Geisinger

Geisinger Health Plan Policies and Procedure Manual

Policy: MP323

Section: Medical Benefit Policy

Subject: Molecular Profiling of Malignant Tumors to Identify Targeted Therapies

Applicable line of business:

Commercial	**x**	**Medicaid**	**x**
Medicare	**x**	**ACA**	**x**
CHIP	**x**		

I. Policy: Molecular Profiling of Malignant Tumors to Identify Targeted Therapies

II. Purpose/Objective:

To provide a policy of coverage regarding Molecular Profiling of Malignant Tumors to Identify Targeted Therapies

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.

Commercial

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicare

Geisinger Gold Medicare Advantage HMO, PPO, and HMO D-SNP plans are offered by Geisinger Health Plan/Geisinger Indemnity Insurance Company, health plans with a Medicare contract. Continued enrollment in Geisinger Gold depends on contract renewal. Geisinger Health Plan/Geisinger Indemnity Insurance Company are part of Geisinger, an integrated health care delivery and coverage organization.

CHIP

Geisinger Health Plan Kids (GHP Kids) is a Children's Health Insurance Program (CHIP) offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicaid

Geisinger Health Plan Family (GHP Family) is a Medical Assistance (Medicaid) insurance program offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

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:
Molecular profiling is a method for identifying multiple biomarkers in the malignant tumors of persons who have cancer. The biomarker information can be used to identify treatment options.

INDICATIONS:

REQUIRES PRIOR AUTHORIZATION BY A PLAN MEDICAL DIRECTOR OR DESIGNEE

FoundationOne, Foundation One CDx (0037U), Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT), or Target Now Molecular Profiling Service Caris Diagnostics) - (Commercial and Medicare Business Segments), Guardant 360 TissueNext

Molecular profiling to identify targeted therapies utilizing one of the following tests: **FoundationOne, Foundation One CDx, Guardant 360 TissueNext, Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT), or MI Profile and MI Tumor Seek (Caris Diagnostics)** will be considered medically necessary when **all of the following** criteria are met:

- A diagnosis of recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer has been established; **and**
- A decision has been made to seek further cancer treatment, such as therapeutic chemotherapy; **and**
- The member has not been previously tested using the same NGS test for the same primary diagnosis of cancer without evidence of progression;
- The test is being used:
    - To establish eligibility for checkpoint inhibition immunotherapy including but not limited to Bavencio (avelumab), Imfinzi (durvalumab), Keytruda (pembrolizumab), Opdivo (nivolumab), Tecentriq (atezolizumab), Yervoy (ipilimumab); **and/or**
    - As a companion diagnostic for drugs including but not limited to: Alecensa (alectinib), Cotellic (cobimetinib) in combination with Zelboraf (vemurafenib), Erbitux (cetuximab), Gilotrif (afatinib), Herceptin (trastuzumab), Iressa (gefitinib), Kadcyla (ado-trastuzumabemtansine), Mekinist (trametinib), Perjeta (pertuzumab), Rubraca (rucaparib), Tarceva (erlotinib), Tafinlar (dabrafenib), Tafinlar (dabrafenib) in combination with Mekinist (trametinib), Tagrisso (osimertinib), Vectibix (panitumumab), Xalkori (crizotinib), Zelboraf (vemurafenib), Zykadia (ceritinib)

FoundationOne Liquid CDx: (Commercial and Medicare Business Segments) (0239U)

FoundationOne Liquid CDx circulating tumor cell free DNA (cfDNA) molecular profiling testing is considered to be medically necessary at diagnosis or progression for the following indications when the criteria are met:

- Member has a diagnosis of solid tumor cancer; and
- Treatment is being considered with a medication for which there is an FDA-approved companion diagnostic assay; and

- FDA label for the drug and indication being considered states companion diagnostic testing is necessary for patient selection

Note: FDA-approved companion diagnostic indications can be found here, https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools

FoundationOne Heme: (Commercial and Medicare Business Segments) (81450), (81455)

- The member has a diagnosis of AML, MDS or MPN. AML, MDS and MPN are herein classified as refractory and/or metastatic cancers and fulfil the NCD 90.2 criteria.
- The test has satisfactorily completed a TA by MolDX® for the stated indications of the test.
- The assay performed includes at least the minimum genes and positions indicated for its intended use, as described in an associated coverage Article or found in the TA forms.
- For members that do not have a diagnosis of a myeloid malignancy, where one is suspected, the member must have an undefined cytopenia for greater than 4 months, other possible causes have been reasonably excluded.
- Testing is performed on bone marrow biopsies, bone marrow aspirates, bone marrow clots, peripheral blood samples, or extramedullary sites suspected of harboring a myeloid malignancy.

