Name of Blue Advantage Policy:
Isolated Limb Perfusion/Infusion for Malignant Melanoma

Policy #: 185
Category: Surgery

Latest Review Date: July 2010
Policy Grade: Effective September 2012: 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:**

Isolated limb perfusion (ILP) is a method of drug delivery that is designed to deliver high local doses of chemotherapeutic agents to isolated anatomic regions while avoiding systemic toxicity. It has been investigated primarily as a treatment of malignant melanoma arising in the extremities. ILP involves the following steps: 1) mobilization and placement of venotomy and arteriotomy catheters into the major blood vessels (axillary, brachial, iliac, or popliteal artery and vein) proximal to the tumor; 2) isolation of the limb via a tourniquet; and 3) perfusion of a chemotherapeutic drug via an extracorporeal circulation system into the affected extremity. Perfusion lasts for approximately 60 minutes. Melphalan is the drug typically used, but more recently melphalan has been combined with the cytokine tumor necrosis factor alpha (TNF-alpha) and/or interferon gamma (IFN-gamma). Temperature is another factor that has been modified. Mild hyperthermia (39° to 40° C) may be used during ILP based on the theoretical rationale that heat may potentiate the tumor killing effect of melphalan. Hyperthermia is performed by warming the perfusate and by wrapping the treated extremity in a warming blanket.

ILP as a treatment for melanoma has been investigated as a treatment of melanoma in these general settings:

1. As adjuvant treatment of surgically treated primary malignant melanoma with no clinical evidence of disease.
2. As adjuvant treatment of surgically treated locally recurrent melanoma with no other evidence of disease.
3. As a therapeutic treatment for local recurrence of non-resectable melanoma (i.e., satellite lesions or “in transit” melanoma).

Similar to IHP is isolated limb infusion (ILI), introduced by Thompson and colleagues from the Sydney Melanoma Unit. Catheters are inserted percutaneously into the axial artery and vein of the affected limb and a pneumatic tourniquet is inflated proximally. Cytotoxic agents are then infused through the arterial catheter and circulated with a syringe for 15 to 20 minutes after which the limb is flushed with a liter of Hartman’s solution. Progressive hypoxia occurs, but normothermia is maintained. This procedure differs from ILP primarily by avoiding the use of an extracorporeal circulation system, making it less expensive, requiring fewer medical personnel, and reducing the total operating room time.

**Policy:**

**Effective for dates of service on or after July 1, 2005:**

Blue Advantage will treat isolated limb perfusion with melphalan as a covered benefit when used as a therapeutic treatment of local recurrence of non-resectable melanoma (i.e., satellite lesions or “in transit” melanoma).

Blue Advantage will treat isolated limb perfusion with melphalan as a non-covered benefit when used for the following indications:

- As an adjuvant treatment of surgically treated primary malignant melanoma with no clinical evidence of disease and is a non-covered benefit.

Proprietary Information of Blue Cross and Blue Shield of Alabama
Blue Advantage Medical Policy #185
• As an adjuvant treatment of surgically treated locally recurrent melanoma with no other evidence of disease and is considered investigational.
• In conjunction with tumor necrosis factor or interferon gamma for primary malignant melanoma, locally recurrent melanoma with no other evidence of disease, or local recurrence of non-resectable melanoma and is considered investigational.

Blue Advantage will treat isolated limb perfusion in conjunction with hyperthermia as a non-covered benefit and as investigational.

Blue Advantage will treat isolated limb infusion (ILI) with melphalan as a covered benefit for the therapeutic treatment of local recurrence of nonresectable melanoma (i.e., satellite lesions or “in transit” melanoma).

Blue Advantage will treat isolated limb infusion in the treatment of melanoma for all other indications 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:
Melanoma is a malignancy of pigment-producing cells (melanocytes) occurring in the skin, eyes, ears, GI tract, leptomeninges of the central nervous system (CNS), and oral and genital mucous membranes. Melanoma accounts for only 4% of all skin cancers; however, it causes the greatest number of skin cancer–related deaths worldwide.

