**Protocol**

Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment and Immunotherapy in Metastatic Colorectal Cancer

(20453)

(Formerly KRAS, NRAS, BRAF Variant Analysis [Including Liquid Biopsy] in Metastatic Colorectal Cancer)

<table>
<thead>
<tr>
<th>Medical Benefit</th>
<th>Effective Date: 02/01/22</th>
<th>Next Review Date: 05/22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preauthorization</td>
<td>Yes</td>
<td>Review Dates: 05/12, 05/13, 05/14, 05/15, 05/16, 07/16, 05/17, 05/18, 05/19, 09/19, 05/20, 05/21, 11/21</td>
</tr>
</tbody>
</table>

**Preauthorization is required.**

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

**RELATED PROTOCOLS**

Circulating Tumor DNA and Circulating Tumor Cells for Cancer Management (Liquid Biopsy)

Comprehensive Genomic Profiling for Selecting Targeted Cancer Therapies

Gene Expression Profile Testing and Circulating Tumor DNA Testing for Predicting Recurrence in Colon Cancer

Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals: With metastatic colorectal cancer</td>
<td>Interventions of interest are: KRAS variant testing to guide treatment</td>
<td>Comparators of interest are: No KRAS variant testing to guide treatment</td>
<td>Relevant outcomes include: Overall survival, Disease-specific survival, Change in disease status, Medication use, Resource utilization, Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals: With metastatic colorectal cancer</td>
<td>Interventions of interest are: NRAS variant testing to guide treatment</td>
<td>Comparators of interest are: No NRAS variant testing to guide treatment</td>
<td>Relevant outcomes include: Overall survival, Disease-specific survival, Change in disease status, Medication use, Resource utilization, Treatment-related morbidity</td>
</tr>
</tbody>
</table>
**DESCRIPTION**

The epidermal growth factor receptor (EGFR) is overexpressed in colorectal cancer (CRC). EGFR-targeted therapy combined with monoclonal antibodies cetuximab and panitumumab has shown a clear survival benefit in patients with metastatic CRC. However, this benefit depends on a lack of variants in certain genes in the signaling pathway downstream from the EGFR. It has been hypothesized that knowledge of tumor cell KRAS, NRAS, BRAF variant status might be used to predict nonresponse to anti-EGFR monoclonal antibody therapy. More recently, testing for microsatellite instability/mismatch repair (MSI/MMR) and tumor mutational burden (TMB) status to select patients for immunotherapy and human epidermal growth factor receptor 2 (HER2) testing to select patients for targeted therapy has been proposed. Typically, the evaluation of biomarker status requires tissue biopsy. Circulating tumor DNA or circulating tumor cell testing (also known as a liquid biopsy) is proposed as a non-invasive alternative.