Guardant360 and Guardant360CDx: (Commercial) (0242U), (0334U)

Molecular profiling to identify targeted therapies utilizing Guardant360 CDx will be considered medically necessary for any the following indications when criteria are met:

1. Guardant360 and Guardant360CDx is considered medically necessary to provide information biomarkers in all solid tumors
    - The member is a candidate for further treatment with a drug that is either FDA-approved for that cancer, or has an NCCN 1 or NCCN 2A recommendation for that cancer, or
    - The FDA-approved indication or NCCN recommendation is based upon information about the presence or absence of a genetic biomarker tested for in the Guardant360 or Guardant360 CDx assay

For the MEDICARE BUSINESS SEGMENT:

Guardant360 and Guardant360 CDx is covered when the member:

- has been diagnosed with a recurrent, relapsed, refractory, metastatic, or advanced solid tumor that did not originate from the central nervous system, **and**
- is untreated for the primary cancer being tested, or is not responding to treatment, **and**
- has decided to seek further cancer treatment with the following conditions:
    - The member is a candidate for further treatment with a drug that is either FDA-approved for that cancer, or has an NCCN 1 or NCCN 2A recommendation for that cancer, **and**
    - The FDA-approved indication or NCCN recommendation is based upon information about the presence or absence of a genetic biomarker tested for in the Guardant360 CDx assay

Guardant360 Response (Commercial and Medicare) (0422U)

Guardant360 Response is considered medically necessary for members who have metastatic or inoperable solid tumors who are on an immune checkpoint inhibitor therapy to monitor response to immunotherapy .

OncoExTra (Commercial and Medicare) (0329U)

OncoExTra is considered medically necessary for any the following indications when criteria are met:

- The member is diagnosed with an unresectable or metastatic solid tumor(s); and
- The test is used to assess tumor mutation burden and identify candidates for checkpoint inhibition immunotherapy;

  and
- The member has progressed following prior treatment

Define MBC Metastatic Breast Cancer Panel (Commercial and Medicare) (0428U)

Define MBC Metastatic Breast Cancer Panel is considered medically necessary for members who have metastatic breast cancer and for whom tissue-based, comprehensive genomic profiling is infeasible.

oncoRevealTM DX Lung and Colon Cancer Assay (Commercial and Medicare) (0448U), (0523U)

oncoRevealTM DX Lung and Colon Cancer Assay is considered medically necessary for members who require EGFR & KRAS therapy selection in non-small cell lung cancer (NSCLC) and colorectal cancer (CRC)

Oncotype MAP™ Pan-Cancer Tissue Test (Commercial and Medicare) (0244U)

Oncotype MAP™ Pan-Cancer Tissue Test is considered medically necessary for members who have:

- Recurrent cancer
- Relapsed cancer
- Refractory cancer
- Metastatic cancer
- Advanced cancer (stages III or IV)

AND has not been previously tested by the same test for the same genetic content, **AND** is seeking further treatment

Tempus xt CDx (0473U) (Commercial and Medicare)

Tempus xt CDx is considered medically necessary for solid tumor profiling, which includes microsatellite instability status and companion diagnostic evaluation for colorectal cancer in members being considered for cetuximab (Erbitux) or panitumumab (Vectibix).

myChoice CDx (0172U) (Commercial and Medicare)

myChoice CDx is considered medically necessary for members with ovarian cancer being considered for PARP inhibitor therapy

EXCLUSIONS:

The Plan currently considers the use of molecular profiling tests such as but not limited to EXaCT-1 Whole Exome Sequencing, GeneKey, GeneTrails Solid Tumor Panel, MatePair, MyAML, OmniSeq, OnkoMatch, OncInsights, LiquidHALLMARK and SmartGenomics to be **unproven** and **NOT COVERED.** At this time, published, peer-reviewed, medical literature to support the use of these tests or any other testing not specifically outlined in this policy is limited and insufficient to establish their analytical validity or clinical utility.

