



Name of Blue Advantage Policy:

Hematopoietic Stem-Cell Transplantation for Breast Cancer

Policy #: 518
Category: Surgical

Latest Review Date: September 2019
Policy Grade: **Active Policy but no longer scheduled for regular literature reviews and updates.**

Background:

Blue Advantage medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
 - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
 - *Furnished in a setting appropriate to the patient's medical needs and condition;*
 - *Ordered and furnished by qualified personnel;*
 - *One that meets, but does not exceed, the patient's medical need; and*
 - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill **Original Medicare for covered services that are related to **clinical trials** that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

Description of Procedure or Service:

The use of high-dose chemotherapy (HDC) and hematopoietic stem cell transplantation (HSCT), instead of standard dose chemotherapy, has been used in an attempt to prolong survival in women with high-risk nonmetastatic and metastatic breast cancer.

Hematopoietic Stem Cell Transplantation

Hematopoietic stem cell transplantation (HSCT) refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs with or without whole body radiation therapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HSCT) or from a donor (allogeneic HSCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naïve” and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD).

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HSCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HSCT. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the Class I and Class II loci on chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci (with the exception of umbilical cord blood).

Conventional Preparative Conditioning for HSCT

The success of autologous HSCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient prior to undergoing bone marrow ablation. As a consequence, autologous HSCT is typically performed as consolidation therapy when the patient’s disease is in complete remission. Patients who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

The conventional (“classical”) practice of allogeneic HSCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy (GVM) effect mediated by non-self-immunologic effector cells that develop after engraftment of allogeneic stem cells within the patient’s bone marrow space. While the slower GVM effect is considered to be the potentially curative component, it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse effects that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HSCT,

immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility of the patient to opportunistic infections.

Reduced-Intensity Conditioning for Allogeneic HSCT

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiation than are used in traditional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated treatment-related morbidity and non-relapse mortality (NRM) in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly totally myeloablative to minimally myeloablative with lympho-ablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allogeneic HSCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells.

For the purposes of this policy, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be non-myeloablative, as opposed to fully myeloablative (traditional) regimens.

HSCT in Solid Tumors in Adults

HSCT is an established treatment for certain hematologic malignancies; however, its use in solid tumors in adults continues to be largely experimental. Initial enthusiasm for the use of autologous transplant with the use of HDC and stem cells for solid tumors has waned with the realization that dose intensification often fails to improve survival, even in tumors with a linear-dose response to chemotherapy. With the advent of reduced-intensity allogeneic transplant, interest has shifted to exploring the generation of alloreactivity to metastatic solid tumors via a graft-versus-tumor (GVT) effect of donor-derived T cells.

Policy:

Blue Advantage will treat **single or tandem autologous hematopoietic stem-cell transplantation when used to treat any stage of breast cancer** as a **non-covered benefit**.

Blue Advantage will treat **allogeneic hematopoietic stem-cell transplantation when used to treat any stage of breast cancer** as a **non-covered benefit** and as **investigational**.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature review was performed through August 28, 2019. Following is a summary of key literature to date.

History of Hematopoietic Stem-Cell Transplant for Breast Cancer

In the late 1980s/early 1990s, initial results of Phase II trials for breast cancer and autologous hematopoietic stem-cell transplant (HSCT) were promising, showing high response rates in patients with metastatic disease who underwent high-dose consolidation, with a subset of up to 30% remaining disease-free for prolonged periods. In the early 1990s, larger prospective comparisons of conventional-dose chemotherapy to high-dose therapy with HSCT were initiated but accrued slowly, with up to a decade from initiation to the reporting of results. The first results from randomized trials at a single institution in early stage and metastatic disease showed survival benefits but were ultimately shown to have been based on fraudulent data. In the interim, however, the treatment became almost standard of care, while many patients received high-dose therapy off protocol, further reducing accrual to ongoing randomized trials. The results of the randomized trials were presented beginning in 1999 and showed little survival benefit; subsequently, the number of HSCT procedures performed for breast cancer decreased from thousands every year to only a few.