**SUMMARY OF EVIDENCE**

For individuals with metastatic CRC who receive KRAS variant testing to guide treatment, the evidence includes multiple systematic reviews including a TEC Assessment. Relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. Variant testing of tumor tissue performed in prospective and retrospective analyses of randomized controlled trials has consistently shown that the presence of a KRAS variant predicts nonresponse to cetuximab and panitumumab, either as monotherapy or in combination with other treatment regimens. Analyses also support the use of KRAS variant analysis of tumor DNA before considering a treatment regimen. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with metastatic CRC who receive NRAS variant testing to guide treatment, the evidence includes prospective-retrospective analyses of randomized controlled trials and retrospective cohort studies. Relevant outcomes are OS, disease-specific survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. Pooled analyses have shown that NRAS variants (beyond the common KRAS exon 2 variants) predict nonresponse to cetuximab and panitumumab and support the use of NRAS variant analysis of tumor DNA before considering a treatment regimen. In addition, there is strong support from the National Comprehensive Cancer Network and the American Society of Clinical Oncology for NRAS and KRAS testing in patients...
with metastatic CRC. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with metastatic CRC who receive BRAF variant testing to guide treatment, the evidence includes two meta-analyses of prospective and retrospective analyses of randomized controlled trials. Relevant outcomes are OS, disease-specific survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. The meta-analyses have shown that anti-EGFR monoclonal antibody therapy did not improve survival in patients with RAS wild-type or BRAF-mutated tumors; however, the individual studies have been small, and the results have been inconsistent. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with metastatic CRC who receive MSI/MMR testing to guide treatment, the evidence includes a RCT of pembrolizumab compared to chemotherapy and nonrandomized trials. Relevant outcomes are OS, disease-specific survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. Effectiveness of pembrolizumab compared to chemotherapy in patients with previously untreated, unresectable or metastatic high-frequency MSI (MSI-H) or deficient MMR (dMMR) CRC was investigated in a multicenter, randomized, open-label, active-controlled trial of 307 patients. The trial demonstrated a statistically significant improvement in progression free survival for patients randomized to pembrolizumab compared with chemotherapy (hazard ratio 0.60; 95% confidence interval [CI] 0.45 to 0.80; p=.0002). The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with metastatic CRC who receive HER2 testing to guide treatment, the evidence includes nonrandomized trials. Relevant outcomes are OS, disease-specific survival, change in disease status, medication use, resource utilization, and treatment-related morbidity. There is no approved targeted treatment or companion diagnostic test for HER2 testing in patients with metastatic CRC. A phase 2 basket trial included 37 patients with HER2-amplified/overexpressed metastatic CRC. Treatment with trastuzumab plus pertuzumab produced partial response in 14 patients (38%; 95% CI, 23% to 55%) and the median duration of response was 11 months (range one to 16+ months; 95% CI, 2.8 months to not estimable). In an open-label, phase 2 trial of trastuzumab deruxtecan, objective response was observed in 24 of 53 patients with HER2-positive metastatic CRC (45.3%; 95% CI 31.6 to 59.6) after a median follow-up of 27.1 weeks (interquartile range 19.3 to 40.1). Preliminary evidence has suggested that patients with HER2-amplified metastatic CRC are less likely to respond to anti-EGFR therapy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with metastatic CRC who receive TMB testing to select treatment with immunotherapy, the evidence includes a prespecified retrospective subgroup analysis of a nonrandomized phase 2 trial. Relevant outcomes are OS, disease-specific survival, and test accuracy. Objective responses were observed in 35% of participants who had both TMB-high status and programmed death-ligand 1 (PD-L1)-positive tumors and in 21% of participants who had TMB-high status and PD-L1-negative tumors. High TMB status was associated with improved response irrespective of PD-L1 status. Median OS and progression free survival were not significantly different between TMB groups. Because no patients with CRC were included in these analyses, it is not possible to draw conclusions about the clinical validity and utility of TMB in this group of patients. Well-designed prospective studies enrolling patients in the population of interest are required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with metastatic CRC who receive circulating tumor DNA or circulating tumor cell testing (liquid biopsy) to guide treatment, the evidence includes observational studies. Relevant outcomes are OS, disease-specific survival, test validity, morbid events, and medication use. Given the breadth of methodologies available to assess circulating tumor DNA and circulating tumor cells, the clinical validity of each commercially available test must be established independently. The clinical validity of the OncoBEAM™ RAS CRC Assay has been studied.
in multiple observational studies. When compared to tissue biopsy, sensitivity ranged from 70% (51% to 84%) to 96% (95% CI 87% to 100%) and specificity ranged from 83% (95% CI 71% to 92%) to 94% (82% to 98%). FoundationOne® Liquid has been compared to tissue biopsy with the FoundationACT™ assay in one observational study; positive percent agreement was 80% overall and 90% when tissue and liquid biopsy were collected less than 270 days apart. Clinical validity studies were limited by unclear reporting of blinding, use of convenience rather than consecutive samples, and variation in the timing of sample collection. There are no published studies reporting clinical outcomes or clinical utility. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

POLICY

KRAS variant analysis may be considered medically necessary for patients with metastatic colorectal cancer to predict nonresponse prior to planned therapy with anti-epidermal growth factor receptor (EGFR) monoclonal antibodies cetuximab or panitumumab.

NRAS variant analysis may be considered medically necessary for patients with metastatic colorectal cancer to predict nonresponse prior to planned therapy with anti-EGFR monoclonal antibodies cetuximab or panitumumab.

BRAF variant analysis is may be considered medically necessary for patients with metastatic colorectal cancer who are found to be wild-type on KRAS and NRAS variant analysis to guide management decisions.

Mismatch repair/microsatellite instability testing may be considered medically necessary to predict treatment response to pembrolizumab:

- for first-line treatment of patients with unresectable or metastatic colorectal cancer; OR
- in patients with colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan; OR
- in patients with colorectal cancer tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.

Human epidermal growth factor receptor 2 testing is considered investigational to predict treatment response to immunotherapy in patients with metastatic colorectal cancer.

Tumor mutational burden testing to predict response to immunotherapy in patients with metastatic colorectal cancer is considered investigational.

