SEPTEMBER–OCTOBER 2019

BCN Provider News

Medical policy updates

The following applies to Blue Care Network members: Noncovered services appear first; covered services follow. The effective date is indicated for the service, technology or procedure.

Noncovered services

Radiofrequency ablation of peripheral nerves to treat pain including Coolief™ Cooled radiofrequency

- **Revised policy**
- **Effective date: July 1, 2019**
- **Procedure code: *64640**

Nerve radiofrequency ablation is a minimally invasive method that involves the use of heat and coagulation necrosis to destroy tissue. A needle electrode is inserted through the skin and then into the tissue to be ablated. A high-frequency electrical current is applied to the target tissue. A small sphere of tissue is coagulated around the needle by the heat generated. It is theorized that the thermal lesioning of the nerve destroys peripheral sensory nerve endings, resulting in the alleviation of pain. Cooled radiofrequency treatment is a variation of nerve RFA using a special device that applies more energy at the desired location without excessive heat diffusing beyond the area, causing less tissue injury away from the nerve. The goal of ablating the nerve is the same. RFA has been evaluated for use in the following conditions: plantar fasciitis, osteoarthritis (hip and knee), occipital neuralgia and cervicogenic headaches.

Radiofrequency ablation of peripheral nerves to treat pain (plantar fasciitis, occipital neuralgia, cervicogenic headache, osteoarthritis) including Coolief™ Cooled RF is experimental. It has not been scientifically demonstrated to improve patient clinical outcomes.

Genetic testing for FMR1 and FMR2 variants (Including Fragile X and Fragile XE syndromes)

- **Revised policy (Added testing for Fragile SE Syndrome)**
- **Effective date: Sept. 1, 2019**
- **Procedure codes: *81171, *81172**

Fragile X syndrome (FXS) is the most common cause of heritable intellectual disability, characterized by moderate intellectual disability in males and mild intellectual disability in females. In addition to intellectual impairment, patients present with typical facial features, such as an elongated face with prominent forehead, protruding jaw and large ears. Connective tissue anomalies include hyperextensible finger and thumb joints, hand calluses, velvet-like skin, flat feet and mitral valve prolapse. FXS is associated with the expansion of the CGG trinucleotide repeat in the Fragile X mental retardation 1 *(FMR1)* gene on the X chromosome. FXS affects approximately one in 4,000 males and one in 8,000 females.

Genetic testing for *FMR1* variants may be considered established in select patient populations.

Fragile XE syndrome is caused by variants in the *FMR2* (or *AFF2*) gene, which is located in close proximity to the *FMR1* gene. Reported clinical features include mild to borderline intellectual disabilities, learning difficulties, speech delays and developmental delay. Some individuals also display autistic behaviors such as repetitive behaviors, intense interest in a particular subject and hand flapping. Symptoms vary from person to person and there are no consistent physical characteristics associated with fragile XE syndrome. Estimates of prevalence of fragile XE syndrome range from one in 25,000 to one in 100,000.

Genetic testing for *FMR2* variants (*AFF2* gene) is considered experimental. This medical literature has not demonstrated the clinical utility of this testing.

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Medical policy updates *Cont.*

Genotype-guided warfarin dosing

- **Revised policy**
- **Effective date: Sept. 1, 2019**
- **Procedure codes: G9143, *81227, *81355**

Genetic variants in genes may result in individual differences in the ability to metabolize warfarin. The drug, warfarin, is administered for preventing and treating thromboembolic events in high-risk individuals. Using information regarding an individual's genotypes, as well as other known characteristics to determine a personalized starting dose may reduce the time to a stable warfarin dose and avoid serious bleeding events.

Genetic testing for warfarin dosing is experimental. The clinical utility of genetic testing to determine cytochrome p450 2C9 (CYP2C9), P450 4F2 (CYP4F2), and vitamin K epoxide reductase subunit C1(VKORC1) genetic polymorphisms and other warfarin responsive testing for the purpose of determining warfarin dosing has not been demonstrated. The peer reviewed medical literature has not yet shown that this testing has sufficient diagnostic accuracy to provide clinically relevant information for patient management.

