Medical Policy
Analysis of Proteomic Patterns for Early Detection of Cancer

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Policy Number: 536
BCBSA Reference Number: 2.04.34A
NCD/LCD: N/A

Related Policies
Tumor Markers for Diagnosis and Management of Cancer, #167
Proteomics-Based Testing Related to Ovarian Cancer, #249

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO Blue^SM and Medicare PPO Blue^SM Members

Analysis of proteomic patterns in serum for screening and detection of cancer is considered **INVESTIGATIONAL**.

Prior Authorization Information
Inpatient
- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient
- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is **not** a covered service.
Commercial PPO and Indemnity	This is **not** a covered service.
Medicare HMO Blue^SM	This is **not** a covered service.
Medicare PPO Blue^SM	This is **not** a covered service.

CPT Codes / HCPCS Codes / ICD Codes
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes
There is no specific code for this type of testing.

Description
The analysis of proteomic patterns in serum for early detection of cancer has been proposed. Several of these proteomic tests are being studied, particularly in ovarian and prostate cancer.

The genetic basis of cancer has been the focus of intense research; however, genetic mutations do not reflect the complicated interactions between individual cells, tissue, and organs. Proteins are the functional units of cells and represent the end product of the interactions among the underlying genes. Research interest has been increasing in the field of proteomics (referring to the protein product of the genome), in an effort to improve on screening and detection efforts for malignancies.

Serum protein biomarkers
Current diagnostic and follow-up serum biomarkers in clinical oncology (e.g., prostate-specific antigen [PSA, prostate cancer], CA-125 [ovarian cancer]) involve identifying and quantifying specific proteins, but limitations may include non-specificity and elevation in benign conditions.

Ovarian cancer is the leading cause of death from gynecologic malignancy in the United States; most patients present with advanced disease, which has a 5-year survival rate from 15–45%. If the disease is diagnosed in Stage I, survival rates are 95%. Therefore, there is great interest in using a biomarker to detect ovarian cancer in its earliest stages, as current screening methods are inadequate.

Serum measurements of PSA are used as a screening method for detecting prostate cancer. Very low or very high serum PSA results are most reliable in determining cancer risk. However, values often fall within a range that is nonspecific, and thus many patients end up undergoing biopsy for benign disease. Proteomics has been proposed as a technique to further evaluate cancer risk in this diagnostic gray zone.

Proteomics
Proteomics involve the use of mass spectrometry to study differences in patterns of protein expression. While patterns of protein expression have been proposed to yield more biologically relevant and clinically useful information than assays of single proteins, many limitations in the use of proteomics exist. (1) In contrast to genomics, in which amplification techniques like polymerase chain reaction (PCR) allow for the investigation of single cells, no technology is available at the protein level. (1) Other issues between studies have been lack of uniform patient inclusion and exclusion criteria, small patient numbers, absence of standardized sample preparations, and limited analytical reproducibility.(1)

Proteomic tests
Correlogic Systems, Inc. developed a serum-based test using proteomics for the early detection of epithelial ovarian cancer called OvaCheck®. The test is based on proteomic patterns detected in the serum, which are further analyzed with the use of a mass spectrometer to profile a population of proteins based on their size and electrical charge. This type of analysis contains thousands of data points, which undergo further sophisticated computer analysis using artificial intelligence-based algorithms to identify a pattern that is consistent with ovarian cancer.

Summary
The use of proteomic pattern analysis for the early detection of cancer is currently in clinical trials and testing is not commercially available. There are no published prospective trials that demonstrate that the use of proteomic analysis for screening or detection of disease improves clinical outcomes, and it is therefore considered investigational.

Policy History

Date	Action
2/2020	Policy updated with literature review through February 1, 2020, references added. Policy statements unchanged.
11/2015	Ongoing investigational indications transferred from medical policy #167, Tumor Markers for Diagnosis and Management of Cancer. 11/1/2015

Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

1. Reymond MA, Schlegel W. Proteomics in cancer. Adv Clin Chem 2007; 44:103-42.
2. Dziadziuszko R, Hirsch FR. Advances in genomic and proteomic studies of non-small-cell lung cancer: clinical and translational research perspective. Clin Lung Cancer 2008; 9(2):78-84.
3. Lin Y, Dynan WS, Lee JR et al. The current state of proteomics in GI oncology. Dig Dis Sci 2009; 54(3):431-57.
4. Lomnytska M, Souchelnytskyi S. Markers of breast and gynecological malignancies: The clinical approach of proteomics-based studies. Proteomics Clin Appl 2007; 1(9):1090-101.
5. Unwin RD, Whetton AD. How will haematologists use proteomics? Blood Rev 2007; 21(6):315-26.
6. Petricoin EF, Ardekani AM, Hitt BA et al. Use of proteomic patterns in serum to identify ovarian cancer. Lancet 2002; 359(9306):572-7.
7. Questions and Answers: OvaCheck and NCI/FDA Ovarian Cancer Clinical Trials Using Proteomic Technology. Available online at: www.cancer.gov/templates/content_nav_print.aspx?viewid=38D1A09A-7C41-4A
8. Diamandis EP. Proteomic patterns in serum and identification of ovarian cancer. Lancet 2002;360(9327):170; author reply 70-1.
9. Diamandis EP. Analysis of serum proteomic patterns for early cancer diagnosis: drawing attention to potential problems. J Natl Cancer Inst 2004; 96(5):353-6.
10. Ornstein DK, Rayford W, Fusaro VA et al. Serum proteomic profiling can discriminate prostate cancer from benign prostates in men with total prostate specific antigen levels between 2.5 and 15.0 ng/ml. J Urol 2004; 172(4 Pt 1):1302-5.
11. McLerran D, Grizzle WE, Feng Z et al. SELDI-TOF MS whole serum proteomic profiling with IMAC surface does not reliably detect prostate cancer. Clin Chem 2008; 54(1):53-60.
12. Bast RC, Jr., Brewer M, Zou C et al. Prevention and early detection of ovarian cancer: mission impossible? Recent Results Cancer Res 2007; 174:91-100.
13. Belluco C, Petricoin EF, Mammano E et al. Serum proteomic analysis identifies a highly sensitive and specific discriminatory pattern in stage 1 breast cancer. Ann Surg Oncol 2007; 14(9):2470-6.
14. Garrisi VM, Abbate I, Quaranta M et al. SELDI-TOF serum proteomics and breast cancer: which perspective? Expert Rev Proteomics 2008; 5(6):779-85.
15. Leman ES, Schoen RE, Weissfeld JL et al. Initial analyses of colon cancer-specific antigen (CCSA)-3 and CCSA-4 as colorectal cancer-associated serum markers. Cancer Res 2007; 67(12):5600-5.
16. Li J, Zhuang Z, Okamoto H et al. Proteomic profiling distinguishes astrocytomas and identifies differential tumor markers. Neurology 2006; 66(5):733-6.
17. Society of Gynecologic Oncologists. Chicago Illinois. *Press release* February 7, 2004.