

Corporate Medical Policy

Radioembolization for Primary and Metastatic Tumors of the Liver

File Name: radioembolization_for_primary_and_metastatic_tumors_of_the_liver
Origination: 5/2004
Last CAP Review: 5/2019
Next CAP Review: 5/2020
Last Review: 5/2019

Description of Procedure or Service

Hepatic tumors can arise either as primary liver cancer or by metastasis to the liver from other organs. Local therapy by surgical resection with tumor-free margins or liver transplantation are the only potentially curative treatments. Unfortunately, most hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, number of lesions, concurrent nonmalignant liver disease, or insufficient hepatic reserve. The use of external beam radiotherapy and the application of more advanced radiotherapy approaches (e.g., IMRT) may be limited in patients with diffuse, multiple lesions, due to the low tolerance of normal liver to radiation compared to the higher doses of radiation needed to kill tumor.

Various nonsurgical ablative techniques have been investigated that seek to cure or palliate unresectable hepatic tumors by improving locoregional control. These techniques rely on extreme temperature changes, particle and wave physics (microwave or laser ablation), or arterial embolization therapy including chemoembolization, bland embolization or radioembolization.

Radioembolization (RE), referred to as selective internal radiation therapy or SIRT in older literature, is the intra-arterial delivery of small beads (microspheres) impregnated with yttrium-90 (90Y) via the hepatic artery. The microspheres, which become permanently embedded, are delivered to tumor preferentially to normal liver, as the hepatic circulation is uniquely organized, whereby tumors greater than 0.5 cm rely on the hepatic artery for blood supply while normal liver is primarily perfused via the portal vein. 90Y is a pure beta-emitter with a relatively limited effective range and short half-life that helps focus the radiation and minimize its spread. Candidates for RE are initially examined by hepatic angiogram to identify and map the hepatic arterial system, and at that time, a mixture of albumin particles are delivered via the hepatic artery to simulate microspheres. After, single photon emission CT gamma imaging is used to detect possible shunting of the albumin particles into gastrointestinal or pulmonary vasculature.

Currently two commercial forms of 90Y microspheres are available: a glass sphere, TheraSphere® (manufactured by Nordion, Inc., Ontario, Canada, used under license by BTG International) and a resin sphere, SIR-Spheres® (Sirtex Medical Limited; Lake Forest, IL). Non-commercial forms are used mostly outside the United States. While the commercial products use the same radioisotope (90Y yttrium-90) and have the same target dose (100 Gy), they differ in microsphere size profile, base material (i.e., resin vs. glass), and size of commercially available doses. These physical characteristics of the active and inactive ingredients affect the flow of microspheres during injection, their retention at the tumor site, spread outside the therapeutic target region, and dosimetry calculations. Note also that the U.S. Food and Drug Administration (FDA) granted premarket approval of SIR-Spheres® for use in combination with 5-fluorouridine (5-FUDR) chemotherapy by hepatic arterial infusion (HAI) to treat unresectable hepatic metastases from colorectal cancer. In contrast, TheraSphere® was approved by humanitarian device exemption (HDE) for use as monotherapy to treat unresectable HCC. In January 2007, this HDE was expanded to include patients with hepatocellular carcinoma who have partial or

Radioembolization for Primary and Metastatic Tumors of the Liver

branch portal vein thrombosis. For these reasons, results obtained with one product do not necessarily apply to other commercial (or non-commercial) products.

Unresectable primary hepatocellular carcinoma (HCC)

The majority of patients with HCC present with unresectable disease, and treatment options are limited secondary to the chemoresistance of HCC and the intolerance of normal liver parenchyma to tumoricidal radiation doses. Results of 2 randomized controlled trials have shown a survival benefit using transarterial chemoembolization (TACE) therapy versus supportive care in patients with unresectable HCC. In one study, patients were randomly assigned to TACE, transarterial embolization (TAE), or supportive care. One-year survival rates for TACE, TAE, and supportive care were 82%, 75%, and 63%, respectively and 2-year survival rates were 63%, 50%, and 27%, respectively. A recent multicenter, randomized, double-blind placebo controlled Phase III trial that enrolled 602 patients with advanced HCC randomly assigned patients to receive sorafenib versus placebo.