Covered services

Artificial pancreas device systems

- **Revised policy**
- **Effective date: July 1, 2019**
- **Plan approval with clinical review**
- **Procedure codes: S1034, S1035, S1036, S1037**

Tight glucose control in patients with diabetes has been associated with improved outcomes. The American Diabetes Association recommends a glycated hemoglobin (HbA1c) level below 7% for most patients. However, hypoglycemia, defined as plasma glucose below 70 mg/dL, may place a limit on the ability to achieve tighter glycemic control. Hypoglycemic events in adults range from mild to severe based on several factors including the glucose nadir, the presence of symptoms and whether the episode can be self-treated or requires help for recovery. Controlling hyperglycemia and avoiding hypoglycemia in insulin dependent diabetics is difficult.

The U.S. Food and Drug Administration describes the basic design of an artificial pancreas device system as a continuous glucose monitor linked to an insulin pump with the capability to automatically stop, reduce or increase insulin infusion based on specified thresholds of measured interstitial glucose. The artificial pancreas device system components are designed to communicate with each other to automate the process of maintaining blood glucose concentrations at or near a specified range or target and to minimize the incidence and severity of hypoglycemic and hyperglycemic events. An artificial pancreas device system control algorithm is embedded in software in an external processor or controller that receives information from the continuous glucose monitor and performs a series of mathematical calculations. Based on these calculations, the controller sends dosing instructions to the infusion pump.

Different artificial pancreas device system types are currently available for clinical use. An artificial pancreas device system may also be referred to as a "closed-loop" system. A closed-loop system has automated insulin delivery and continuous glucose sensing and insulin delivery without patient intervention. The systems utilize a control algorithm that autonomously and continually increases and decreases the subcutaneous insulin delivery based on real-time sensor glucose levels. A hybrid closed-loop system also uses automated insulin delivery with continuous basal insulin delivery adjustments. However, at mealtime, the patient enters the number of carbohydrates he or she is consuming so the insulin pump can determine the bolus meal dose of insulin. A hybrid system option with the patient administration of a premeal or partial premeal insulin bolus can be used in either control-to-range or control-to-target systems.

The safety and effectiveness of an FDA-approved artificial pancreas device systems with a low glucose suspend feature may be considered established in patients with insulin-requiring diabetes who meet specified patient selection criteria. It is a useful therapeutic option for selected patients.

Inclusions

Use of a U.S. Food and Drug Administration-approved artificial pancreas device system with a low-glucose suspend feature may be considered established in patients with insulin-requiring diabetes who meet all of the following criteria:

- Age 14 or older
- Insulin requiring diabetes
- Used continuous glucose monitor system pump for more than six months
- Individuals with demonstrated hypoglycemia unawareness

Cont.

Medical policy updates *Cont.*

Use of an FDA-approved automated insulin delivery system (artificial pancreas device system) designated as hybrid closed loop insulin delivery system (with low glucose suspend and suspend before low features) is considered established in patients with insulin requiring diabetes who meet all of the following criteria:

- Age 7 and older
- Insulin requiring diabetes
- Used continuous glucose monitor system pump for more than six months
- Individuals with demonstrated hypoglycemia unawareness

Exclusions

- Use of an artificial pancreas device system is considered experimental in all other situations.
- Use of an artificial pancreas device system not approved by the FDA is experimental.