Circulating tumor DNA testing (liquid biopsy) in patients with metastatic colorectal cancer is considered investigational.

POLICY GUIDELINES

There is support from the evidence to use BRAF V600 variant testing for prognostic stratification. Clinical input suggests that patients who are positive for this variant may be considered for clinical trials.

It is uncertain whether the presence of a BRAF V600 variant in patients with metastatic colorectal cancer who are wild-type on KRAS and NRAS variant analysis is predictive of response to anti-epidermal growth factor receptor therapy. Furthermore, there is mixed opinion in clinical guidelines and clinical input on the use of BRAF variant analysis to predict response to treatment.
MEDICARE ADVANTAGE

For Medicare Advantage the following gene analysis is considered **medically necessary** in patients with colorectal cancer when needed to determine if a Medicare approved therapy is a reasonable option given the individual’s specific clinical presentation.

- KRAS gene analysis, variants in codons 12 and 13 and KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146)
- NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)

For Medicare Advantage BRAF gene analysis is considered **medically necessary** in patients with metastatic colorectal cancer when needed to determine if a Medicare approved therapy is a reasonable option given the individual’s specific clinical presentation.

Genomic Sequential Analysis Panel may be considered **medically necessary** when the test is performed in a CLIA-certified laboratory qualified to perform high complexity testing, ordered by a treating physician, and the patient has:

1. metastatic CRC; and
2. is a candidate for intensive chemotherapy with an anti-EGFR biologic agent; and
3. has not had prior RAS/BRAF testing (except after initiation of anti-EGFR therapy with evidence of acquired resistance).

The oncology (gastrointestinal neuroendocrine tumors), real-time PCR expression analysis of 51 genes, utilizing whole peripheral blood, algorithm reported as a nomogram of tumor disease index for its use in treating neuroendocrine tumors is considered **not medically necessary**.

BACKGROUND

**KRAS, NRAS, AND BRAF VARIANTS**

Cetuximab (Erbitux®; ImClone Systems) and panitumumab (Vectibix®; Amgen) are monoclonal antibodies that bind to the epidermal growth factor receptor (EGFR), preventing intrinsic ligand binding and activation of downstream signaling pathways vital for cancer cell proliferation, invasion, metastasis, and stimulation of neovascularization. The RAS-RAF-MAP kinase pathway is activated in the EGFR cascade. The RAS proteins are G proteins that cycle between active (RAS guanosine triphosphate) and inactive (RAS guanosine diphosphate) forms in response to stimulation from a cell surface receptor, such as EGFR, and they act as a binary switch between the cell surface EGFR and downstream signaling pathways. The **KRAS** gene can harbor oncogenic variants that result in a constitutively activated protein, independent of EGFR ligand binding, rendering antibodies to the upstream EGFR ineffective. Approximately 40% of colorectal cancers (CRCs) have **KRAS** variants in codons 12 and 13 in exon 2. Another proto-oncogene that acts downstream from **KRAS-NRAS** harbors oncogenic variants in codons 12, 13, or 61 that result in constitutive activation of the EGFR-mediated pathway. These variants are less common compared with **KRAS**, detected in 2% to 7% of CRC specimens. It is unclear whether **NRAS** variants predict poor response due to anti-EGFR monoclonal antibody therapy or are prognostic of poor CRC outcomes in general. A third proto-oncogene, **BRAF**, encodes a protein kinase and is involved in intracellular signaling and cell growth; **BRAF** is also a principal downstream effector of **KRAS**. **BRAF** variants occur in fewer than 10% to 15% of CRCs and appear to be a marker of poor prognosis. **KRAS** and **BRAF** variants are considered to be mutually exclusive.
Cetuximab and panitumumab have marketing approval from the U.S. Food and Drug Administration (FDA) for the treatment of metastatic CRC in the refractory disease setting. The FDA approval for panitumumab indicates that panitumumab is not indicated for the treatment of patients with KRAS or NRAS variant-positive disease in combination with oxaliplatin-based chemotherapy.1

A large body of literature has shown that metastatic CRC tumors with a variant in exon 2 (codon 12 or 13) of the KRAS gene do not respond to cetuximab or panitumumab therapy. More recent evidence has shown that variants in KRAS outside exon 2 (i.e., in exons 3 [codons 59 and 61] and exon 4 [codons 117 and 146]) and variants in NRAS exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146) also predict a lack of response to these monoclonal antibodies. Variant testing of these exons outside the KRAS exon 2 is referred to as extended RAS testing.

HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 AMPLIFICATION/OVEREXPRESSION

Human epidermal growth factor receptor 2 (HER2) is a member of the HER (EGFR) family of tyrosine kinase receptors and has no specific ligand. When activated, it forms dimers with other EGFR family members. Amplification of HER2 is detected in approximately 3% of patients with CRC, with higher prevalence in RAS/BRAF-wild type tumors (5% to 14%). In addition to its role as a predictive marker for HER2-targeted therapy, HER2 amplification/overexpression is being investigated as a predictor of resistance to EGFR-targeting monoclonal antibodies.

MISMATCH REPAIR DEFICIENCY/MICROSATELLITE INSTABILITY

Mismatch repair deficiency (dMMR) and high levels of microsatellite instability (MSI-H) describe cells that have alterations in certain genes involved in correcting errors made when DNA is replicated. Tumors with dMMR are characterized by a high tumor mutational load and potential responsiveness to anti-PD-L1-immunotherapy. Deficiency in MMR is most common in CRC, other types of gastrointestinal cancer, and endometrial cancer, but it may also be found in other cancers including breast cancer. Testing of MSI is generally performed using polymerase chain reaction (PCR) for five biomarkers, although other biomarker panels and next generation sequencing are sometimes performed. High MSI is defined as two or more of the five biomarkers showing instability or more than 30% of the tested biomarkers showing instability depending on what panel is used. Microsatellite instability testing is generally paired with immunohistochemistry assessing lack of protein expression from four DNA mismatch repair genes thereby reflecting dMMR.

TUMOR MUTATIONAL BURDEN

Tumor mutational burden (TMB), a measure of gene mutations within cancer cells, is an emerging biomarker of outcomes with immunotherapy in multiple tumor types. Initially, assessments of TMB involved whole exome sequencing. More recently, targeted next generation sequencing panels are being adapted to estimate TMB. Currently FoundationOne CDx is the only U.S. Food and Drug Administration (FDA) approved panel for estimating TMB, but others are in development.

DETECTING CIRCULATING TUMOR DNA AND CIRCULATING TUMOR CELLS (LIQUID BIOPSY)

Normal and tumor cells release small fragments of DNA into the blood, which is referred to as cell-free DNA. Cell-free DNA from nonmalignant cells is released by apoptosis. Most cell-free tumor DNA is derived from apoptotic and/or necrotic tumor cells, either from the primary tumor, metastases, or circulating tumor cells. Unlike apoptosis, necrosis is considered a pathologic process and generates larger DNA fragments due to incomplete and random digestion of genomic DNA. The length or integrity of the circulating DNA can potentially distinguish between apoptotic and necrotic origin. Circulating tumor DNA can be used for genomic characterization of the tumor.
Typically, the evaluation of RAS mutation status requires tissue biopsy. Circulating tumor DNA (ctDNA) testing is proposed as a non-invasive alternative.

Detection of ctDNA is challenging because ctDNA is diluted by nonmalignant circulating DNA and usually represents a small fraction (<1%) of total ctDNA. Therefore, more sensitive methods than the standard sequencing approaches (e.g., Sanger sequencing) are needed.

Highly sensitive and specific methods have been developed to detect ctDNA, for both single nucleotide variants (e.g., BEAMing [which combines emulsion polymerase chain reaction with magnetic beads and flow cytometry] and digital polymerase chain reaction) and copy-number variants. Digital genomic technologies allow for enumeration of rare variants in complex mixtures of DNA.

Approaches to detecting ctDNA can be considered targeted, which includes the analysis of known genetic mutations from the primary tumor in a small set of frequently occurring driver mutations, or untargeted without knowledge of specific variants present in the primary tumor, which includes array comparative genomic hybridization, next-generation sequencing, and whole exome and genome sequencing. Targeted testing may impact therapy selection.

Circulating tumor cell assays usually start with an enrichment step that increases the concentration of circulating tumor cells, either by biologic properties (expression of protein markers) or physical properties (size, density, electric charge). Circulating tumor cells can then be detected using immunologic, molecular, or functional assays.

A number of liquid biopsy tests related to targeted treatment of metastatic colorectal cancer have been developed (Table 1).