In the United States, the incidence of melanoma has more than tripled in the white population during the last 40 years, and melanoma currently is the seventh most common cancer. Approximately 53,600 Americans will develop invasive cutaneous melanoma in 2002, with an additional estimated 30,000-50,000 cases of melanoma in situ. Currently, the lifetime risk for melanoma is 1 in 71 Americans. The lifetime risk is estimated to rise to 1 in 50 by 2010. Melanoma is responsible for 75% of skin cancer deaths in the United States. White males have the highest mortality rates from melanoma.

Isolated limb perfusion has been used in either the adjuvant or therapeutic setting for the treatment of melanoma. In the adjuvant setting in patients with complete resection of the primary lesion without evidence of metastatic disease, ILP has been the subject of numerous inconclusive case control trials using either matched or historical controls. Results of a large international randomized clinical trial of adjuvant ILP as an adjuvant treatment in patients with high-risk primary melanoma (>1.5 mm in thickness) have been published are summarized below.
Koops, et al (1998), reported on a Phase III international study of 832 patients from 16 centers to evaluate whether prophylactic ILP could prevent regional recurrence and influence survival. In this study, 412 patients were randomized to wide excision (WE) only and 420 patients were randomized to wide excision plus ILP with melphalan and mild hyperthermia. At median follow-up of 6.4 years, patients who had ILP plus wide excision had fewer in-transit (3.3% vs. 6.6%) and regional lymph node (12.6% vs. 16.7%) mets compared to those treated with WE alone. However, there was no benefit from ILP in terms of time to distant metastasis or survival. The authors concluded that ILP cannot be recommended as an adjunct to standard surgery in high-risk primary limb melanoma. The presence of negative data from a large randomized trial provides the rationale for considering this adjuvant role of ILP as not medically necessary.

Two randomized controlled trials have focused on the adjuvant use of ILP in patients with surgically resected satellite lesions or in transit disease. These are by Ghussen (1988) and Hafstrom (1991) and are summarized below.

Ghussen, et al (1988) reported on a randomized controlled trial of 107 patients with malignant melanoma of the extremities. In the control group A (n = 54), the tumors were excised and regional lymph nodes excised. In the perfusion group B (n = 53), patients had surgery plus hyperthermic perfusion with melphalan. At an average follow up of 550 days, group A had 21 recurrences and group B had 4 recurrences. At a follow up of 3 ½ years, group A had 26 recurrences and group B had 6 recurrences. Although this trial showed a significant improvement in overall survival with ILP, the results were so inconsistent with prior experience that researchers remain skeptical about the results of this study.

Hafstrom et al (1991), reported on a randomized control trial of 69 patients with recurrent melanoma of the extremities. One group had surgery (n = 36) and the other group had surgery plus regional perfusion (n = 33). The median tumor-free survival was 17 months in the perfusion group and 10 months in the control group. The perfusion group had 15 recurrences and the control group had 24. The median survival time was 57 months in the perfusion group and 35 months in the control group, not statistically significant. The authors recommended that regional hyperthermic perfusion after surgery of recurrent malignant melanoma should only be recommended in prospective and controlled trials.

The lack of definitive data in these two trials of either proving or disproving the role of ILP in this adjuvant setting provides the rationale for considering this role of ILP as investigational.

As pointed out in the 1992 TEC Assessment, there are no randomized controlled trials focusing on the therapeutic use of ILP as a treatment of locally recurrent melanoma that cannot be surgically resected. However, large case series have consistently reported impressive complete response rates compared to systemic chemotherapy. For example, as summarized by Balch, et al, complete response rates range from 40%-60% with an overall response rate of 80%. According to Balch, there are no randomized controlled trials because there is currently no alternative therapy that would provide a meaningful comparison to ILP with melphalan in this setting. Since there are few treatment options, ILP with melphalan is currently considered the
gold standard. Two of the studies that show good complete response rates are summarized below.

