling E, Dentener MA, et al. Childhood asthma: exhaled markers of airway inflammation, asthma control score, and lung function tests. *Pediatr Pulmonol*. 2004 Aug 2004;38(2):107-114.
25. Sverrild A, Malinowski A, Porsbjerg C, Backer V, Alving K. Predicting airway hyperreactivity to mannitol using exhaled nitric oxide in an unselected sample of adolescents and young adults. *Respir Med*. Jan 2013;107(1):150-152.
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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1-800-368-1019, 800-537-7697 (TDD). Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nilinígíí Blue Cross Blue Shield of Arizona haada yit'éego bina'idilkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yina'idilkidgo beehaz'áanii hólo díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilinígóó. Ata' halne'ígíí kojį' bich'į' hodilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أية تكلفة. للتحدث مع مترجم اتصل بـ 877-475-4799.

