Comprehensive Genomic Profiling for Selecting Targeted Cancer Therapies

Policy #  00423
Original Effective Date: 07/16/2014
Current Effective Date: 07/13/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: BRAF Gene Variant Testing to Select Melanoma or Glioma Patients for Targeted Therapy is addressed separately in medical policy 00320.

Note: Genetic Cancer Susceptibility Panels Using Next-Generation Sequencing is addressed separately in medical policy 00382.

Note: Molecular Analysis for Targeted Therapy of Non-Small-Cell Lung Cancer is addressed separately in medical policy 00452.

Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of comprehensive genomic profiling for selecting targeted cancer treatment to be investigational.*

Policy Guidelines
Genetics Nomenclature Update
The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion...
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from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

<table>
<thead>
<tr>
<th>Previous</th>
<th>Updated</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutation</td>
<td>Disease-associated variant</td>
<td>Disease-associated change in the DNA sequence</td>
</tr>
<tr>
<td>Variant</td>
<td>Change in the DNA sequence</td>
<td></td>
</tr>
<tr>
<td>Familial variant</td>
<td>Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives</td>
<td></td>
</tr>
</tbody>
</table>

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

<table>
<thead>
<tr>
<th>Variant Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic</td>
<td>Disease-causing change in the DNA sequence</td>
</tr>
<tr>
<td>Likely pathogenic</td>
<td>Likely disease-causing change in the DNA sequence</td>
</tr>
<tr>
<td>Variant of uncertain significance</td>
<td>Change in DNA sequence with uncertain effects on disease</td>
</tr>
<tr>
<td>Likely benign</td>
<td>Likely benign change in the DNA sequence</td>
</tr>
<tr>
<td>Benign</td>
<td>Benign change in the DNA sequence</td>
</tr>
</tbody>
</table>

ACMG: American College of Medical Genetics and Genomics; AMP: Association for Molecular Pathology.

**Background/Overview**

**Traditional Therapeutic Approaches to Cancer**

Tumor location, grade, stage, and the patient's underlying physical condition have traditionally been used in clinical oncology to determine the therapeutic approach to specific cancer, which could include surgical resection, ionizing radiation, systemic chemotherapy, or combinations thereof. Currently, some 100 different types are broadly categorized according to the tissue, organ, or body compartment in which they arise. Most treatment approaches in clinical care were developed and
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evaluated in studies that recruited subjects and categorized results based on this traditional classification scheme.

This traditional approach to cancer treatment does not reflect the wide diversity of cancer at the molecular level. While treatment by organ type, stage, and grade may demonstrate statistically significant therapeutic efficacy overall, only a subgroup of patients may derive clinically significant benefits. It is unusual for cancer treatment to be effective for all patients treated in a traditional clinical trial. Spear et al (2001) analyzed the efficacy of major drugs used to treat several important diseases. They reported heterogeneity of therapeutic responses, noting a low rate of 25% for cancer chemotherapeutics, with response rates for most drugs falling in the range of 50% to 75%. The low rate for cancer treatments is indicative of the need for better identification of characteristics associated with treatment response and better targeting of treatment to have higher rates of therapeutic responses.

Targeted Cancer Therapy

Much of the variability in clinical response may result from genetic variations. Within each broad type of cancer, there may be a large amount of variability in the genetic underpinnings of cancer. Targeted cancer treatment refers to the identification of genetic abnormalities present in the cancer of a particular patient, and the use of drugs that target the specific genetic abnormality. The use of genetic markers allows cancers to be further classified by "pathways" defined at the molecular level. An expanding number of genetic markers have been identified. These may be categorized into three classes (1) genetic markers that have a direct impact on care for the specific cancer of interest, (2) genetic markers that may be biologically important but are not currently actionable, and (3) genetic markers of uncertain importance.

