CMS Measure ID/CMS QCDR ID: CAP 15

Measure Title: BRAF Biomarker Testing to Inform Clinical Management and Treatment Decisions in Patients with Metastatic Colorectal Adenocarcinoma

Measure Specifications

Measure Description	Percentage of metastatic colorectal adenocarcinoma surgical pathology reports that address biomarker evaluation for BRAF mutation. INSTRUCTIONS: This measure is to be reported each time a primary colorectal adenocarcinoma pathology report is finalized during the performance period. This measure may be submitted by eligible clinicians who perform the quality actions described in the measure based on the services provided and the measure-specific denominator coding. The results of BRAF testing of a sample are frequently needed at some point during a patient's treatment. Pathologists are uniquely well positioned at the time of signing out the surgical pathology report to detail the disposition of BRAF testing for that sample. Referring physicians depend on both the pathologists' interpretations of and any recommendations for tests in order to provide quality patient care. If the status is not indicated in each pathology report for the patient, important tests may be missed or unnecessary repeat testing may be performed delaying treatment and increasing cost. This measure monitors the success of pathologists in effectively communicating this important information for the purpose of care coordination and efficient use of resources.
Denominator Statement	All surgical pathology reports with a diagnosis of metastatic colorectal adenocarcinoma CPT®: 88305, 88307, 88309 **AND** ICD10: • C18.0: Malignant neoplasm of cecum • 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 • C78.0: Secondary malignant neoplasm of lung • C78.1: Secondary malignant neoplasm of mediastinum • C78.2: Secondary malignant neoplasm of pleura • C78.3: Secondary malignant neoplasm of other and unspecified 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 • C78.8: Secondary malignant neoplasm of other and unspecified digestive organs • C79.0: Secondary malignant neoplasm of 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 • C79.1: Secondary malignant neoplasm of bladder and other and unspecified urinary organs • 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 • C79.3: Secondary malignant neoplasm of brain and cerebral meninges • C79.31: Secondary malignant neoplasm of brain • C79.32: Secondary malignant neoplasm of cerebral meninges • C79.4: Secondary malignant neoplasm of other and unspecified parts of nervous system • C79.40: Secondary malignant neoplasm of unspecified part of nervous system • C79.49: Secondary malignant neoplasm of other parts of nervous system • C79.5: Secondary malignant neoplasm of bone and bone marrow • C79.51: Secondary malignant neoplasm of bone • C79.52: Secondary malignant neoplasm of bone marrow • C79.6: Secondary malignant neoplasm of ovary • C79.60: Secondary malignant neoplasm of unspecified ovary • C79.61: Secondary malignant neoplasm of right ovary • C79.62: Secondary malignant neoplasm of left ovary C79.7: • C79.7: Secondary malignant neoplasm of adrenal gland • 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 C79.8: • C79.8: Secondary malignant neoplasm of other specified sites • 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
Denominator Exclusions	None

