

BRAF Mutation Analysis

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Definition

BRAF gene (serine/threonine-protein kinase B-Raf, v-raf murine sarcoma viral oncogene homolog B1), is an oncogene that encodes a protein kinase, which is part of the RAS/MAPK signaling pathway that regulates intracellular signaling and mediates cell growth, division, differentiation, cell movement and self-destruction. It is a principle downstream effector of NRAS and KRAS.

BRAF gene mutations are seen most commonly in melanoma, but have also been found in acute leukemias, lymphoma, colon, lung and thyroid cancer. BRAF gene mutations occur in less than 15% of colorectal cancers and approximately 50% of cutaneous melanomas.

Guideline

BRAF mutation analysis in tumor tissue of members with Langerhans Cell Histiocytosis, Erdheim Chester Disease (ECD), unresectable or metastatic melanoma, metastatic colorectal cancer, non-small cell lung cancer, thyroid cancer or hairy cell leukemia is considered medically necessary to select those who would benefit from treatment with an FDA-approved BRAF inhibitor.

Limitations/Exclusions

BRAF mutation analysis is considered investigational and not medically necessary for all other indications that do not meet the criteria above.

Results will help select or maintain therapy.

Revision History

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| Dec. 12, 2021 | Added note communicating that results must impact therapeutic decision-making |
| Dec. 11, 2020 | Added thyroid cancer as covered indication |
| Oct. 11, 2019 | Added Langerhans Cell Histiocytosis, Erdheim Chester Disease (ECD) as covered indications (eff. Jan. 11, 2020) |
| Oct. 14, 2016 | Added non-small cell lung cancer and hairy cell leukemia as covered indications. |

Applicable Procedure Codes

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| 81210 | BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s) |
| 88363 | Examination and selection of retrieved archival (ie, previously diagnosed) tissue(s) for molecular analysis (e.g., KRAS mutational analysis) [when specified in relation to BRAF testing] |

Applicable ICD-10 Diagnosis Codes

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| C17.0 | Malignant neoplasm of duodenum |
| C17.1 | Malignant neoplasm of jejunum |
| C17.2 | Malignant neoplasm of ileum |
| C17.3 | Meckel's diverticulum, malignant |
| C17.8 | Malignant neoplasm of overlapping sites of small intestine |
| C17.9 | Malignant neoplasm of small intestine, unspecified |
| C18.0 | Malignant neoplasm of cecum |
| C18.1 | Malignant neoplasm of appendix |
| C18.2 | Malignant neoplasm of ascending colon |
| C18.3 | Malignant neoplasm of hepatic flexure |
| C18.4 | Malignant neoplasm of transverse colon |
| C18.5 | Malignant neoplasm of splenic flexure |
| C18.6 | Malignant neoplasm of descending colon |
| C18.7 | Malignant neoplasm of sigmoid colon |
| C18.8 | Malignant neoplasm of overlapping sites of colon |
| C18.9 | Malignant neoplasm of colon, unspecified |
| C19 | Malignant neoplasm of rectosigmoid junction |
| C20 | Malignant neoplasm of rectum |
| C21.1 | Malignant neoplasm of anal canal |
| C21.2 | Malignant neoplasm of cloacogenic zone |
| C21.8 | Malignant neoplasm of overlapping sites of rectum, anus and anal canal |
| C33 | Malignant neoplasm of trachea |
| C34.00 | Malignant neoplasm of unspecified main bronchus |
| C34.01 | Malignant neoplasm of right main bronchus |
| C34.02 | Malignant neoplasm of left main bronchus |
| C34.10 | Malignant neoplasm of upper lobe, unspecified bronchus or lung |
| C34.11 | Malignant neoplasm of upper lobe, right bronchus or lung |
| C34.12 | Malignant neoplasm of upper lobe, left bronchus or lung |
| C34.2 | Malignant neoplasm of middle lobe, bronchus or lung |
| C34.30 | Malignant neoplasm of lower lobe, unspecified bronchus or lung |
| C34.31 | Malignant neoplasm of lower lobe, right bronchus or lung |
| C34.32 | Malignant neoplasm of lower lobe, left bronchus or lung |
| C34.80 | Malignant neoplasm of overlapping sites of unspecified bronchus and lung |
| C34.81 | Malignant neoplasm of overlapping sites of right bronchus and lung |