A smaller number of individual genetic markers fall into the first category (ie, have established utility for a particular cancer type). The utility of these markers has been demonstrated by randomized controlled trials that select patients with the marker and report significant improvements in outcomes with targeted therapy compared with standard therapy. Testing for individual variants with established utility is not covered in this evidence review. In some cases, limited panels may be offered that are specific to one type of cancer (eg, a panel of several markers for non-small-cell lung cancer). This review also does not address the use of cancer-specific panels that include a few variants. Rather, this review addresses expanded panels that test for many potential variants that do not have established efficacy for the specific cancer in question.
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When advanced cancers are tested with expanded molecular panels, most patients are found to have at least one potentially pathogenic variant. The number of variants varies widely by types of cancers, different variants included in testing, and different testing methods among the available studies. In a study by Schwaederle et al (2015), 439 patients with diverse cancers were tested with a 236-gene panel. A total of 1813 molecular alterations were identified, and almost all patients (420/439 [96%]) had at least 1 molecular alteration. The median number of alterations per patient was 3, and 85% (372/439) of patients had 2 or more alterations. The most common alterations were in the TP53 (44%), KRAS (16%), and PIK3CA (12%) genes.

Some evidence is available on the generalizability of targeted treatment based on a specific variant among cancers that originate from different organs. There are several examples of variant-directed treatment that is effective in one type of cancer but ineffective in another. For example, targeted therapy for epidermal growth factor receptor variants have been successful in non-small-cell lung cancer but not in trials of other cancer types. Treatment with tyrosine kinase inhibitors based on variant testing has been effective for renal cell carcinoma but has not demonstrated effectiveness for other cancer types tested. "Basket" studies, in which tumors of various histologic types that share a common genetic variant are treated with a targeted agent, also have been performed. One such study was published by Hyman et al (2015). In this study, 122 patients with BRAF V600 variants in nonmelanoma cancers were treated with vemurafenib. The authors reported that there appeared to be an antitumor activity for some but not all cancers, with the most promising results seen for non-small-cell lung cancer, Erdheim-Chester disease, and Langerhans cell histiocytosis.

**Expanded Cancer Molecular Panels**
Table 1 provides a select list of commercially available expanded cancer molecular panels.

**Table 1. Commercially Available Molecular Panels for Solid and Hematologic Tumor Testing**

<table>
<thead>
<tr>
<th>Test</th>
<th>Manufacturer</th>
<th>Tumor Type</th>
<th>Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>FoundationOne® CDx test (F1CDx)</td>
<td>Foundation Medicine</td>
<td>Solid</td>
<td>NGS</td>
</tr>
<tr>
<td>FoundationOne® CDx Heme test</td>
<td>Foundation Medicine</td>
<td>Hematologic</td>
<td>RNA sequencing</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Test</th>
<th>Manufacturer</th>
<th>Tumor Type</th>
<th>Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>OnkoMatch™‡</td>
<td>GenPath Diagnostics</td>
<td>Solid</td>
<td>Multiplex PCR</td>
</tr>
<tr>
<td>GeneTrails®‡ Solid Tumor Panel</td>
<td>Knight Diagnostic Labs</td>
<td>Solid</td>
<td></td>
</tr>
<tr>
<td>Tumor profiling service</td>
<td>Caris Molecular Intelligence through Caris Life Sciences</td>
<td>Solid</td>
<td>Multiple technologies</td>
</tr>
<tr>
<td>SmartGenomics™‡</td>
<td>PathGroup</td>
<td>Solid and hematologic</td>
<td>NGS, cytogenomic array, other technologies</td>
</tr>
<tr>
<td>Guardant 360 panel</td>
<td>GuardantHealth</td>
<td>Solid</td>
<td>Digital sequencing</td>
</tr>
<tr>
<td>Paradigm Cancer Diagnostic (PcDx™‡) Panel</td>
<td>Paradigm</td>
<td>Solid</td>
<td>NGS</td>
</tr>
<tr>
<td>Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets</td>
<td>MSK-IMPACT™‡; Memorial Sloan Kettering Cancer Center</td>
<td>Solid</td>
<td>NGS</td>
</tr>
<tr>
<td>TruSeq™‡ Amplicon Panel</td>
<td></td>
<td>Solid</td>
<td>NGS</td>
</tr>
<tr>
<td>Illumina TruSight™‡ Tumor</td>
<td>Illumina</td>
<td>Solid</td>
<td>NGS</td>
</tr>
<tr>
<td>Ion AmpliSeq™‡ Comprehensive Cancer Panel</td>
<td></td>
<td>Solid</td>
<td>NGS</td>
</tr>
<tr>
<td>Ion AmpliSeq™‡ Cancer Hotspot Panel v2</td>
<td>Thermo Fisher Scientific</td>
<td>Solid</td>
<td>NGS</td>
</tr>
<tr>
<td>OmniSeq Comprehensive™‡</td>
<td>OmniSeq</td>
<td>Solid</td>
<td>NGS</td>
</tr>
</tbody>
</table>