Storm et al (1985) reported on 26 patients with lower extremity advanced melanoma mets who underwent ILP. A complete response was noted in 21/26 patients (81%). In five patients, a response lasted a median of five months, but most patients died by 15 months.

Thompson, et al (1997), reviewed 114 cases of locally recurrent limb melanoma treated with ILP. Complete remission was seen in 81/111 (73%) and partial remission in 14/111 (13%). Recurrence occurred in 44/81 (54%) at a median time of 9.5 months. The authors noted that in 12 series previously reported in the literature, the initial complete remission rate was 50% and partial remission rate 32%.

Research has focused on the addition of cytokines and immunomodulating substances to perfusion schedules to improve tumor response rates. Specifically, the have been trials using ILP with melphalan and tumor necrosis factor-alpha (TNF-alpha) with or without interferon-gamma (IFN-gamma).

Fraker et al (1996) evaluated response rates of hyperthermic ILP with escalating doses of TNF in conjunction with melphalan and IFN. Twenty-six patients received 4 mg TNF and had a complete response rate of 76% with an overall response rate of 92%. Escalating the TNF dose to 6 mg did not increase the complete response rate.

Lienard et al (1999) reported on a Phase II trial of 64 patients who were randomized to receive either a two-drug regimen (TNF-alpha and melphalan) or a three-drug regimen (TNF-alpha, melphalan, and IFN-gamma). A total of 47 complete responses were reported. The overall response rate was 91% in the two-drug group and 100% in the three-drug group. This study did not include a control group, but the authors compared the treatment results with historical control data. In the historical control group, 103 patients received melphalan alone, with 54 complete responses (52%) and 80 complete or partial responses (78%). The median survival time was 819 days for the two drug group and > 705 days for the three drug group. The estimate for recurrence was 327 days for the two drug group, > 498 days for the three drug group, and 338 days for the control group. The authors concluded that ILP with TNF-alpha may be superior to ILP with melphalan alone. However, the lack of randomized trial data limits any conclusion as to whether perfusion with melphalan may be improved by adding TNF-alpha and IFN-gamma. Further studies are needed.

Bartlett et al (1997) reported that there is currently an ongoing study (since 1999) to see if there is a benefit to adding TNF-alpha to standard melphalan ILP. The ACOSOG Trial Z0020 is a randomized prospective multi-institutional study of melanoma patients randomly assigned to receive either standard ILP with hyperthermia and melphalan or standard ILP with hyperthermia, melphalan, and TNF-alpha. They will assess the overall, complete, and partial response rates to the two treatment arms. However, at the present time, TNF is not a U.S. Food and Drug Administration (FDA) approved drug, so the use of TNF in an ILP procedure is considered investigational.
Temperature is another factor that has been studied. Pitts and Malony (2000) discussed regional isolated perfusion to treat melanoma. They noted that early investigators used hyperthermia (41°-42° C), but found increased regional toxicity. So, studies were performed using mild hyperthermia (39°-40°C).

Klaase et al (1995) reported on 218 patients treated with mild hyperthermic perfusion compared to 166 patients perfused under normothermic conditions. The use of mild hyperthermia did not influence limb recurrence-free interval or survival. The authors concluded that there was no benefit from mild hyperthermia in ILP.

The National Comprehensive Cancer Network (NCCN) practice guidelines in Oncology, 2004, state that one standard option for patients with unresectable in-transit metastases is regional treatment with hyperthermic isolation limb perfusion with melphalan as a single agent.