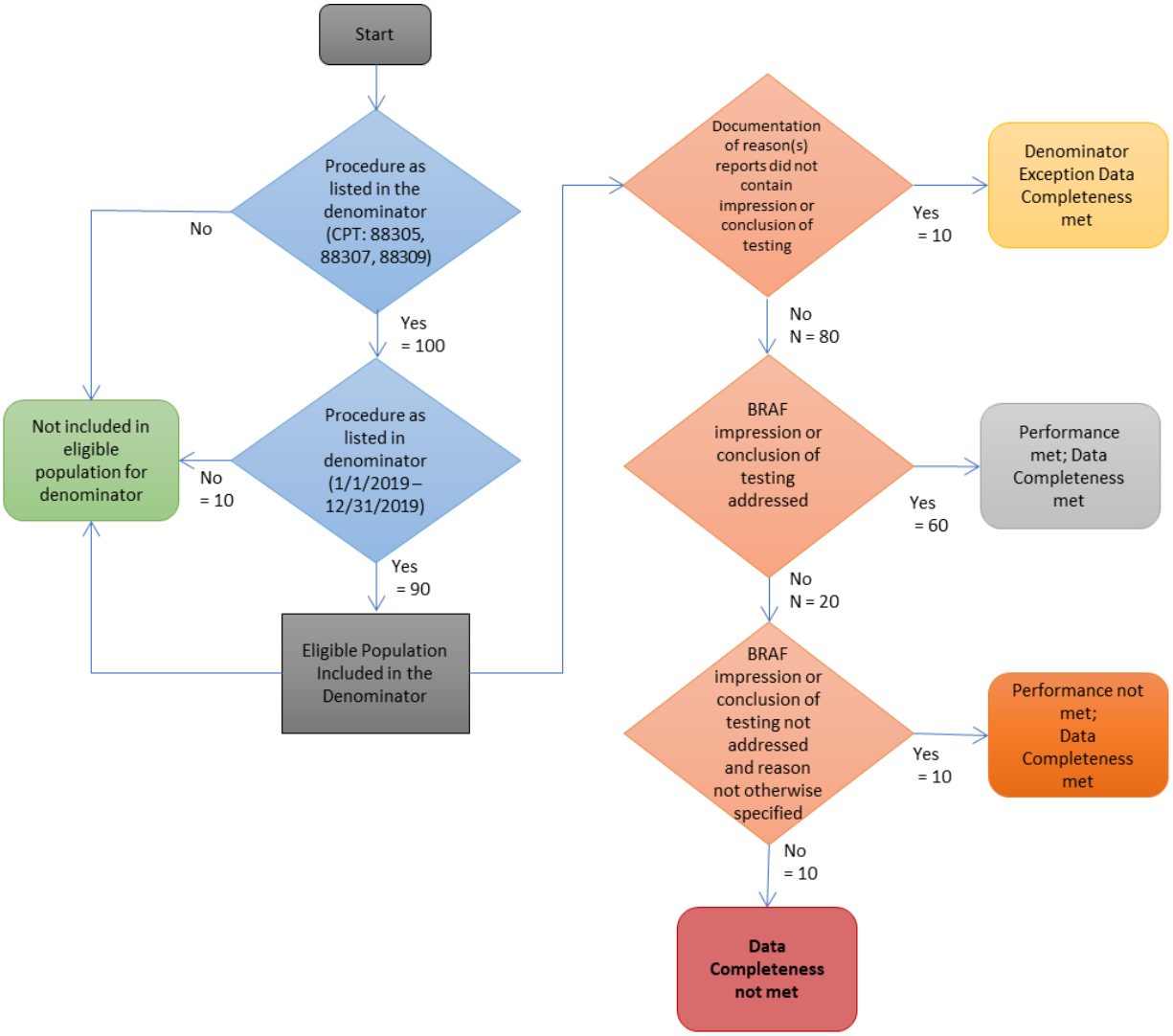
Denominator Exceptions	Documentation of reason(s) BRAF test was not performed (e.g., payor-related limitations, patients receiving hospice)
Numerator Statement	Surgical pathology reports that contain impression or conclusion of, or recommendation for BRAF testing. Numerator guidance: A short note can be made in the final report, such as: • BRAF mutation / positive • No BRAF mutations detected / negative • BRAF previously performed • BRAF mutation testing recommended • BRAF mutation cannot be determined BRAF mutation status may be derived from either the primary or a reference laboratory. CPT®: 81210, 81212, 81445, 81455
Numerator Exclusions	None
Measure Information	
NQS Domain	Communication and Care Coordination
Meaningful Measures Area(s)	Transfer of Health Information and Interoperability
Meaningful Measure Rationale	NCCN recommends that all patients with metastatic CRC should have tumor tissue genotyped for BRAF mutations (1). BRAF V600 mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor. In the Molecular Biomarkers for the Evaluation of Colorectal Cancer guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology it is recommended that BRAF p.V600 (BRAF c.1799 [p.V600]) position mutational analysis should be performed in CRC tissue in selected patients with colorectal carcinoma for prognostic stratification (2). BRAF activating mutations occur in about 8% of advanced disease patients with CRC and in approximately 14% of patients with localized stage II and III CRC. As such, mutations in BRAF constitute a substantial subset of patients with CRC (2). This recommendation is supported by seven systematic reviews (3-9), three of which included meta-analysis (4, 5, 9). The measure is designed to account for situations where it is not appropriate, safe or possible to obtain BRAF evaluation due to the patient receiving hospice or palliative care or resources to perform the evaluation are not available. In addition, it is intended to reflect factors relating to patient choice. For all