NGS: next-generation sequencing; PCR: polymerase chain reaction.

**FDA or Other Governmental Regulatory Approval**

**U.S. Food and Drug Administration (FDA)**

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
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Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing.

In 2017, FoundationOne CDx (Foundation Medicine) received premarket approval by the U.S. Food and Drug Administration (P170019) as a companion diagnostic to identify patients who may benefit from treatment with the targeted therapies listed in Table 2. "Additionally, F1CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms." Food and Drug Administration product code: PQP

MSK-IMPACT (Memorial Sloan Kettering) received de novo marketing clearance in 2017 (DEN170058). "The test is intended to provide information on somatic mutations (point mutations and small insertions and deletions) and microsatellite instability for use by qualified health care professionals in accordance with professional guidelines, and is not conclusive or prescriptive for labeled use of any specific therapeutic product." Food and Drug Administration product code: PZM

OmniSeq Comprehensive is approved by the New York State Clinical Laboratory Evaluation Program.

Table 2. Companion Diagnostic Indications for F1CDx

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Biomarker(s) Detected</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-small cell lung cancer (NSCLC)</td>
<td><em>EGFR</em> exon 19 deletions and <em>EGFR</em> exon 21 L858R alterations</td>
<td>Gilotrif®‡ (afatinib), Iressa®‡ (gefitinib), Tagrisso®‡ (osimertinib), or Tarceva® (erlotinib)</td>
</tr>
<tr>
<td></td>
<td><em>EGFR</em> exon 20 T790M alterations</td>
<td>Tagrisso®‡ (osimertinib)</td>
</tr>
<tr>
<td>ALK rearrangements</td>
<td><em>ALK</em> rearrangements</td>
<td>Alecensa®‡ (alectinib), Xalkori®‡ (crizotinib), or Zykadia®‡ (ceritinib)</td>
</tr>
<tr>
<td>BRAF V600E</td>
<td></td>
<td>Tafinlar®‡ (dabrafenib) in combination with Mekinist®‡ (trametinib)</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Relevant Genetic Markers</th>
<th>Targeted Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>BRAF V600E</td>
<td>Tafinlar®‡ (dabrafenib) or Zelboraf®‡ (vemurafenib)</td>
</tr>
<tr>
<td></td>
<td>BRAF V600E and V600K</td>
<td>Mekinist®‡ (trametinib) or Cotell®‡ (cobimetinib) in combination with Zelboraf®‡ (vemurafenib)</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>ERBB2 (HER2) amplification</td>
<td>Herceptin®‡ (trastuzumab), Kadcyla®‡ (ado-trastuzumabemtansine), or Perjeta®‡ (pertuzumab)</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>KRAS wild-type (absence of mutations in codons 12 and 13)</td>
<td>Erbitux®‡ (cetuximab)</td>
</tr>
<tr>
<td></td>
<td>KRAS wild-type (absence of mutations in exons 2, 3, and 4) and NRAS wild type (absence of mutations in exons 2, 3, and 4)</td>
<td>Vectibix®‡ (panitumumab)</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>BRCA1/2 alterations</td>
<td>Lynparza®‡ (olaparib) or Rubraca®‡ (rucaparib)</td>
</tr>
</tbody>
</table>