Table 1. Examples of Liquid Biopsy Tests Related to Targeted Treatment of Metastatic Colorectal Cancer

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Test</th>
<th>Type of Liquid Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biocept</td>
<td>Target SElector ctDNA EGFR Kit</td>
<td>ctDNA</td>
</tr>
<tr>
<td>Foundation Medicine</td>
<td>FoundationOne Liquid (Previously FoundationAct)</td>
<td>ctDNA</td>
</tr>
<tr>
<td>Guardant Health</td>
<td>Guardant360®</td>
<td>ctD</td>
</tr>
<tr>
<td>IV Diagnostics</td>
<td>Velox™</td>
<td>CTC</td>
</tr>
<tr>
<td>Personal Genome Diagnostics</td>
<td>PlasmaSELECT</td>
<td>ctD</td>
</tr>
<tr>
<td>Sysmex Inostics</td>
<td>OncoBEAM</td>
<td>ctD</td>
</tr>
<tr>
<td>Circulogene</td>
<td>Theranostics</td>
<td>ctD</td>
</tr>
</tbody>
</table>

CTC: circulating tumor cell; ctDNA: circulating tumor DNA.

REGULATORY STATUS

Table 2 summarizes the targeted treatments approved by the U.S. Food and Drug Administration (FDA) for patients with CRC, along with the approved companion diagnostic tests. The information in Table 2 was current as of June 18, 2021; FDA maintains a list of cleared or approved companion diagnostic devices that is updated regularly.²

Table 2. Targeted Treatments for Metastatic Colorectal Cancer and FDA Approved Companion Diagnostic Tests

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Indications in Metastatic Colorectal Cancer</th>
<th>Companion Diagnostics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab</td>
<td>KRAS wild-type, EGFR-expressing, metastatic colorectal cancer as determined by an FDA-approved test</td>
<td>cobas KRAS Mutation Test</td>
</tr>
<tr>
<td>(Erbitux)</td>
<td>• in combination with FOLFIRI for first-line treatment,</td>
<td>Dako EGFR pharmDx Kit</td>
</tr>
<tr>
<td></td>
<td>• in combination with irinotecan in patients who are refractory to</td>
<td>therascreen KRAS RGQ PCR Kit</td>
</tr>
</tbody>
</table>

Page 7 of 12
### Treatment Indications in Metastatic Colorectal Cancer

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Indications in Metastatic Colorectal Cancer</th>
<th>Companion Diagnostics</th>
</tr>
</thead>
</table>
| Panitumumab (Vectibix) | Treatment of wild-type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use) metastatic CRC:  
- In combination with FOLFOX for first-line treatment.  
- As monotherapy following disease progression after prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy.  
Limitation of Use: Vectibix is not indicated for the treatment of patients with RAS-mutant mCRC or for whom RAS mutation status is unknown. | cobas KRAS Mutation Test  
Dako EGFR pharmDx Kit  
FoundationOne CDx  
Praxis Extended RAS Panel  
therascreen KRAS RGQ PCR Kit |
| Pembrolizumab (Keytruda®) | Unresectable or metastatic, MSI-H or dMMR  
- solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or  
- CRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan  
First-line treatment of patients with unresectable or metastatic MSI-H or dMMR CRC | FoundationOne CDx |

### Companion Diagnostics
- cobas KRAS Mutation Test
- Dako EGFR pharmDx Kit
- FoundationOne CDx
- Praxis Extended RAS Panel
- therascreen KRAS RGQ PCR Kit

### Source: FDA (2021)

CRC: colorectal cancer; dMMR: mismatch repair deficient; EGFR: epidermal growth factor receptor; FOLFIRI: leucovorin, fluorouracil and irinotecan; FOLFOX: leucovorin, fluorouracil, and oxaliplatin; HER2: human epidermal growth factor receptor 2; mCRC: metastatic CRC; MSI-H: microsatellite instability-high

### LABORATORY-DEVELOPED TESTS

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). Laboratories that offer laboratory-developed tests must be licensed under CLIA for high-complexity testing. To date, the FDA has chosen not to require any regulatory review of this test.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.
REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


<table>
<thead>
<tr>
<th>Protocol</th>
<th>Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment and Immunotherapy in Metastatic Colorectal Cancer</th>
<th>Last Review Date: 11/21</th>
</tr>
</thead>
</table>


60. National Government Services, Inc. (Primary Geographic Jurisdiction 06 & K - Illinois, Minnesota, Wisconsin, Connecticut, New York - Entire State, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) Local Coverage Determination (LCD): Molecular Pathology Procedures (L35000), Revision Effective Date for services performed on or after 07/01/2020.