Geisinger

Geisinger Health Plan Policies and Procedure Manual

Policy: MP197

Section: Medical Benefit Policy

Subject: Janus Kinase 2 (JAK 2), CALR and MPL Gene Mutation Analysis

Applicable Lines of Business

Commercial	**X**	**CHIP**	**X**
Medicare	**X**	**ACA**	**X**
Medicaid	**X**		

I. Policy: Janus Kinase 2 (JAK 2), CALR and MPL Gene Mutation Analysis

II. Purpose/Objective:

To provide a policy of coverage regarding Janus Kinase 2 (JAK 2), CALR and MPL Gene Mutation Analysis

III. Responsibility:

A. Medical Directors
B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an

illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

DESCRIPTION:
Janus Kinase 2 (JAK 2, JAK 2^{V617F}) mutation analysis has been established as a laboratory test to aid in the diagnosis and clinical management and prognosis of patients with primary myelofibrosis (PMF), myeloproliferative disorder (MPD) and myeloproliferative neoplasms (MPN).

The JAK2 ^{V617F} mutation occurs in exon 14 and is found in greater than 90% of individuals with polycythemia vera, and in nearly 60% of individuals with essential thrombocytopenia (ET) or myelofibrosis (MF). Rare insertions and deletions have been found in exon 12 in 2-3% of patients with polycythemia vera.

Hereditary thrombocytosis has also been reported with germline JAK2 mutation (JAK2 V617I) and associated with vascular events, but not fibrotic/leukemic progression.

Activating mutations in the thrombopoietin receptor gene (MPL) W515L/K) are reported in approximately 5% to 8% of all patients with MF and 1% to 4% of all patients with ET

Frameshift mutations in exon 9 of the calreticulin gene (CALR) are reported in approximately 20% to 35% of all patients with essential ET and MF, which accounts for 60%–80% of patients with JAK2/MPL-negative ET and MF.

Testing of specific variants in JAK2, MPN, and/or MPN has been found to be useful in patients with clinical, laboratory, or pathological findings suggesting essential thrombocythemia or myelofibrosis and who have tested negative for the V617F mutation in JAK2 ^{V617F}.

INDICATIONS:
JAK 2^{V617F} mutation analysis is considered medically necessary in the evaluation of:

- Adults, age 21 or older, presenting with clinical, laboratory, or pathological findings suggesting classic forms of polycythemia vera; or
- Adults with isolated idiopathic erythrocytosis, AND a serum erythropoietin level <10.

JAK2 mutation analysis is considered medically necessary in the evaluation of:

- Adult's initial diagnostic evaluation of clinical or laboratory findings suggestive of either:
    a. essential thrombocythemia
    b. primary myelofibrosis

If JAK2 testing is negative, serial testing of MPL followed by CALR is recommended

Janus Kinase 2 (JAK2; JAK2^{V617F}) gene mutation analysis is considered medically necessary in members presenting with clinical, laboratory, or pathological findings suggesting classic forms of MPD/MPN/PMF.

In members presenting with clinical, laboratory, or pathological findings suggesting classic forms of MPD/MPN/PMF who were negative for Janus Kinase 2 (JAK2; JAK2^{V617F}) gene mutation, testing for the JAK2 exon 12 gene mutation, CALR and MPL is considered medically necessary.

Additional mutations in ASXL1, EZH2, TET2, IDH1, IDH2, SRSF2, and SF3B1 genes are noted to be of use in determining the clonal nature of disease. In the absence of JAK2, CALR, and MPL mutations, the presence of another clonal marker is included as one of the major diagnostic criteria for PMF and may be considered medically necessary if JAK2, CALR, and MPL testing is negative or inconclusive.

EXCLUSIONS:
Testing for Janus Kinase 2 (JAK 2, JAK 2^{V617F}) gene mutation is considered not medically necessary for any other indication including but not limited to:
- Myeloproliferative disorders (MPD) in children under the age of 21
- Quantitative JAK 2^{V617F} allele burden subsequent to qualitative detection of JAK 2^{V617F}.

Testing for the CALR or MPL gene mutation is considered not medically necessary when the criteria above have not been met.

Medicaid Business Segment:

Any requests for services, that do not meet criteria set in the PARP, may be evaluated on a case by case basis.

CODING ASSOCIATED WITH: Janus Kinase 2 (JAK 2) Gene Mutation Analysis

The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.

81219 CALR (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9
81270 JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) Variant
81279 JAK2 (Janus kinase 2)(eg, myeloproliferative disorder) targeted sequence analysis (eg, exons 12 and 13)
81402 Molecular pathology procedure, Level 3 (eg, > 10 SNP's 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD]) [when specified as the following]:
MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (eg myeloproliferative disorder), common variants (eg, W515A, W515K, W515L, W515R)
81403: Molecular pathology procedure, Level 4 (e.g., analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR [polymerase chain reaction] in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) - which includes: o JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder), exon 12 sequence and exon 13 sequence, if performed
0017U Oncology (hematolymphoid neoplasia), JAK2 mutation, DNA, PCR amplification of exons 12-14 and sequence analysis, blood or bone marrow, report of JAK2 mutation not detected or detected
0027U JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, targeted sequence analysis exons 12-15

LINE OF BUSINESS: Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

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This policy will be revised as necessary and reviewed no less than annually.

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