### Rationale/Source

Comprehensive genomic profiling offers the potential to evaluate a large number of genetic markers at a single time to identify cancer treatments that target specific biologic pathways. Some individual markers have established benefit in certain types of cancers; they are not addressed in this evidence review. Rather, this review focuses on "expanded" panels, which are defined as molecular panels that test a wide variety of genetic markers in cancers without regard for whether a specific targeted treatment has demonstrated benefit. This approach may result in treatment different from that usually selected for a patient based on the type and stage of cancer.

For individuals who have advanced cancer that is being considered for targeted therapy who receive comprehensive genomic profiling of tumor tissue, the evidence includes a randomized controlled trial, nonrandomized trials, and systematic reviews of these studies. The relevant outcomes are...
overall survival, disease-specific survival, test validity, and quality of life. A large number of variants and many types of cancer preclude determination of the clinical validity of the panels as a whole, and clinical utility has not been demonstrated for the use of expanded molecular panels to direct targeted cancer treatment. The one published randomized controlled trial (SHIVA trial) that used an expanded panel reported no difference in progression-free survival compared with standard treatment. Additional randomized and nonrandomized trials for drug development, along with systematic reviews of these trials, have compared outcomes in patients who received molecularly targeted treatment with patients who did not. Generally, trials in which therapy was targeted to a gene variant resulted in improved response rates, progression-free survival, and overall survival compared to patients in trials who did not receive targeted therapy. A major limitation in the relevance of these studies for comprehensive genomic profiling is that treatment in these trials was guided both by the tissue source and the molecular target for drug development, rather than being matched solely by the molecular marker (ie, basket trials). As a result, these types of studies do not provide evidence of the benefit of broad molecular profiling compared to more limited genetic assessments based on known tumor-specific variants. Basket trials that randomize patients with various tumor types to a strategy of comprehensive genomic profiling followed by targeted treatment are needed, and several are ongoing. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Supplemental Information**

**Practice Guidelines and Position Statements**

The National Comprehensive Cancer Network guidelines do not contain recommendations for the general strategy of testing a tumor for a wide range of variants. The guidelines do contain recommendations for specific genetic testing for individual cancers, based on situations where there is a known mutation-drug combination that has demonstrated benefits for that specific tumor type. Some examples of recommendations for testing of common solid tumors are listed below:

**Breast cancer**
- *HER2* testing for all new primary or newly metastatic breast cancers,

**Colon cancer**
- *KRAS*, *NRAS*, and *BRAF* mutation testing and microsatellite instability or mismatch repair testing for patients with metastatic colon cancer.
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Non-small-cell lung cancer
- *EGFR, ALK, ROS1, BRAF, KRAS,* and *NTRK* fusions.

Cutaneous Melanoma
- *BRAF, NRAS, KIT*
- Uncommon mutations with next-generation sequencing are *ALK, ROS,* and *NTRK* fusions

Ovarian cancer
- *BRCA*

Chronic myeloid leukemia
- *BCR-ABL1*

Gastric cancer
- *HER2,* microsatellite instability
- *CDH1* for hereditary cancer predisposition syndromes.