Autologous SCT

The PBT-1 trial randomly assigned patients with a complete response (CR) or partial response (PR) to induction therapy for previously untreated metastatic breast cancer to autologous HSCT (n=101) or to conventional-dose maintenance chemotherapy (n=83) for up to two years. Of 553 patients enrolled and given initial induction therapy, only 310 achieved a PR (n=252) or CR (n=58), and only 199 were randomized. Of 72 partial responders assigned to the HSCT arm after initial induction therapy, only five (7%) were converted to complete responses. Median survival (24 vs. 26 months, respectively) and overall survival (OS) at three years (32% vs. 38%, respectively) did not differ between arms. There also were no statistically significant differences between arms in time to progression (TTP) or progression-free survival (PFS) at three years. While treatment duration was substantially shorter for those randomly assigned to HSCT, acute morbidity was markedly more severe than after conventional-dose maintenance.

Four trials reported final outcomes analyses from randomized comparisons of autologous HSCT versus conventional-dose chemotherapy for adjuvant therapy of high-risk non-metastatic breast cancer. Two of the studies involved women with at least four positive axillary lymph nodes, and the other two involved at least ten positive lymph nodes. The four studies pooled included 2,337 patients.

Evidence from these trials did not support the conclusion that autologous HSCT improved outcomes when compared with conventional-dose adjuvant therapy, as no OS difference was seen in any of the studies. An editorial that accompanied one of the trials briefly reviewed and commented on factors contributing to the diffusion of autologous HSCT into routine practice of the treatment of certain breast cancer patients, without adequate testing in randomized clinical trials (RCTs).

A Cochrane systematic review and meta-analysis published with pooled data from six RCTs on metastatic breast cancer (n=438 randomly assigned to autologous HSCT, 412 to conventional-dose therapy). The relative risk (RR) for treatment-related mortality was significantly higher in the arm randomly assigned to HSCT (15 vs. two deaths; RR: 4.07; 95% confidence interval [CI]: 1.39–11.88). Treatment-related morbidity also was more severe among those randomly assigned to HSCT. Overall survival did not differ significantly between groups at one, three, or five years after treatment. Statistically significant differences in event-free survival (EFS) at one year (RR: 1.76; 95% CI: 1.40–2.21) and five years (RR: 2.84; 95% CI: 1.07–7.50) favored the HSCT arms. Only one of the six RCTs included trials that had followed up all patients for at least five years. Reviewers recommended further follow-up for patients randomized in the other five trials. They also concluded that, in the interim, patients with metastatic breast cancer should not receive HSCT outside of a clinical trial, since available data showed greater treatment-related mortality and toxicity without improved OS.

A second Cochrane systematic review and meta-analysis, included data from 13 RCTs on patients with high-risk (poor prognosis) early breast cancer (N=2,535 randomly assigned to HSCT, 2,529 to conventional-dose therapy). Treatment-related mortality was significantly greater among those randomly assigned to high-dose chemotherapy/autologous SCT (HDC/AuSCT) (65 vs. four deaths; RR: 8.58; 95% CI: 4.13, 17.80, respectively). Treatment-related morbidity also was more common and more severe in the high-dose arms. There were no significant differences between arms in OS rates at any time after treatment. Event-free survival was significantly greater in the HSCT group at three years (RR: 1.12; 95% CI: 1.06, 1.19, respectively) and four years (RR: 1.30; 95% CI: 1.16, 1.45, respectively) after treatment. However, the two groups did not differ significantly with respect to EFS at five and six years after treatment. Quality-of-life scores were significantly worse in the HSCT arms than in controls soon after treatment, but differences were no longer statistically significant by one year. Reviewers concluded that available data were insufficient to support routine use of HSCT for patients with poor-prognosis early breast cancer.

Hanrahan and colleagues, with a median follow-up of 12 years, demonstrated no recurrence-free or OS advantage for patients with high-risk primary breast cancer treated with autologous HSCT after standard dose chemotherapy (n=39) versus standard chemotherapy alone (n=39). Coombes and colleagues reported on autologous HSCT as adjuvant therapy for primary breast cancer in women free of metastatic disease, with a median follow-up of 68 months. A total of 281 patients were randomly assigned to receive standard chemotherapy or high-dose chemotherapy (HDC) with HSCT. They found no significant difference in relapse-free survival or OS (OS hazard ratio [HR]: 1.18, 95% CI: 0.80-1.75, p=0.40).

