BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 2.04.97 Microarray-Based Gene Expression Profile Testing for Multiple Myeloma Risk Stratification

Annual Effective Policy Date: January 1, 2024

Original Policy Date: December 2015

Related Policies:

None

Microarray-Based Gene Expression Profile Testing for Multiple Myeloma Risk Stratification

Description

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Multiple myeloma is a genetically complex-and invariably fatal-disease. A host of well-characterized factors related to tumor biology, tumor burden, and patient-centered characteristics are used to stratify patients into high-, intermediate-, and standard-risk categories for prognostic purposes, as well as determining treatment intensity. However, clinical outcomes have varied among patients in the same risk category who received similar therapy. Thus, more specific methods have been sought to classify multiple myeloma; one such method being proposed is the utilization of a microarray-based gene expression profile (GEP) analysis, which serves to reveal the underlying activity of cellular biologic pathways. This method lends itself to a variety of benefits including the ability to risk-stratify patients with multiple myeloma, as well as guide treatment decisions.

OBJECTIVE

The objective of this evidence review is to determine whether risk stratification using a gene expression profile risk score improves the net health outcome in individuals with multiple myeloma.

POLICY STATEMENT

Microarray-based gene expression profile testing for multiple myeloma is considered **investigational** for all indications.

POLICY GUIDELINES

According to Mayo Clinic recommendations, a large number of prognostic factors have been validated and categorized into 3 main groups: tumor biology, tumor burden, and patient-related factors. These factors must be considered to individualize the choice of therapy in individuals with multiple myeloma (Table PG1).

Table PG1. Prognostic Factors in Multiple Myeloma

Tumor Biology	Tumor Burden	Patient-Related
• Ploidy • 17p (p53 deletion) • t(14;16) • t(14;20) • t(4;14) • Deletion 13 on conventional cytogenetics • Alterations in chromosome 1 • t(11;14) • t(6;14) • Lactate dehydrogenase levels • Plasma cell proliferative rate • Presentation as plasma cell leukemia • High-risk GEP signature[a]	• Durie-Salmon stage • International Staging System stage • Extramedullary disease	• ECOG Performance Status • Age • Renal function

Adapted from Mikhael et al (2013).
ECOG: Eastern Cooperative Oncology Group; GEP: gene expression profile.
[a] The Mayo Clinic does not currently recommend or routinely perform GEP analysis in a non-research setting. However, Mikhael et al (2013) have suggested GEP analysis will likely play a greater role in the management of multiple myeloma as evidence develops.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient's existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

FDA REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). The MyPRS™/MyPRS *Plus*™ GEP70 test was acquired by Quest Diagnostics in December 2016. Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

RATIONALE

Summary of Evidence

For individuals who have multiple myeloma who received risk stratification using a gene expression profile (GEP) test, the evidence includes retrospective series that correlate risk scores with survival. Relevant outcomes are progression-free survival, overall survival, disease-specific survival, test validity, and other test performance measures. The microarray-based GEP70 test (MyPRS/MyPRS *Plus*) has been reported to risk-stratify multiple myeloma patients. Some predictive models in the body of evidence combine risk status as determined by the GEP70 test with additional clinical or genetic variables. Patients with a high GEP70 risk score have a substantially increased risk of mortality compared with patients without a high score. However, there is no evidence (from available studies) that this test would add incremental value to existing risk stratification methods; nor have any studies demonstrated the need to prospectively allocate patients to risk-based therapies based on the GEP70 score. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Mayo Clinic Stratification of Multiple Myeloma and Risk-Adapted Therapy

Guidelines from the Mayo Clinic (2017) have stated that "if indicated, gene expression profiling may be performed to further understand the behavior of the disease and guide therapy."[30,]

National Comprehensive Cancer Network

The National Comprehensive Cancer Network practice guidelines (v4.2023) on multiple myeloma do not provide recommendations regarding use of gene expression profiling.[31,]

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2015	New policy	Microarray-based gene expression profile testing for multiple myeloma is considered investigational for all indications.
December 2018	Replace policy	Policy updated with literature review through August 6, 2018; references 30-31 added. Policy statement unchanged.
December 2019	Replace policy	Policy updated with literature review through August 6, 2019; no references added, reference on NCCN updated. Policy statement unchanged.
December 2020	Replace policy	Policy updated with literature review through August 20, 2020; references added. Policy statement unchanged.
December 2021	Replace policy	Policy updated with literature review through August 22, 2021; no references added. Policy statement unchanged.
December 2022	Replace policy	Policy updated with literature review through August 22, 2022; reference added. Minor editorial refinements to Policy Guideline statements; intent unchanged.
December 2023	Replace policy	Policy updated with literature review through September 1, 2023; reference added. Policy statement unchanged.