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.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

CODING ASSOCIATED WITH: Molecular Profiling of Malignant Tumors

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

81445 Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed *[Signatera]*

81449 targeted genomic sequence analysis panel, solid organ neoplasm, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, MET, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements,

81450 Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NOTCH1, NPM1, NRAS), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis *[NeoTYPE Myeloid Disorders Profile, OncoHeme Next-Generation Sequencing for Myeloid Neoplasms, Onkosight Myeloid Disorder Panel]*

81455 Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MET, MLL, NOTCH1, NPM1, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression

levels, if performed; DNA analysis or combined DNA and RNA analysis *[FoundationOne Heme, MI Profile, OmniSeq, OnkoSight, Tempus|xT,]*

81456 Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MET, MLL, NOTCH1, NPM1, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis *{FoundationOne RNA}*

0013U Oncology (solid organ neoplasia), gene rearrangement detection by whole genome next-generation sequencing, DNA, fresh or frozen tissue or cells, report of specific gene rearrangement(s) [*MatePair Targeted Rearrangements*]

0014U Hematology (hematolymphoid neoplasia), gene rearrangement detection by whole genome next-generation sequencing, DNA, whole blood or bone marrow, report of specific gene rearrangement(s) [*MatePair Targeted Rearrangements*]

0334U Oncology (solid organ), targeted genomic sequence analysis, formalin-fixed paraffin-embedded (FFPE) tumor tissue, DNA analysis, 84 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden *[Guardant360 TissueNext™]*

0036U Exome (ie, somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal specimen, sequence analyses [*EXaCT-1 Whole Exome Testing*]

0037U Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden [*FoundationOne CDx (F1CDx)]*

0048U Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s) *[MSK-IMPACT (Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets*)]

0050U Targeted genomic sequence analysis panel, acute myelogenous leukemia, DNA analysis, 194 genes, interrogation for sequence variants, copy number variants or rearrangements [*MyAML NGS Panel*]

0056U Hematology (acute myelogenous leukemia), DNA, whole genome next generation sequencing to detect gene rearrangement(s), blood or bone marrow, report of specific gene rearrangement(s) [*MatePair Acute Myeloid Leukemia Panel*]

0172U Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score *{myChoice CDx}*

0179U Oncology (non-small cell lung cancer), cell-free DNA, targeted sequence analysis of 23 genes (single nucleotide variations, insertions and deletions, fusions without prior knowledge of partner/breakpoint, copy number variations), with report of significant mutation(s) **(Non-covered for Medicare per A57867)**

0211U Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association *[MI Cancer Seek- Caris]*

0239U Targeted genomic sequence analysis panel 311 genes [*FoundationOne® Liquid CDx*]

0244U Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single-nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor-mutational burden and microsatellite instability, utilizing formalin-fixed paraffin-embedded tumor tissue *[Oncotype MAP™ Pan-Cancer Tissue Test]*

0329U Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor mutational burden and microsatellite instability, utilizing formalin-fixed paraffin embedded tumor tissue [*OncoExTra*]

0391U Oncology (solid tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded (FFPE) tissue, 437 genes, interpretive report for single nucleotide variants, splice-site variants, insertions/deletions, copy number alterations, gene fusions, tumor mutational burden, and microsatellite instability, with algorithm quantifying immunotherapy response score

0409U Oncology (solid tumor), DNA (80 genes) and RNA (36 genes), by next-generation sequencing from plasma, including single nucleotide variants, insertions/deletions, copy number alterations, microsatellite instability, and fusions, report showing identified mutations with clinical actionability

0422U Oncology (pan-solid tumor), analysis of DNA biomarker response to anti-cancer therapy using cell-free circulating DNA, biomarker comparison to a previous baseline pre-treatment cell-free circulating DNA analysis using next-generation sequencing, algorithm reported as a quantitative change from baseline, including specific alterations, if appropriate *{ Guardant360 Response}*

0428U Oncology (breast), targeted hybrid-capture genomic sequence analysis panel, circulating tumor DNA (ctDNA) analysis of 56 or more genes, interrogation for sequence variants, gene copy number amplifications, gene

rearrangements, microsatellite instability, and tumor mutation burden *{ Epic Sciences ctDNA Define MBC Metastatic Breast Cancer Panel}*

0448U Oncology (lung and colon cancer), dna, qualitative, nextgeneration sequencing detection of single-nucleotide variants and deletions in egfr and kras genes, formalin-fixed paraffinembedded (ffpe) solid tumor samples, reported as presence or absence of targeted mutation(s), with recommended therapeutic options *{oncoRevealTM DX Lung and Colon Cancer Assay}*