A systematic review and meta-analysis included RCTs comparing autologous HSCT to standard-dose chemotherapy in women with early, poor prognosis breast cancer, which included 13 trials with a total of 5,064 patients. Major conclusions were that, at five years, EFS approached statistical significance for the high-dose group, but no OS differences were seen. There were more transplant-related deaths in the high-dose group. The end conclusion was that there was insufficient evidence to support routine use of autologous HSCT for treating early, poor prognosis breast cancer.

Crump and colleagues reported the results of a randomized trial of women who had not previously been treated with chemotherapy and had metastatic breast cancer or locoregional recurrence after mastectomy. After initial response to induction therapy, 112 women were allocated to standard chemotherapy and 112 to autologous HSCT. After a median follow-up of 48 months, 79 deaths were observed in the high-dose group and 77 in the standard chemotherapy group. No difference in OS was observed between the two groups after a median follow-up of 48 months, with a median OS of 24 months in the HSCT group (95% CI: 21–35 months) and 28 months for the standard chemotherapy group (95% CI: 22–33 months; HR: 0.9; 95% CI: 0.6–1.2; p=0.43).

Biron and colleagues reported the results of a Phase III, open, multicenter, prospective trial of women with metastatic breast cancer (and/or local or regional relapse beyond curative treatment by surgery or radiation). After a CR or at least 50% PR to induction therapy, 88 women were randomly assigned to HSCT and 91 to no further treatment. No OS difference was seen between the two groups, with three-year survival of 33.6% in the high-dose group and 27.3% in the observation group (p=0.8).

Zander and colleagues reported survival data after six years of follow-up on a trial that had previously been reported after 3.8 years of follow-up. Women with surgically resected breast cancer and axillary lymph node dissection with ten or more positive axillary lymph nodes but no evidence of metastatic disease were randomly assigned to standard chemotherapy (n=152) or HSCT (n=150). No difference in OS was observed; the estimated five-year OS rate in the standard arm was 62% (95% CI: 54-70%) and 64% (95% CI: 56-72%) in the high-dose transplant group.

Nieto and Shpall performed a meta-analysis of all randomized trials published or updated since 2006, focusing on those that compared HDC with standard-dose chemotherapy for high-risk primary breast cancer. The meta-analysis of 15 randomized trials involving patients with high-risk primary breast cancer or metastatic disease (n=6,102) detected an absolute 13% EFS benefit in favor of HDC and autologous HSCT (p=0.0001) at a median follow-up of six years. The absolute differences in disease-specific and OS did not reach statistical significance (7 % and 5%, respectively). Subset analyses suggested that HDC could be particularly effective in patients with triple negative tumors (hormone receptor and HER2-negative). The authors concluded that HDC remains a valid research strategy in certain subpopulations with high-risk primary breast cancer, for example those with triple negative tumors.

Berry and colleagues performed a meta-analysis with individual patient data from 15 randomized trials comparing autologous HSCT with HDC (n=3,118) to standard chemotherapy (n= 3,092) for patients with high-risk primary breast cancer. A survival analysis was adjusted for trial, age, number of positive lymph nodes, and hormone receptor status. HSCT was associated with a non-significant 6% reduction in risk of death (HR: 0.94; 95% CI: 0.87-1.02; p=0.13) and a significant reduction in the risk of recurrence (HR: 0.87; 95% CI: 0.81-0.93; p<0.001). Toxic death was higher in the HSCT group with 72 (6%) of 1,207 deaths in these trial arms compared to 17 (1.4%) of 1,261 deaths in the standard therapy arms. In a subgroup analysis, the authors investigated whether age, number of positive lymph nodes, tumor size, histology, hormone receptor status, or HER2 status impacted survival when comparing HSCT

versus standard treatment. The authors found that HER2-negative patients receiving HSCT had a 21% reduction in the risk of death and HER2-negative and hormone receptor negative patients receiving HSCT had a 33% reduction in the risk of death. In their discussion, the authors state that this relationship could be spurious due to the amount of missing data on HER2 status and suggest that HSCT is unlikely to show much benefit in these subgroups of patients.