Genetic testing-assays of genetic expression in tumor tissue as a technique to determine prognosis in patients with breast cancer

- **Revised policy**
- **Effective date: July 1, 2019**
- **Plan approval with clinical review**
- **Procedure codes: *81519, *81520, *81521, *84999**

Most women with newly diagnosed breast cancer in the United States present with early-stage or locally advanced (for example, nonmetastatic) disease. However, almost a third of women who are disease-free after initial local and regional treatment develop distant recurrences during follow-up. Current breast cancer treatment regimens involve systemic adjuvant chemotherapy, hormonal therapy, biologic therapy or a combination, depending on a patient's baseline level of recurrence risk, hormonal markers and risk tolerance.

An important part of treatment planning for women with breast cancer involves determining which patients could benefit from adjuvant treatments. In other clinical scenarios involving breast cancer, accurate assessment of prognosis may affect the decision to offer certain treatments. Recently, several groups have identified panels of gene expression markers ("signatures") that appear to predict the baseline risk of breast cancer recurrence after surgery, radiation therapy and hormonal therapy (for hormone-receptor-positive tumors).

The safety and effectiveness of the use of the 21-gene reverse transcriptase-polymerase chain reaction (RT-PCR) assay (i.e., Oncotype DX®), the EndoPredict®, the Breast Cancer Index℠, MammaPrint and Prosigna™ tests to determine recurrence risk for deciding whether to undergo adjuvant chemotherapy have been established. They are useful diagnostic tests for determining the likelihood of distant cancer recurrence in women for patients who meet the inclusionary guidelines.

Other genetic testing for determining the likelihood of distant cancer recurrence in women is experimental. (Refer to exclusions).

Inclusions (must meet all):

The use of Oncotype Dx®, the EndoPredict®, the Breast Cancer Index℠, MammaPrint and Prosigna™ tests to determine recurrence risk for deciding whether to undergo adjuvant chemotherapy may be considered established in women with breast cancer meeting all of the following characteristics:

- Unilateral tumor
- Hormone receptor-positive (that is, estrogen-receptor [ER] positive or progesterone-receptor [PR]-positive
- Human epidermal growth factor receptor (HER) 2-negative
- Tumor size 0.6-1 cm with moderate/poor differentiation or unfavorable features or tumor size larger than 1 cm
- Node negative (Lymph nodes with micrometastases [less than 2 mm in size] are considered node negative for this policy.)
- Treatment with adjuvant endocrine therapy, for example, tamoxifen or aromatase inhibitors
- When the test result will aid the patient in making the decision regarding chemotherapy (for example, when chemotherapy is a therapeutic option)
- When ordered within six months after diagnosis, since the value of the test for making decisions regarding delayed chemotherapy is unknown

Use of multigene assay to assess prognosis and determine chemotherapy benefit for node-positive, ER+, HER2- breast cancer with pN1mi (≤2 mm axillary node metastasis) or N1 (<4 nodes is established.

Cont.

Medical policy updates *Cont.*

These tests should only be ordered on a tissue specimen obtained during surgical removal of the tumor and after subsequent pathology examination of the tumor has been completed and determined to meet the above criteria; the test should not be ordered on a preliminary core biopsy. The test should be ordered in the context of a physician-patient discussion regarding risk preferences when the test result will aid in making decisions regarding chemotherapy.

For patients who otherwise meet the above characteristics but who have multiple ipsilateral primary tumors, a specimen from the tumor with the most aggressive histological characteristics should be submitted for testing. It is not necessary to conduct testing on each tumor; treatment is based on the most aggressive lesion.

Exclusions:

- Gene expression assays when used in tandem with other similar assays is considered investigational; only a single assay should be used (Oncotype DX and MammaPrint should not be ordered on the same patient).
- Use of a subset of genes from the 21-gene RT-PCR assay for predicting recurrence risk in patients with noninvasive ductal carcinoma in situ (DCIS) (for example, Oncotype DX® DCIS) to inform treatment planning following excisional surgery is considered experimental.
- The use of other gene expression assays (for example, Mammostrat® Breast Cancer Test, the BreastOncPx™, NexCourse® Breast IHC4, BreastPRS™) for any indication is experimental.
- The use of gene expression assays in men with breast cancer is considered experimental.
- The use of gene expression assays to molecularly subclassify breast cancer (for example, BluePrint®) is considered experimental.
- The use of gene expression assays for quantitative assessment of ER, PR and HER2 overexpression (for example, TargetPrint®) is considered experimental.