The Blue Cross and Blue Shield Association reviewed isolated limb perfusion February 2004, and concluded the following: “There continues to be interest in using TNF in conjunction with melphalan as the infusate. However, final results of the randomized studies of TNF have not yet been published. In addition, TNF is not FDA approved for any indication. Noorda and colleagues examined the use of true hyperthermia ILP (in the range of 42 to 43 degrees Celsius) used sequentially with normothermic ILP with melphalan in 17 patients with grossly recurrent limb melanoma. With this approach, the maximum tolerable dosages can be applied with each treatment sequentially in attempts to avoid the toxicity that occurs with simultaneous use. The authors report complete remission in 11 (65%) patients with a five-year limb recurrence-free interval of 63%. While these results are promising in extensive disease, this approach requires two surgical procedures within a one- to two-week timeframe, doubling surgical risk. Also, larger studies are needed to determine whether sequential true hyperthermia ILP and ILP with melphalan is superior to ILP with melphalan alone.”

July 2007 Update
A literature search was performed and no information was located that would alter the coverage statement of this policy.

July 2010 Update
Isolated limb perfusion (ILP) and isolated limb infusion (ILI) have been used in the adjuvant and therapeutic settings.

Therapeutic treatment of local recurrence of nonresectable melanoma (i.e., satellite lesions or in transit melanoma)
No randomized, controlled trials are currently focusing on the therapeutic use of ILP as a treatment of locally recurrent melanoma that cannot be surgically resected. However, large case series have consistently reported impressive complete response rates, compared to systemic chemotherapy. For example, as summarized by Balch et al, complete response rates range from 40%-60%, with an overall response rate of 80%. According to the authors, no randomized, controlled trials are available, because currently no alternative therapy would provide a meaningful comparison to ILP with melphalan. In this population of patients with few treatment options, ILP with melphalan is currently considered the gold standard.
As with ILP, no data from randomized, controlled trials exist to assess the efficacy of ILI. Introduced by Thompson and colleagues, they first reported on case series of 82 patients treated with ILI for melanoma with six months of follow-up. Complete response (CR) was reported for 39% and partial response (PR) for 52% following a single ILI session; after two sessions CR was 45% and PR was 42%. Beasley and colleagues published papers on two data sets. The first, in 2008, was a database study of 120 regionally treated melanoma patients (over the time frame of 1995-2007); 58 patients received ILI and 54 patients were treated with ILP and variables were compared using Chi-square analysis. Response was defined at three months using the Response Evaluation Criteria in Solid Tumors (RECIST). Complete, partial, and no response was seen in 30%, 14%, and 56% or ILI recipients, respectively, versus 57%, 31%, and 12% (p<0.0001) of those getting ILP, respectively. ILP recipients did, however, have a greater number of Grade 3 or greater toxicities: 18% vs. 32%, respectively (p=0.037). The second study published in 2009 looked at response and toxicity associated with ILI only. Patient characteristics from 162 ILI procedures performed at eight institutions (over the time frame of 2001-2008) were compared with Chi-square and t-statistics. Complete, partial, and no response was seen in 31%, 33%, and 36% respectively. Thirty-six percent had Grade 3 or greater toxicity, with one toxicity-related amputation. The authors reporting the first multi-institutional analysis of ILI concluded that the procedure is a reasonable alternative to hyperthermic isolated limb perfusion in the management of advanced extremity melanoma.

Few centers in the United States have any sizable experience with ILI. The majority of procedures have been performed in Australia at the Sydney Melanoma Unit (SMU), where upward of 300 procedures have been performed. At SMU, they report a better overall response rate than has been reported by Beasley and colleagues (84% vs. 64%). ILI is a rare procedure with a learning curve for the technique, which can contribute to response variation. Many centers in the Beasley study had completed less than 10 ILI procedures. At SMU, response was measured at a medial time of 1.4 months, whereas in the United States, response is measured at three months, also potentially contributing to the difference in rates.

Due to the small numbers, inability to blind to treatment assignment, and potentially the lack of good comparators, there may never be a randomized control trial of either ILI or ILP. The body of evidence for these procedures could however be strengthened by prospectively designed studies with standardized response data, allowing for comparisons between trials and centers.