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| C34.82 | Malignant neoplasm of overlapping sites of left bronchus and lung |
| C34.90 | Malignant neoplasm of unspecified part of unspecified bronchus or lung |
| C34.91 | Malignant neoplasm of unspecified part of right bronchus or lung |
| C34.92 | Malignant neoplasm of unspecified part of left bronchus or lung |
| C43.0 | Malignant melanoma of lip |
| C43.10 | Malignant melanoma of unspecified eyelid, including canthus |
| C43.111 | Malignant melanoma of right upper eyelid, including canthus |
| C43.112 | Malignant melanoma of right lower eyelid, including canthus |
| C43.121 | Malignant melanoma of left upper eyelid, including canthus |
| C43.122 | Malignant melanoma of left lower eyelid, including canthus |
| C43.20 | Malignant melanoma of unspecified ear and external auricular canal |
| C43.21 | Malignant melanoma of right ear and external auricular canal |
| C43.22 | Malignant melanoma of left ear and external auricular canal |
| C43.30 | Malignant melanoma of unspecified part of face |
| C43.31 | Malignant melanoma of nose |
| C43.39 | Malignant melanoma of other parts of face |
| C43.4 | Malignant melanoma of scalp and neck |
| C43.51 | Malignant melanoma of anal skin |
| C43.52 | Malignant melanoma of skin of breast |
| C43.59 | Malignant melanoma of other part of trunk |
| C43.60 | Malignant melanoma of unspecified upper limb, including shoulder |
| C43.61 | Malignant melanoma of right upper limb, including shoulder |
| C43.62 | Malignant melanoma of left upper limb, including shoulder |
| C43.70 | Malignant melanoma of unspecified lower limb, including hip |
| C43.71 | Malignant melanoma of right lower limb, including hip |
| C43.72 | Malignant melanoma of left lower limb, including hip |
| C43.8 | Malignant melanoma of overlapping sites of skin |
| C43.9 | Malignant melanoma of skin, unspecified |
| C44.1021 | Unspecified malignant neoplasm of skin of right upper eyelid, including canthus |
| C44.1022 | Unspecified malignant neoplasm of skin of right lower eyelid, including canthus |
| C44.1091 | Unspecified malignant neoplasm of skin of left upper eyelid, including canthus |
| C44.1092 | Unspecified malignant neoplasm of skin of left lower eyelid, including canthus |
| C44.1921 | Other specified malignant neoplasm of skin of right upper eyelid, including canthus |
| C44.1922 | Other specified malignant neoplasm of skin of right lower eyelid, including canthus |
| C44.1991 | Other specified malignant neoplasm of skin of left upper eyelid, including canthus |
| C44.1992 | Other specified malignant neoplasm of skin of left lower eyelid, including canthus |
| C73 | Malignant neoplasm of thyroid gland |
| C77.0 | Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck |
| C77.1 | Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes |
| C77.2 | Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes |
| C77.3 | Secondary and unspecified malignant neoplasm of axilla and upper limb lymph nodes |
| C77.4 | Secondary and unspecified malignant neoplasm of inguinal and lower limb lymph nodes |