Unresectable intrahepatic cholangiocarcinoma

Cholangiocarcinomas are tumors that arise from the epithelium of the bile duct and are separated into intrahepatic and extrahepatic types. Intrahepatic cholangiocarcinomas appear in the hepatic parenchyma and are also known as peripheral cholangiocarcinomas. Resection is the only treatment with the potential for cure and 5 year survival rates have been in the range of 20% to 43%.⁽⁴⁾ Patients with unresectable disease may select among fluoropyrimidine-based or gemcitabine-based chemotherapy, fluoropyrimidine chemoradiation or best supportive care.

Unresectable metastatic colorectal carcinoma

Fifty to sixty percent of patients with colorectal cancer will develop metastases, either synchronously or metachronously. Select patients with liver-only metastases that are surgically resectable can be cured, with some reports showing 5-year survival rates exceeding 50%. Emphasis on treating these patients with potentially curable disease is on complete removal of all tumor with negative surgical margins. The majority of patients diagnosed with metastatic colorectal disease are initially classified as having unresectable disease. In patients with metastatic disease limited to the liver, preoperative chemotherapy is sometimes used in an attempt to downsize the metastases in order to convert the metastatic lesions to a resectable status (conversion chemotherapy).

In patients with unresectable disease that cannot be converted to resectable disease, the primary treatment goal is palliative, with survival benefit shown with both second and third-line systemic chemotherapy. Recent advances in chemotherapy, including oxaliplatin, irinotecan and targeted antibodies like cetuximab, have doubled the median survival in this population from less than 1 year to more than 2 years. Palliative chemotherapy by combined systemic and HAI may increase disease-free intervals for patients with unresectable hepatic metastases from colorectal cancer.

Radiofrequency ablation (RFA) has been shown to be inferior to resection in local recurrence rates and 5-year overall survival and is generally reserved for patients with potentially resectable disease that cannot be completely resected due to patient comorbidities, location of metastases (i.e., adjacent to a major vessel), or an estimate of inadequate liver reserve following resection. RFA is generally recommended to be used with the goal of complete resection with curative intent. The role of local (liver-directed) therapy (including radioembolization, chemoembolization, and conformal radiation therapy) in debulking unresectable metastatic disease remains controversial.

Unresectable metastatic neuroendocrine tumors

Neuroendocrine tumors are an uncommon, heterogeneous group of mostly slow-growing, hormone-secreting malignancies, with an average patient age of 60 years. Primary neuroendocrine tumors vary in location, but most are either carcinoids (which most commonly arise in the midgut) or pancreatic islet cells. Carcinoid tumors, particularly if they metastasize to the liver, can result in excessive vasoactive amine secretion including serotonin and are commonly associated with the carcinoid syndrome (diarrhea, flush, bronchoconstriction, and right valvular heart failure).

Although they are considered to be indolent tumors, at the time of diagnosis, up to 75% of patients have liver metastases, and with metastases to the liver, 5-year survival rates are less than 20%. Surgical resection of the metastases is considered the only curative option; however, less than 10% of patients are eligible for resection, as most patients have diffuse, multiple lesions.

Radioembolization for Primary and Metastatic Tumors of the Liver

Conventional therapy is largely considered to be palliative supportive care, to control, eradicate, or debulk hepatic metastases, often to palliate carcinoid syndrome or local pain from liver capsular stretching. Therapies for unresectable metastatic neuroendocrine tumors include medical (somatostatin analogs like octreotide), systemic chemotherapy, ablation (radiofrequency or cryotherapy), transcatheter arterial embolization (TAE) or chemoembolization (TACE), or radiation. Although patients often achieve symptom relief with octreotide, the disease eventually becomes refractory, with a median duration of symptom relief of approximately 13 months, with no known effect on survival. Systemic chemotherapy for these tumors has shown modest response rates of limited duration, is better for pancreatic neuroendocrine tumors compared to carcinoids, and is frequently associated with significant toxicity. Chemoembolization has shown response rates of nearly 80%, but the effect is of short duration and a survival benefit has not been demonstrated.