Of note, use of ILI in the treatment of melanoma is considered investigational (except for use of ILI in treatment of local recurrence of nonresectable melanoma) due to lack of sufficient data concerning outcomes.

**Adjuvant treatment of surgically treated locally recurrent melanoma with no other evidence of disease**

Two randomized, controlled trials have focused on the adjuvant use of ILP in patients with surgically resected recurrent satellite lesions or in transit disease. While one of these trials reported a highly significant improvement in overall survival, the results were inconsistent with prior experience with ILP and researchers remain skeptical about the results of this study. The other randomized study was a small single-institution study that did not report a statistically...
significant improvement in overall survival. The lack of definitive data either proving or disproving the role of ILP in this adjuvant setting provides the rationale for considering this role of ILP as investigational.

**Isolated limb perfusion using melphalan in conjunction with tumor necrosis factor, interferon gamma or hyperthermia**

Current research is focused on ways to enhance the results of ILP with melphalan such as the use of tumor necrosis factor (TNF) or interferon gamma along with melphalan. An initial European Phase II trial combining TNF with melphalan reported a complete response rate of 90% among 28 patients, with only two recurrences within 14 months. These results were considered so impressive that it was considered unethical to withhold TNF in any randomized trial. A subsequent randomized trial from the same group of investigators studied the use of ILP with TNF and melphalan (two-drug regimen) with and without additional interferon gamma (three-drug regimen) in 64 patients with in-transit metastases. No significant difference was noted between the two groups in terms of complete or overall response rate. Continued interest in the use of TNF in conjunction with melphalan as the infusate prompted a series of studies. In 2008, the results of a randomized, multicenter trial were published in which patients with locally advanced extremity melanoma received melphalan-based hyperthermic ILP treatment with randomization as to whether they received TNF alpha as well. The intervention was completed in 124 of 133 enrolled patients, and 116 of the patients had data available at three months. The primary clinical endpoint of the study was tumor response, assessed at three months. Secondary objectives included evaluation of treatment toxicity, local recurrence-free survival, regional disease symptoms, and overall survival. A response to treatment at three months was seen in 64% of patients in the melphalan-alone group versus 69% in the melphalan plus TNF-alpha group (p=0.435), with a complete response in 25% of the melphalan alone and 26% of the melphalan plus TNF-alpha patients (p=0.890). The authors concluded that the addition of TNF alpha to melphalan in the treatment of locally advanced extremity melanoma with hyperthermic ILP did not demonstrate a significant difference in short-term response rates. In addition, the TNF-alpha plus melphalan regimen was associated with a higher complication rate.

Mild hyperthermia is often used in conjunction with ILP, as in the cited clinical trial. However, no published controlled trials compare the outcomes of ILP with and without hyperthermia. Retrospective analyses of case series suggest that no significant improvement occurs when hyperthermia is added to the ILP regimen. Noorda and colleagues examined the use of true hyperthermia ILP (in the range of 42 to 43 degrees Celsius) used sequentially with normothermic ILP with melphalan in 17 patients with grossly recurrent limb melanoma. With this approach, the maximum tolerable dosages can be applied with each treatment sequentially in attempts to avoid the toxicity that occurs with simultaneous use. The authors report complete remission in 11 patients (65%) with a five-year limb recurrence-free interval of 63%. While these results are promising in extensive disease, this approach requires two surgical procedures within a one- to two-week timeframe, doubling surgical risk. Also, larger studies are needed to determine whether sequential true hyperthermia ILP and ILP with melphalan is superior to ILP with melphalan alone. In a study of 20 patients with in-transit melanoma metastases treated with hyperthermia ILP with melphalan and low-dose TNF alpha, Rossi et al reported disease-free survival in six patients while seven patients experienced local and/or distant disease.
recurrence and seven patients died of disease progression at 18-month follow-up. The authors found this approach to have acceptable local toxicity and outcomes comparable to treatment with more toxic levels of cytokines. However, this study does not address questions of hyperthermia versus normothermia ILP nor does it address ILP with melphalan with or without TNF alpha. Noorda and colleagues concluded ILP with melphalan (with or without TNF alpha and interferon gamma) is appropriate for local recurrence of unresectable melanoma. However, ILP with melphalan could not be recommended as an adjuvant treatment for primary or locally recurrent melanoma. The conclusions of this meta-analysis are consistent with the policy statements here.