A meta-analysis by Wang et al included aggregate data from 14 trials (n=5,747) published since March 2010. Clinical trials of patients receiving HSCT as a first-line treatment for primary breast cancer were eligible for inclusion. A higher treatment-related mortality was found among the patients who received HSCT compared to standard chemotherapy (RR=3.42, 95% CI: 1.32-8.86). Overall survival did not differ significantly between groups with a hazard ratio of 0.91 (95% CI: 0.82-1.00) for the HSCT compared to standard treatment. Risk of secondary, non-breast cancer was higher in the HSCT group (RR=1.28, 95% CI: 0.82-1.98). Disease free survival was better in the HSCT group compared to chemotherapy alone (RR=0.89, 95% CI: 0.79-0.99). Patients receiving HSCT had a greater risk of dying during remission than patients treated with nonmyeloablative chemotherapy due to the toxicity of the regimen. This increase in treatment-related mortality may help explain why there was no observed overall survival benefit for patients receiving HSCT when disease-free survival was observed to be superior to standard chemotherapy.

The Italian Group of Bone Marrow and Hematopoietic Stem-Cell Transplantation and Cellular Therapy (GITMO) published registry data on 415 patients with metastatic breast cancer who received high-dose chemotherapy and autologous HSCT between 1990 and 2005. More than 95% of the transplants performed used peripheral blood stem cells. Sixteen percent of patients received a tandem transplant. Estrogen-receptor (ER) status was known in 328 patients, 65% of whom were ER positive. Her-2 expression data were insufficient for subset analysis. After a median follow-up of 27 months (range 0-172 months), PFS at five and ten years was 23% and 14% and OS was 47% and 32%, respectively. The authors reported statistically significant survival benefit in patient subgroups including those with ER-positive tumors and those without visceral metastases; however, these are established positive prognostic factors compared with factors for patients with ER-negative tumors and visceral metastases, respectively. In addition, the authors did not report which patients received hormonal therapy, nor was it known if/which patients received targeted HER-2 therapy, and it is unclear what impact on survival therapies other than HSCT may have had.

In 2013, GITMO published registry data on the use of adjuvant HDC with autologous HSCT in 1183 patients with high-risk primary breast cancer (three or more involved lymph nodes), treated between 1990 and 2005. Data on ER and HER-2 status were available in 85% and 48% of patients, respectively. The majority of patients with hormone receptor-positive tumors received tamoxifen after HSCT. The median lymph node involvement at surgery was 15 (range 4-63). Greater than 95% of the patients received peripheral blood-mobilized stem cells. After a median follow-up of 7.1 years, disease free survival was 9.6 years, with 65% of patients free of disease at five years. Median OS was not reached, with 75% of patients alive at five years post-transplantation. Subgroup analysis showed significantly better OS in endocrine responsive tumors and in patients who received multiple transplant procedures. Transplant-related

mortality was 0.8% and late cardiac and secondary tumor-related mortality were approximately 1% overall.

Tandem Autologous Transplantation

Kroger and colleagues reported on the comparison of single versus tandem autologous HSCT in 187 patients with chemotherapy-sensitive metastatic breast cancer. Only 52 of 85 patients completed the second HDC cycle in the tandem arm, mostly due to withdrawal of consent (most common reason), adverse effects, progressive disease, or death. The rate of CR was 33% in the single-dose arm versus 37% in the tandem arm ($p=0.48$). Although there was a trend toward improved PFS after tandem HSCT, median OS tended to be greater after single versus tandem HDC (29 vs. 23.5 months, respectively; $p=0.4$). The authors concluded that tandem HSCT cannot be recommended for patients with chemotherapy-sensitive metastatic breast cancer because of a trend for shorter OS and higher toxicity compared with single HSCT.