Drug testing of urine, oral fluids and hair

- **New policy — Clarification**
- **Effective date: May 1, 2019**
- **No referral required — Use appropriate contracted vendor**
- **Procedure codes: *80305 - 80307, *80320 - 80377, *83992 (for reporting purposes), G0480 - G0483, G0659**

Note: The original medical policy was published in the July-August issue of *BCN Provider News*. We've added clarifications to the Policy Guidelines section, as follows:

Policy guidelines

One presumptive and one definitive test code may be billed per date of service.

Billing guidelines - Definitive drug testing - Effective Aug. 1, 2019

- Bill G0480-G0483, G0659 as appropriate, for the number of drug classes tested.
- Bill *80XXX and *83992 to report the appropriate drug or metabolite testing. The codes are no longer individually reimbursed. For the purpose of this policy; however, we request that they are reported with the appropriate G code.

Genetic testing-expanded molecular panel testing of cancers to identify targeted therapies

- **Revised policy**
- **Effective date: July 1, 2019**
- **No referral required — Use appropriate contracted vendor**
- **Procedure codes: *81445, *81450**

Note: The original article was published in the July-August issue. We've made a correction to the "Inclusions" section, italicized, as follows.

Cont.

Medical policy updates *Cont.*

Inclusions:

Testing for appropriate actionable genomic alterations that influence therapy may be performed through a panel test for the following conditions:

- Non-small-cell lung cancer
- Colorectal cancer
- Cutaneous melanoma
- Gastrointestinal stromal tumor
- Glioma
- Acute myeloid leukemia
- Thyroid *nodule, to determine a diagnosis of cancer*

Exclusions:

Molecular panel testing for conditions other than those listed in the Inclusions section is considered experimental.

Genetic testing for hereditary hemochromatosis

- **Revised policy**
- **Effective date: Sept. 1, 2019**
- **No referral required — Use appropriate contracted vendor**
- **Procedure code: *81256**

Iron overload syndromes, if untreated, can lead to secondary tissue damage in a wide range of organs resulting in chronic liver disease (hepatic fibrosis, cirrhosis, hepatocellular carcinoma), endocrine dysfunction (diabetes, hypogonadism), arthralgia or arthritis (typically involving the second and third metacarpophalangeal joints), and cardiomyopathy (with either symptomatic cardiac failure or arrhythmias).

Hereditary hemochromatosis (HH), an autosomal recessive disorder, is the most common identified genetic disorder in Caucasians, with an estimated prevalence of one in 250. HH leads to inappropriate iron absorption from the intestine and progressive increase in intracellular iron concentrations. Untreated HH leads to premature death, usually by liver complications. Most individuals with HH have variants in the *HFE* gene, located on the short arm of chromosome 6.

The safety and effectiveness of genetic testing for hereditary hemochromatosis have been established. It may be considered a useful diagnostic tool when indicated. Genetic testing should be performed in conjunction with appropriate pre- and post-test genetic counseling.

Inclusions:

Testing for *HFE* variants may be performed in, either

- Individuals with a fasting transferrin saturation (the ratio of serum iron to total iron-binding capacity) ≥45%
- Individuals with a serum ferritin level above the upper limit of normal
- Individuals with a first-degree relative* diagnosed with *HFE*-related hereditary hemochromatosis

*A first-degree relative is a biological parent, full-sibling or child (someone who shares 50% of the individual's genes).