0473U Oncology (solid tumor), next-generation sequencing (NGS) of DNA from formalin-fixed paraffin-embedded (FFPE) tissue with comparative sequence analysis from a matched normal specimen (blood or saliva), 648 genes, interrogation for sequence variants, insertion and deletion alterations, copy number variants, rearrangements, microsatellite instability, and tumor-mutation burden (xT CDx, Tempus AI)

0485U Oncology (solid tumor), cell-free DNA and RNA by next-generation sequencing, interpretative report for germline mutations, clonal hematopoiesis of indeterminate potential, and tumor-derived single-nucleotide variants, small insertions/deletions, copy number alterations, fusions, microsatellite instability, and tumor mutational burden

0486U Oncology (pan-solid tumor), next-generation sequencing analysis of tumor methylation markers present in cell-free circulating tumor DNA, algorithm reported as quantitative measurement of methylation as a correlate of tumor fraction

0487U Oncology (solid tumor), cell-free circulating DNA, targeted genomic sequence analysis panel of 84 genes, interrogation for sequence variants, aneuploidy-corrected gene copy number amplifications and losses, gene rearrangements, and microsatellite instability

0511U Oncology (solid tumor), tumor cell culture in 3D microenvironment, 36 or more drug panel, reported as tumor-response prediction for each drug (PARIS, Tempus AI)

0523U Oncology (solid tumor), DNA, qualitative, next-generation sequencing (NGS) of single-nucleotide variants (SNV) and insertion/deletions in 22 genes utilizing formalin-fixed paraffin-embedded tissue, reported as presence or absence of mutation(s), location of mutation(s), nucleotide change, and amino acid change *{oncoRevealTM CDx}*

0530U Oncology (pan-solid tumor), ctDNA, utilizing plasma, next-generation sequencing (NGS) of 77 genes, 8 fusions, microsatellite instability, and tumor mutation burden, interpretative report for single-nucleotide variants, copy-number alterations, with therapy association

0538U Oncology (solid tumor), next-generation targeted sequencing analysis, formalin-fixed paraffin embedded (FFPE) tumor tissue, DNA analysis of 600 genes, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, and copy number alterations, microsatellite instability, tumor mutation burden, reported as actionable variant *{PredicineATLASTM Assay}*

0539U Oncology (solid tumor), cellfree circulating tumor DNA (ctDNA), 152 genes, next-generation sequencing, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, copy number alterations, and microsatellite instability, using whole-blood samples, mutations with clinical actionability reported as actionable variant {*PredicineCARETM Assay}*

LINE OF BUSINESS:
Eligibility and contract specific benefits, 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.

REFERENCES:
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MolDx LCD L37649 Guardant360® Plasma-Based Comprehensive Genomic Profiling in Non-Small Cell Lung Cancer (NSCLC)

NCCN Clinical Practice Guidelines in Oncology. Colon cancer v2.2024

NCCN Clinical Practice Guidelines in Oncology. Non-small cell lung cancer v5.2024

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MolDX: Next-Generation Sequencing for Solid Tumors (L38119)

MolDX: Plasma-Based Genomic Profiling in Solid Tumors (L38043)

MolDx: Next-Generation Sequencing Lab-Developed Tests for Myeloid Malignancies and Suspected Myeloid Malignancies (L38047)

MolDx: Targeted and Comprehensive Genomic Profile Next-Generation sequencing Testing in Cancer (A56518)

NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma v2.2024

NCCN Clinical Practice Guidelines in Oncology. Gastric Cancer v1.2024

NCCN Clinical Practice Guidelines in Oncology. Breast cancer v2.2024

NCCN Clinical Practice Guidelines in Oncology. Esophageal and Esophagogastric Junction Cancers v3.2024

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MolDx A57772 Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT)

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

Devised: 12/18

Revised: 12/19 (add FoundationOne Liquid); 2/20(Add Medicare Guardant360 indication); 9/20(add indications for Guardant 360CDx and FoundationOne CDx); 6/21 (add indications for Oncotype MAP Pan Cancer); 3/23 (add indications for FoundationOne Heme), 10/23 (revise Guardant360 criteria); 5/24 (add coverage for Define MBC, Guardant360 Response, oncoReveal, and Oncotype MAP™ Pan-Cancer Tissue Test); 02/25 (add coverage for myChoice CDx, and Tempus xt CDx)

Reviewed: 6/22, 6/23

CMS UM Oversight Committee Approval: 12/23, 7/24, 4/25