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| C77.5 | Secondary and unspecified malignant neoplasm of intrapelvic lymph nodes |
| C77.8 | Secondary and unspecified malignant neoplasm of lymph nodes of multiple regions |
| C77.9 | Secondary and unspecified malignant neoplasm of lymph node, unspecified |
| C78.00 | Secondary malignant neoplasm of unspecified lung |
| C78.01 | Secondary malignant neoplasm of right lung |
| C78.02 | Secondary malignant neoplasm of left lung |
| C78.1 | Secondary malignant neoplasm of mediastinum |
| C78.2 | Secondary malignant neoplasm of pleura |
| C78.30 | Secondary malignant neoplasm of unspecified respiratory organ |
| C78.39 | Secondary malignant neoplasm of other respiratory organs |
| C78.4 | Secondary malignant neoplasm of small intestine |
| C78.5 | Secondary malignant neoplasm of large intestine and rectum |
| C78.6 | Secondary malignant neoplasm of retroperitoneum and peritoneum |
| C78.7 | Secondary malignant neoplasm of liver and intrahepatic bile duct |
| C78.80 | Secondary malignant neoplasm of unspecified digestive organ |
| C78.89 | Secondary malignant neoplasm of other digestive organs |
| C79.00 | Secondary malignant neoplasm of unspecified kidney and renal pelvis |
| C79.01 | Secondary malignant neoplasm of right kidney and renal pelvis |
| C79.02 | Secondary malignant neoplasm of left kidney and renal pelvis |
| C79.10 | Secondary malignant neoplasm of unspecified urinary organs |
| C79.11 | Secondary malignant neoplasm of bladder |
| C79.19 | Secondary malignant neoplasm of other urinary organs |
| C79.2 | Secondary malignant neoplasm of skin |
| C79.31 | Secondary malignant neoplasm of brain |
| C79.32 | Secondary malignant neoplasm of cerebral meninges |
| C79.40 | Secondary malignant neoplasm of unspecified part of nervous system |
| C79.49 | Secondary malignant neoplasm of other parts of nervous system |
| C79.51 | Secondary malignant neoplasm of bone |
| C79.52 | Secondary malignant neoplasm of bone marrow |
| C79.60 | Secondary malignant neoplasm of unspecified ovary |
| C79.61 | Secondary malignant neoplasm of right ovary |
| C79.62 | Secondary malignant neoplasm of left ovary |
| C79.70 | Secondary malignant neoplasm of unspecified adrenal gland |
| C79.71 | Secondary malignant neoplasm of right adrenal gland |
| C79.72 | Secondary malignant neoplasm of left adrenal gland |
| C79.81 | Secondary malignant neoplasm of breast |
| C79.82 | Secondary malignant neoplasm of genital organs |
| C79.89 | Secondary malignant neoplasm of other specified sites |
| C79.9 | Secondary malignant neoplasm of unspecified site |
| C91.40 | Hairy cell leukemia not having achieved remission |
| C91.41 | Hairy cell leukemia, in remission |
| C91.42 | Hairy cell leukemia, in relapse |
| C96.6 | Unifocal Langerhans-cell histiocytosis |

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| D03.0 | Melanoma in situ of lip |
| D03.10 | Melanoma in situ of unspecified eyelid, including canthus |
| D03.111 | Melanoma in situ of right upper eyelid, including canthus |
| D03.112 | Melanoma in situ of right lower eyelid, including canthus |
| D03.121 | Melanoma in situ of left upper eyelid, including canthus |
| D03.122 | Melanoma in situ of left lower eyelid, including canthus |
| D03.20 | Melanoma in situ of unspecified ear and external auricular canal |
| D03.21 | Melanoma in situ of right ear and external auricular canal |
| D03.22 | Melanoma in situ of left ear and external auricular canal |
| D03.30 | Melanoma in situ of unspecified part of face |
| D03.39 | Melanoma in situ of other parts of face |
| D03.4 | Melanoma in situ of scalp and neck |
| D03.51 | Melanoma in situ of anal skin |
| D03.52 | Melanoma in situ of breast (skin) (soft tissue) |
| D03.59 | Melanoma in situ of other part of trunk |
| D03.60 | Melanoma in situ of unspecified upper limb, including shoulder |
| D03.61 | Melanoma in situ of right upper limb, including shoulder |
| D03.62 | Melanoma in situ of left upper limb, including shoulder |
| D03.70 | Melanoma in situ of unspecified lower limb, including hip |
| D03.71 | Melanoma in situ of right lower limb, including hip |
| D03.72 | Melanoma in situ of left lower limb, including hip |
| D03.8 | Melanoma in situ of other sites |
| D03.9 | Melanoma in situ, unspecified |
| E88.2 | Lipomatosis, not elsewhere classified |
| E88.81 | Metabolic syndrome |
| E88.89 | Other specified metabolic disorders |
| E88.9 | Metabolic disorder, unspecified |
| Z85.038 | Personal history of other malignant neoplasm of large intestine |
| Z85.048 | Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus |
| Z85.820 | Personal history of malignant melanoma of skin |

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