Exclusions:

- Screening for non-HFE related hereditary hemochromatosis
- Screening for HFE variants in the general population

Reconstructive breast surgery / management of implants

- **Revised policy**
- **Effective date: Sept. 1, 2019**
- **Plan approval with clinical review**
- **Procedure codes: Multiple**

Reconstructive breast surgery is surgery performed to restore the normal appearance of the breast after surgery, accidental injury, trauma, or to correct a congenital defect. Prosthetic breast implants are silicone or saline-filled sacs that may be used for breast reconstruction or cosmetic breast augmentation. These devices are made of an outer silicone shell and filled with either saline or silicone gel. Breast implants are not lifetime devices and may require replacement. Removal of a breast implant may be medically necessary depending on the significance of the complication.

The safety and effectiveness of breast implant and breast reconstruction procedures have been established. Insertion, removal and reinsertion of silicone gel or saline filled breast implants are established procedures for breast reconstruction and implant surgery when specific clinical criteria are met.

Cont.

Medical policy updates *Cont.*

Implants

Inclusions:

Implant removal for documented:

- Baker Class III contractures (only if initial implant was for reconstructive purposes)
- Baker Class IV contracture
- Recurrent infection
- Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)
- Suspected BIA-ALCL (symptoms of pain, swelling, redness or lump in the area of the implant; seroma; asymmetry of the breast). Bilateral removal is covered if requested.
- Extrusion
- Silicone implant rupture
- Surgery for a new diagnosis of breast cancer
- Textured-surface breast implant, when the surgeon determines it is in the best interest of the patient. Reinsertion of an implant will not be covered.

Exclusions:

The following indications for removal of breast implant are considered not medically necessary:

- Patient anxiety
- Pain not related to contractures or rupture
- Baker Class III contractures in patients with implants for cosmetic purposes
- Removal of a ruptured saline breast implant(s) when the original insertion was for a cosmetic purpose
- Systemic symptoms, attributed to connective tissue diseases, autoimmune diseases, etc.

Reduction mammaplasty

- **Revised policy**
- **Effective date: Sept. 1, 2019**
- **Plan approval with clinical review**
- **Procedure code: *19318**

Macromastia may result in clinical symptoms such as shoulder, neck, or back pain, or recurrent intertrigo in the mammary folds. Reduction mammaplasty is a surgical procedure designed to remove a variable portion of breast tissue to relieve the associated symptoms.

The safety and effectiveness of reduction mammoplasty have been established. It may be considered a useful therapeutic option (and not considered cosmetic) when either:

- The patient meets specified patient selection guidelines
- When performed in conjunction with medically necessary breast reconstruction for the purposes of attaining breast symmetry

Patients under the age of 18 years cannot give legal consent for surgery. The parent or legal guardian must support and authorize a reduction mammaplasty.

Emancipated minors may be extended individual consideration.

Inclusions:

A. Must meet both criteria (1-2):

1. Patient's breasts are fully grown (breast size stable for approximately over one year)
2. Removal of more than 500 grams of tissue per breast

Or

Must meet both B and C:

B. Two of the following criteria (1-3) must be met:

1. Pain
   - Documented pain in the neck and/or shoulders or postural backache which must be of long-standing duration, and
   - Failure of conservative therapy (for example, an appropriate support bra, exercises, heat/cold treatments, non-steroidal anti-inflammatory agents or muscle relaxants)
2. Shoulder grooving
3. Recurrent intertrigo between the breasts and the chest wall

And

C. Must meet both criteria:

1. Patient's breasts are fully grown (breast size stable for approximately over one year)
2. The amount of tissue to be removed must be greater than or equal to the 22nd percentile on the Schnur Scale.

Medical policy updates *Cont.*

Genetic testing for FLT3, NPM1, CEBPA, IDH1 and IDH2 variants in acute myeloid leukemia

- **New policy**
- **Effective date: Sept. 1, 2019**
- **Plan approval with clinical review**
- **Procedure codes: *81120, *81121, *81218, *81245, *81246, *81310, *81450 (may be appropriate when all variants are being tested)**

Acute myeloid leukemia (AML) is a group of diverse hematologic malignancies characterized by the clonal expansion of myeloid blasts in the bone marrow, blood, or other tissues. It is the most common type of leukemia in adults and is generally associated with a poor prognosis. The most recent World Health Organization classification (2016) reflects the increasing number of acute leukemias that can be categorized based on underlying cytogenetic abnormalities (for example, at the level of the chromosome including chromosomal translocations or deletions) or molecular genetic abnormalities (at the level of the function of individual genes, including gene variants).