Bladder cancer
- *FGFR*

Soft Tissue Sarcomas
- *NTRK* fusions

**College of American Pathologists et al**
The College of American Pathologists and 2 other associations (2018) updated their joint guidelines on molecular testing of patients with non-small-cell lung cancer. The groups gave a strong recommendation for *EGFR, ALK,* and *ROS1* testing. Based on expert consensus opinion *KRAS* was recommended as a single gene test if *EGFR, ALK,* and *ROS* were negative. Tests that were not recommended for single gene testing outside of a clinical trial were *BRAF, RET, ERBB2 (HER2),* and *MET,* although these genes should be tested if included in a panel.
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American Society of Clinical Oncology
The American Society of Clinical Oncology (2018) affirmed the majority of these guidelines. The Society guidelines also recommended \textit{BRAF} testing on all patients with advanced lung adenocarcinoma.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
The Centers for Medicare and Medicaid Services will cover diagnostic testing with next-generation sequencing for beneficiaries with recurrent, relapsed, refractory, metastatic cancer, or advanced stages III or IV cancer if the beneficiary has not been previously tested using the same next-generation sequencing test, unless a new primary cancer diagnosis is made by the treating physician, and if the patient has decided to seek further cancer treatment (CAG-00450N). The test must have a Food and Drug Administration approved or cleared indication as an in vitro diagnostic, with results and treatment options provided to the treating physician for patient management.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 14. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Ongoing}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02693535\textsuperscript{a}</td>
<td>TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)</td>
<td>3123</td>
<td>Dec 2021</td>
</tr>
<tr>
<td>NCT02152254</td>
<td>Randomized Study Evaluating Molecular Profiling and Targeted Agents in Metastatic Cancer: Initiative for Molecular Profiling and Advanced Cancer Therapy (IMPACT 2)</td>
<td>1362</td>
<td>May 2020</td>
</tr>
</tbody>
</table>

\textsuperscript{a} \text{For more information, please see clinicaltrials.gov.}
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<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02299999*</td>
<td>Evaluation of the Efficacy of High Throughput Genome Analysis as a Therapeutic Decision Tool for Patients with Metastatic Breast Cancer (SAFIR02_Breast)</td>
<td>1460</td>
<td>Dec 2022</td>
</tr>
<tr>
<td>NCT02465060</td>
<td>Molecular Analysis for Therapy Choice (MATCH)</td>
<td>6452</td>
<td>Jun 2022</td>
</tr>
<tr>
<td>NCT02029001</td>
<td>Adapting Treatment to the Tumor Molecular Alterations for Patients with Advanced Solid Tumors: My Own Specific Treatment</td>
<td>560</td>
<td>Oct 2022</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
* Industry-sponsored or co-sponsored.

References

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Policy History
Original Effective Date: 07/16/2014
Current Effective Date: 07/13/2020
07/10/2014 Medical Policy Committee review
07/16/2014 Medical Policy Implementation Committee approval. New policy.

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06/04/2015   Medical Policy Committee review
06/17/2015   Medical Policy Implementation Committee approval. Updated rationale and references. No change in coverage.
08/03/2015   Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
06/02/2016   Medical Policy Committee review
06/20/2016   Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017   Coding update: Removing ICD-9 Diagnosis Codes
06/01/2017   Medical Policy Committee review
06/21/2017   Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2018   Coding update
06/07/2018   Medical Policy Committee review
06/20/2018   Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/01/2018   Coding update
01/01/2019   Coding update
06/06/2019   Medical Policy Committee review
06/19/2019   Medical Policy Implementation Committee approval. Title changed from "Molecular Panel Testing of Cancers to Identify Targeted Therapies" to "Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies". Changed "mutation" to "molecular" in the INV statement.
04/21/2020   Coding update
05/11/2020   Coding update
06/04/2020   Medical Policy Committee review
06/10/2020   Medical Policy Implementation Committee approval. Title changed from "Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies" to "Comprehensive Genomic Profiling for Selecting Targeted Cancer Therapies". Language in policy statement changed from "expanded cancer molecular panels" to "comprehensive genomic profiling". The intent of coverage eligibility is unchanged.
09/22/2020   Coding update

Next Scheduled Review Date:  06/2021
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**Coding**

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Add code eff 7/1/2020: 0174U</td>
</tr>
<tr>
<td></td>
<td>Add code eff 10/1/2020: 0016M, 0211U</td>
</tr>
<tr>
<td>HCPCS</td>
<td>No codes</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>All related diagnoses</td>
</tr>
</tbody>
</table>
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.