Schmid and colleagues published results of 93 patients without prior chemotherapy for metastatic breast cancer who were randomly assigned to standard-dose chemotherapy or double HDC with autologous HSCT. The primary study objective was to compare CR rates. Objective response rates for the patients in the high-dose group were 66.7% versus 64.4% for the standard group ($p=0.82$). There were no significant differences between the two treatments in median TTP, duration of response, or OS (OS 26.9 months vs. 23.4 months for the double high-dose arm versus the standard arm, respectively; $p=0.60$).

Allogeneic SCT

To date, allogeneic HSCT for breast cancer has mostly been used in patients who have failed multiple lines of conventional chemotherapy.

Ueno and colleagues reported the results of allogeneic HSCT in 66 women with poor-risk metastatic breast cancer from 15 centers who underwent transplantation between 1992 and 2000. Thirty-nine (59%) received myeloablative and 27 (41%) reduced-intensity conditioning (RIC) regimens. A total of 17 (26%) patients had received a prior autologous HSCT. Median follow-up time for survivors was 40 months (range 3–64 months). Treatment-related mortality was lower in the RIC group (7% vs. 29% at 100 days; $p=0.03$). Progression-free survival at one year was 23% in the myeloablative group versus 8% in the RIC group ($p=0.09$). Overall survival rates after myeloablative conditioning versus the RIC group were 51% (95% CI: 36–67%) versus 26% (95% CI: 11–45%) [$p=0.04$] at one year, 25% (95% CI: 13–40%) versus 15% (95% CI: 3–34%; $p=0.33$) at two years, and 19% (95% CI: 8–33%) versus 7% (95% CI: <1–25%; $p=0.21$) at three years, respectively.

Fleskens and colleagues reported the results of a Phase II study of 15 patients with metastatic breast cancer treated with HLA-matched reduced-intensity allogeneic HSCT. Median patient age was 49.5 years (range: 39.7–60.8 years), and all patients had been extensively pretreated and had undergone at least one palliative chemotherapy regimen for metastatic disease. Treatment-related mortality was 2/15 (13%). One-year PFS was 20% and one- and two-year OS was 40% and 20%, respectively. The authors noted no objective tumor responses but concluded that the relatively long PFS suggests a graft-versus-tumor (GVT) effect.

Summary

Randomized trials of autologous hematopoietic stem cell transplantation (HSCT) versus standard dose chemotherapy for patients with high-risk non-metastatic or metastatic breast cancer have not shown a survival advantage with HSCT, with greater treatment-related mortality and toxicity. Therefore, autologous HSCT is considered not medically necessary for this indication.

Nonrandomized studies using reduced-intensity or myeloablative allogeneic HSCT for metastatic breast cancer have suggested a possible graft-versus-tumor effect, but remains investigational for this indication.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network guidelines (V2.2019) do not address the use of HSCT in the treatment of breast cancer.

U.S. Preventive Services Task Force Recommendations

Not applicable.

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Key Words:

Hematopoietic stem cell transplantation for breast cancer, stem cell transplant, breast cancer, HSCT, autologous SCT, allogeneic SCT

Approved by Governing Bodies:

Not applicable at this time.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

Current Coding:

CPT Codes:

38204	Management of recipient hematopoietic cell donor search and cell acquisition
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, autologous
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	; thawing of previously frozen harvest, with washing, per donor

38210	; specific cell depletion with harvest, T cell depletion
38211	; tumor cell depletion
38212	; red blood cell removal
38213	; platelet depletion
38214	; plasma (volume) depletion
38215	; cell concentration in plasma, mononuclear, or buffy coat layer
38220	Diagnostic bone marrow; aspiration(s)
38221	Diagnostic bone marrow; biopsy(ies)
38222	Diagnostic bone marrow; biopsy(ies) and aspiration(s) (Effective 01/01/2018)
38230	Bone marrow harvesting for transplantation; allogeneic
38232	; autologous (Effective 1/1/12)
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	; autologous transplantation
38242	Allogeneic lymphocyte infusions

HCPCS:

S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood derived stem-cell transplantation, allogeneic
S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of posttransplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic, and emergency services)

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Medical Policy Group, March 2013

Medical Policy Group, February 2014

Medical Policy Group, February 2015

Medical Policy Group, March 2015

Medical Policy Group, July 2016

Medical Policy Group, December 2017

Medical Policy Group, September 2019

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.