Molecular variants have been analyzed to subdivide AML with normal cytogenetics into prognostic subsets. Most frequent molecular changes with prognostic impact are variants of FLT3, CEBPA, NPM1, IDH1 and IDH2. Testing may be done on individual variants or may require testing of all variants.

Genetic testing for *FLT3* internal tandem duplication (*FLT3*-ITD), *FLT3* tyrosine kinase domain (*FLT3-TKD), NPM1, CEBPA, IDH1 and IDH2* variants may be considered established in cytogenetically normal acute myeloid leukemia (if testing for all variants, panel testing [code *81450] may be appropriate).

Genetic testing for *FLT3-ITD, FLT3-TKD, NPM1, CEBPA, IDH1 and IDH2* variants is considered experimental in all other situations.

Genetic testing for *FLT3, NPM1, and CEBPA* variants to detect minimal residual disease is considered experimental.

Genetic testing for cytogenetically normal acute myeloid leukemia is intended to guide management decisions in patients who would receive treatment other than low-dose chemotherapy or best supportive care.

Genetic testing for IDH1 and IDH2 variants is intended for use as diagnostic and prognostic value in hematologic disorders, such as acute myeloid leukemia.

Genetic testing- molecular markers in fine needle aspirates (FNA) of the thyroid

- **Revised policy**
- **Effective date: Sept. 1, 2019**
- **Plan approval with clinical review**
- **Procedure codes: *81445, *81545, *0018U, *0026U, *81479**

Fine needle aspiration (FNA) of a thyroid lesion to identify which patients need to undergo surgery has diagnostic limitations and has led to the development of molecular markers in an attempt to improve the accuracy of patient selection.

FNA of the thyroid is currently the most accurate procedure to distinguish benign thyroid lesions and malignant ones, reducing the rate of unnecessary thyroid surgery for patients with benign nodules and triaging patients with thyroid cancer to appropriate surgery.

The use of either Afirma® Gene Expression Classifier or ThyroSeq™ v3 in fine needle aspirates of thyroid nodules with indeterminate cytologic findings (for example, Bethesda diagnostic category III [atypia/follicular lesion of undetermined significance] or Bethesda diagnostic category IV [follicular neoplasm/suspicion for a follicular neoplasm]) is established in patients who have the following characteristics:

- Thyroid nodules without strong clinical or radiologic findings suggestive of malignancy
- In those whom surgical decision-making would be affected by test results

The use of any of the following types of molecular marker testing or gene variant analysis in fine needle aspirates of thyroid nodules with indeterminate findings (Bethesda diagnostic category III [atypia/follicular lesion of undetermined significance] or Bethesda diagnostic category IV [follicular neoplasm/suspicion for a follicular neoplasm]) or suspicious findings (Bethesda diagnostic category V [suspicious for malignancy]) to rule in malignancy to guide surgical planning for initial resection rather than a two-stage surgical biopsy followed by definitive surgery may be considered established:

- ThyroSeq™ v3
- ThyraMIR™ microRNA®/ThyGenX™
- Afirma® BRAF after Afirma® Gene Expression Classifier
- Afirma® MTC after Afirma® Gene Expression Classifier

Cont.

Medical policy updates *Cont.*

Gene expression classifiers, genetic variant analysis, and molecular marker testing in fine needle aspirates of the thyroid not meeting criteria outlined above, including but not limited to use of RosettaGX™ Reveal and single-gene TERT testing, are considered experimental.

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