	metastatic colorectal adenocarcinoma cases, whether BRAF V600 was conducted or not, a standard statement addressing BRAF should be included in pathology reports.1. Febbo PG, Ladanyi M, Aldape KD, et al. NCCN task force report: evaluating the clinical utility of tumor markers in oncology. J Natl Compr Cancer Netw. 2011;9(suppl 5):S1–S33. 2. Sepulveda AR, et al. Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. Arch Pathol Lab Med. 2017 May;141(5):625-657. 3. Baas JM, Krens LL, Guchelaar HJ, et al. Concordance of predictive markers for EGFR inhibitors in primary tumors and metastases in colorectal cancer: a review. Oncologist. 2011;16:1239–1249. doi 0.1634/theoncologist. 2011-0024. 4. Xu Q, Xu AT, Zhu MM, et al. Predictive and prognostic roles of BRAF mutation in patients with metastatic colorectal cancer treated with anti-epidermal growth factor receptor monoclonal antibodies: a meta-analysis. J Dig Dis. 2013; 14:409–416. doi 10.1111/1751-2980.12063]. 5. Yuan ZX, Wang XY, Qin QY, et al. The prognostic role of BRAF mutation in metastatic colorectal cancer receiving anti-EGFR monoclonal antibodies: a meta-analysis. PLoS One. 2013;8:e65995. doi 10.1371/journal.pone.0065995. 6. Lin JS, Webber EM, Senger CA, et al. Systematic review of pharmacogenetics testing for predicting clinical benefit to anti-EGFR therapy in metastatic colorectal cancer. Am J Cancer Res. 2011;1:650–662. 7. Mao C, Liao RY, Qiu LX, et al. BRAF V600E mutation and resistance to anti-EGFR monoclonal antibodies in patients with metastatic colorectal cancer: a meta-analysis. Mol Biol Rep. 2011;38:2219–2223. doi 10.1007/s11033-010-0351-4. 8. Parsons MT, Buchanan DD, Thompson B, et al. Correlation of tumour BRAF mutations and MLH1 methylation with germline mismatch repair (MMR) gene mutation status: a literature review assessing utility of tumour features for MMR variant classification. J Med Genet. 2012;49:151–157. doi 10.1136/jmedgenet-2011-100714]. 9. Cui D, Cao D, Yang Y, et al. Effect of BRAF V600E mutation on tumor response of anti-EGFR monoclonal antibodies for first-line metastatic colorectal cancer treatment: a meta-analysis of randomized studies. Mol Biol Rep. 2014;41:1291–1298 doi 10.1007/s11033-013-2974-8.
Measure Type	Process
Data Source	Laboratory Information Systems; pathology reports
Summary of Performance	In May 2017, the American Society for Clinical Pathology (ASCP), the College of American Pathologists (CAP), the Association for Molecular Pathology (AMP), and the American Society of Clinical Oncology (ASCO) collaborated to