Data also suggest that ILP using TNF is an effective palliative treatment for patients with bulky melanomas causing pain, decreased mobility, or skin breakdown. However, at the present time, TNF is not a drug approved by the U.S. Food and Drug Administration (FDA) for any indication, and thus, on this basis, the use of TNF in an ILP procedure is considered investigational. Similarly, the additional benefit of interferon gamma as part of the ILP drug regimen has not been validated and is considered investigational.

**Adjuvant treatment of surgically treated primary malignant melanoma with no clinical evidence of disease**

In the adjuvant setting in patients with complete resection of the primary lesion without evidence of metastatic disease, ILP has been the subject of numerous inconclusive case control trials using either matched or historical controls. Results of a large international randomized clinical trial of adjuvant ILP as an adjuvant treatment in patients with high-risk primary melanoma (i.e., >1.5 mm in thickness) have been published. While the incidence of local recurrence decreased in the treatment group, the overall survival was unchanged. The presence of negative data from a large randomized trial provides the rationale for considering this adjuvant role of ILP as not medically necessary.

**Current Clinical Trials and Guidelines**

A search of the National Cancer Institute’s Physician Data Query database returned no active phase III trials involving isolated limb perfusion and melanoma, as of November 2009.

The National Cancer Comprehensive Cancer Network (NCCN) guidelines for unresectable in-transit melanoma or in-transit recurrence include hyperthermic limb perfusion or infusion with melphalan; these are category 2-B recommendation (meaning the recommendation is based on “lower level evidence’ and nonuniform NCCN consensus” without major disagreement).

**Physician Specialty Society and Academic Medical Center Input**

In response to requests by the Blue Cross Blue Shield Association, responses were received from two academic medical centers while this policy was being reviewed. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement of position statement by the physician specialty societies or academic medical centers, unless otherwise noted. One academic center declined comment, indicating they do not perform this procedure because it is so specialized but instead refer potential candidates (one to two patients per year) to specific center. The reviewer from the second center agreed with the policy conclusions. Citing Cornett et al, the reviewer commented
that no data from trials address whether hyperthermia contributes to the effect of ILP with melphalan.

**Key Words:**
Isolated limb perfusion, ILP, melphalan, malignant melanoma, tumor necrosis factor, interferon gamma, hyperthermia, isolated limb infusion, ILI

**Approved by Governing Bodies:**
TNF is not FDA approved for any indication
Melphalan is FDA approved

**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

**Coding:**
CPT codes: 36823
Insertion of arterial and venous cannula(s) for isolated extracorporeal circulation and regional chemotherapy perfusion to an extremity, with or without hyperthermia, with removal of cannula(s) and repair of arteriotomy and venotomy sites

HCPCS: Q0083-Q0085 Chemotherapy administration code range (hospital use only)

**References:**
6. Cornett WR, McCall LM, Petersen RP, et al. Randomized multicenter trial of hyperthermic isolated limb perfusion with melphalan alone compared with melphalan plus tumor necrosis


Policy History:
Adopted for Blue Advantage, March 2005
Available for comment May 1-June 14, 2005
Medical Policy Group, July 2007
Medical Policy Group, July 2010
Available for comment June 18-August 2, 2010
Medical Policy Group, September 2010: Active but no longer scheduled for regular literature reviews and updates
Medical Policy Group, October 2013

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.