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The Department of Vermont Health Access Clinical Criteria

Subject: Myeloproliferative Disease Genetic Testing
Last Review: December 17, 2024*
Past Revisions: N/A

***Please note: Most current content changes will be highlighted in yellow.**

Description of Service or Procedure

Myeloproliferative disorders are a group of conditions that cause abnormal growth of blood cells in the bone marrow. They include polycythemia vera (PV), essential thrombocytopenia (ET), primary myelofibrosis (PMF), and chronic myelogenous leukemia (CML). The World Health Organization (WHO) further classifies PV, ET, and PMF as Philadelphia chromosome negative myeloproliferative neoplasms (MPNs). The diagnosis of an MPN is suspected based upon clinical, laboratory, and pathological findings (i.e. bone marrow morphology). MPNs are related, but distinct form, myelodysplastic syndromes (MDS). In general, MDS are characterized by ineffective or dysfunctional blood cells, while MPN are characterized by an increase in the number of blood cells.

Polycythemia Vera (PV): PV is a chronic MPD characterized by increased hemoglobin, hematocrit, and red blood cell mass. Members with PV are often asymptomatic though there is an associated increased risk for thrombosis and transformation to acute myelogenous leukemia (AML) or PMF.

Essential Thrombocythemia (ET): ET is a disorder of sustained increased platelet count. Most ET patients (60%) carry a somatic JAK2 V617F mutation, while a smaller percentage (5-10%) have activating MPL mutations.

Primary Myelofibrosis (PMF): PMF is a rare disorder in which the bone marrow is replaced with fibrous tissue, leading to bone marrow failure. Clinical features are similar to ET and the approximate incidence is 1 in 100,000 individuals. Those with PMF can be asymptomatic in the early stages of the disease and treatment may not initially be necessary. Progression of the disease can include transformation to AML.

Disclaimer

Coverage is limited to that outlined in Medicaid Rule or Health Care Administrative Rules that pertain to the member's aid category. Prior Authorization (PA) is only valid if the member is eligible for the applicable item or service on the date of service.

Medicaid Rule

Medicaid and Health Care Administrative Rules can be found at https://humanservices.vermont.gov/rules-policies/health-care-rules/health-care-administrative-rules-hcar/adopted-rules

7102.2 Prior Authorization Determination
4.101 Medical Necessity for Covered Services
4.104 Medicaid Non-Covered Services
4.106 Early and Periodic Screening, Diagnostic and Treatment (EPSDT) Services
4.218 Laboratory and Radiology Services

Coverage Position

Myeloproliferative disease genetic testing may be covered for members:

- When the test is prescribed by a licensed medical provider, enrolled in the Vermont Medicaid program, operating within their scope of practice as described on the Vermont Office of Professional Regulation's website*, Statute, or rule who is knowledgeable regarding MPL genetic testing and who provides medical care to the member AND
- When the clinical criteria below are met.

* Vermont's Office of Professional Regulation's website: https://sos.vermont.gov/opr/

Coverage Criteria

This policy provides coverage for multi-gene non-next generation sequencing (NGS) panel testing and NGS testing for the diagnostic workup for myeloproliferative disease (MPD), and limited coverage for single-gene testing of patients with BCR-ABL negative MPD. BCR-ABL negative MPD includes polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF).

For laboratories performing single gene technologies, a sequential genetic testing approach is expected. Once a positive result is obtained and the appropriate diagnosis is established, further testing should stop. Reflex testing to the next gene will be considered reasonable and necessary if the following sequence of genetic tests produce a negative result:

1. BCR-ABL negative test results, progress to #2
2. JAK 2 (JAK2 V617F) negative test results, progress to #3 or #4
3. JAK, exon 12 (JAK2 exon 12 is only performed when PV is suspected)
4. Calreticulin (CALR)/MPL (CALR/MPL is only done when either ET or PMF is suspected; testing for CALR/MPL does NOT require a negative JAK2 exon 12, just a negative JAK2 V617F result)

Genetic testing of the JAK2 V617F mutation is medically necessary and may be covered for members when the following criteria are met:

- Are 18 years or older, AND

- Meet criteria for polycythemia vera (PV), essential thrombocythemia (ET) or primary myelofibrosis (PMF) in accordance with the World Health Organization's diagnostic criteria for myeloproliferative neoplasms, AND
- Medical management will be impacted by this genetic testing.

Genetic testing of JAK2 exon 12, performed to identify PV, is medically necessary and may be covered for members when the following criteria are met:

- Genetic testing impacts medical management; and
- Patient meets the WHO's diagnostic criteria for PV, if JAK2 exon 12 testing were positive; and
- JAK2 V617F mutation analysis was previously completed and was negative.

Genetic testing of the CALR gene (only found in ET and PMF) is medically necessary and may be covered for members when the following criteria are met:

- Genetic testing impacts medical management; and
- JAK2 V617F mutation analysis was previously completed and negative; and
- Member meets the WHO's diagnostic criteria for MPD (i.e., ET, PMF) if a clonal marker were identified.

Genetic testing of the MPL gene is medically necessary and may be covered for members when the following criteria are met:

- Genetic testing impacts medical management; and
- JAK2 V617F mutation analysis was previously completed and negative; and
- Member meets the WHO's diagnostic criteria for MPD (i.e., ET, MPF) if a clonal marker were identified.

For laboratories performing NGS or "hotspot" testing platforms: Molecular testing for BCR-ABL, JAK 2, JAK2 exon 12, and CALR/MPL genes by NGS is covered as medically necessary for the identification of myeloproliferative disorders.

2016 World Health Organization diagnostic criteria for PV and ET

2016 World Health Organization diagnostic criteria for PMF

The National Comprehensive Cancer Network (NCCN) guidelines (Version 1.2024) on myeloproliferative neoplasms, recommend for patients with suspected MPN, "molecular testing (blood) for JAK2 V617F mutation; if negative, test for CALR and MPL mutations (for patients with ET and MF) and JAK2 Exon 12 mutations (for patients with PV) or molecular testing using multigene NGS panel that includes JAK2, CALR, and MPL." The NCCN recommends following the 2016 WHO diagnostic criteria to diagnose MPNs (NCCN, 2024).

Considerations: Providers requesting this test should provide pre- and post-test genetic counseling for the member and family, if applicable.

Early and Periodic Screening, Diagnostic and Treatment (EPSDT): Vermont Medicaid will provide comprehensive services and furnish all Medicaid coverable, appropriate, and medically necessary services needed to correct and ameliorate health conditions for Medicaid members under age 21.

Please note, Vermont Medicaid Clinical Criteria is reviewed based on available literature, evidence- based guidelines/standards, Medicaid rule and policy, and Medicare coverage determinations that may be appropriate to incorporate when applicable.

Clinical criteria for repeat service or procedure

Repeat service is not applicable for this genetic testing. If JAK 2 results are negative, Vermont Medicaid does not cover BCR-ABL genetic testing.

Type of service or procedure not covered (this list may not be all inclusive)

- For children younger than 18 years of age
- JAK2 tyrosine, CALR, and MPL mutation testing for the following situations, which are considered **investigational**:
    - Diagnosis of nonclassic forms of myeloproliferative neoplasms (MPNs)
    - Molecular phenotyping of individuals with MPNs
    - Monitoring, management, or selecting treatment in patients with myeloproliferative neoplasms.

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