Gap Evidence	develop a clinical practice guideline on molecular biomarker testing for patients with early and advanced colorectal cancer. This evidence-based clinical practice guideline was developed to help establish standard molecular biomarker testing, guide targeted therapy decisions, and advance personalized care for these patients (1). Prior to the release of this guideline, the utility of incorporating prognostic biomarkers in the management of patients with CRC had not been well defined in clinical practice and treatment decisions are not made based on prognostic markers (1-9). However, as chemotherapeutic regimens become refined and as panels of prognostic markers are put in place to determine which CRC patients should receive therapy, these data will become essential. Laboratories and regulatory agencies are faced with challenges to rapidly and efficiently provide new test results for the management of patients with cancer. There is a need for current evidence-based recommendations for the molecular testing of CRC tissues to guide targeted therapies and conventional chemotherapy regimens. Therefore, the current evidence-based recommendations for the molecular testing of CRC tissues were developed so that new advances in the molecular testing for clinical management of CRC can be integrated (1). 1. Sepulveda AR, et al. Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. Arch Pathol Lab Med. 2017 May;141(5):625-657. 2. Febbo PG, Ladanyi M, Aldape KD, et al. NCCN task force report: evaluating the clinical utility of tumor markers in oncology. J Natl Compr Cancer Netw. 2011;9(suppl 5):S1–S33. 3. Baas JM, Krens LL, Guchelaar HJ, et al. Concordance of predictive markers for EGFR inhibitors in primary tumors and metastases in colorectal cancer: a review. Oncologist. 2011;16:1239–1249. doi 0.1634/theoncologist. 2011-0024. 4. Xu Q, Xu AT, Zhu MM, et al. Predictive and prognostic roles of BRAF mutation in patients with metastatic colorectal cancer treated with anti-epidermal growth factor receptor monoclonal antibodies: a meta-analysis. J Dig Dis. 2013; 14:409–416. doi 10.1111/1751-2980.12063]. 5. Yuan ZX, Wang XY, Qin QY, et al. The prognostic role of BRAF mutation in metastatic colorectal cancer receiving anti-EGFR monoclonal antibodies: a meta-analysis. PLoS One. 2013;8:e65995. doi 10.1371/journal.pone.0065995. 6. Lin JS, Webber EM, Senger CA, et al. Systematic review of pharmacogenetics testing for predicting clinical benefit to anti-EGFR therapy in metastatic colorectal cancer. Am J Cancer Res. 2011;1:650–662. 7. Mao C, Liao RY, Qiu LX, et al. BRAF V600E mutation and resistance to anti-EGFR monoclonal antibodies in patients with metastatic colorectal

	cancer: a meta-analysis. Mol Biol Rep. 2011;38:2219–2223. doi 10.1007/s11033-010-0351-4. 8. Parsons MT, Buchanan DD, Thompson B, et al. Correlation of tumour BRAF mutations and MLH1 methylation with germline mismatch repair (MMR) gene mutation status: a literature review assessing utility of tumour features for MMR variant classification. J Med Genet. 2012;49:151–157. doi 10.1136/jmedgenet-2011-100714]. 9. Cui D, Cao D, Yang Y, et al. Effect of BRAF V600E mutation on tumor response of anti-EGFR monoclonal antibodies for first-line metastatic colorectal cancer treatment: a meta-analysis of randomized studies. Mol Biol Rep. 2014;41:1291–1298 doi 10.1007/s11033-013-2974-8.
Measure Owner	College of American Pathologists
NQF ID	N/A
Number of Performance Rates	1
Overall Performance Rate	1st Performance Rate
High-priority	Yes
Improvement Notation	Inverse Measure: No **Proportional Measure: Yes (Higher score indicates better quality)** Continuous Variable Measure: No Ratio Measure: No Risk-adjusted: No
Specialty	Pathology
Current Clinical Guideline the Measure is Derived From	BRAF p.V600 (BRAF c.1799 [p.V600]) mutational analysis should be performed in CRC tissue in selected patients with colorectal carcinoma for prognostic stratification. (Recommendation) (1). All patients with metastatic colorectal cancer should have tumor tissue genotyped for BRAF mutations (Strong recommendation) (2). 1. Sepulveda AR, et al. Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. Arch Pathol Lab Med. 2017 May;141(5):625-657. 2. Febbo PG, Ladanyi M, Aldape KD, et al. NCCN task force report: evaluating the clinical utility of tumor markers in oncology. J Natl Compr Cancer Netw. 2011;9(suppl 5):S1–S33.

Measure Flow



Data Completeness =
Denominator Exceptions + Performance Met + Performance Not Met $= \frac{10 + 60 + 10}{90} = 88\%$
Eligible Population

Performance Rate =
Performance Met $= \frac{60}{80} = 75\%$
Data completeness Numerator – Denominator Exceptions