Miscellaneous metastatic tumors

Small case reports have been published on the use of RE in many other types of cancer with hepatic metastases, including breast, melanoma, head, and neck (including parotid gland), pancreaticobiliary, anal, thymic, thyroid, endometrial, lung, kidney, gastric, small bowel, esophageal, ovarian, cervical, prostatic, bladder, and for melanoma, sarcoma, and lymphoma

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for radioembolization for primary and metastatic tumors of the liver when determined to be medically necessary because the medical criteria and guidelines shown below are met.

Some patients may be eligible for coverage under Clinical Trials. Refer to the policy on Clinical Trial Services.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Radioembolization for Primary and Metastatic Tumors of the Liver is covered

Radioembolization may be considered medically necessary for the following:

- to treat primary hepatocellular carcinoma that is unresectable and limited to the liver. (See Policy Guidelines)
- in primary hepatocellular carcinoma as a bridge to liver transplantation.
- to treat hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and symptomatic disease when systemic therapy has failed to control symptoms.
- to treat unresectable hepatic metastases from colorectal carcinoma, melanoma (ocular or cutaneous), or breast cancer that are both progressive and diffuse, in patients with liver-dominant disease who are refractory to chemotherapy or are not candidates for chemotherapy or other systemic therapies.
- to treat primary intrahepatic cholangiocarcinoma in patients with unresectable tumors.

Radioembolization for Primary and Metastatic Tumors of the Liver

When Radioembolization for Primary and Metastatic Tumors of the Liver is not covered

Radioembolization is considered investigational for all other hepatic metastases, except as noted above.

Radioembolization is considered investigational for all other indications not described above.

BCBSNC does not provide coverage for investigational services or procedures.

Policy Guidelines

In general, radioembolization (RE) is used for unresectable hepatocellular carcinoma (HCC) that is >3cm.

RE should be reserved for patients with adequate functional status (Eastern Cooperative Oncology Group [ECOG] 0-2), adequate liver function-and reserve, Child Pugh score A or B, and liver-dominant metastases.

Symptomatic disease from metastatic neuroendocrine tumors refers to symptoms related to excess hormone production.

For the use of RE in the treatment of hepatocellular carcinoma (HCC), the evidence consists primarily of retrospective and prospective observational studies, with limited evidence from randomized controlled trials (RCTs). Observational studies suggest that RE has high response rates compared with historical controls. Two small pilot RCTs have compared RE with alternative therapies for HCC, including transarterial chemoembolization (TACE) and TACE with drug-eluting beads, both of which demonstrated similar outcomes for RE. Evidence from observational studies demonstrates that RE can allow successful liver transplantation in certain patients. The available evidence, including clinical input, is sufficient to draw conclusions and to determine that outcomes are improved for the use of RE for the treatment of primary HCC that is unresectable and limited to the liver or as a bridge to liver transplantation.

For the use of RE in the treatment of hepatic metastases from neuroendocrine tumors, the evidence consists of 1 open-label phase 2 study, retrospective reviews, and case series, some of which compare RE with other transarterial liver-directed therapies. This evidence suggests that RE has similar outcomes to standard therapies and historical controls for patients with neuroendocrine tumor-related symptoms or progression of liver tumor burden. There was support from clinical input for the use of RE for the treatment of hepatic metastases from neuroendocrine tumors. Therefore, the available evidence is sufficient to determine that RE is associated with improved outcomes for the treatment of hepatic metastases from neuroendocrine tumors.

A major cause of morbidity and mortality in patients with colorectal disease metastatic to the liver is liver failure, as this disease tends to progress to diffuse, liver-dominant involvement. For the use of RE in the treatment of unresectable metastases from colorectal carcinoma (CRC), the evidence consists of several small- to moderate-sized RCTs, prospective trials, and retrospective studies using a variety of comparators, along with systematic reviews of these studies. Although this evidence describes wide ranges of clinical response to therapy, there was strong support from clinical input for the use of RE for the treatment of hepatic metastases from CRC; the use of RE to decrease tumor bulk, and/or halt the time to tumor progression and liver failure, may lead to prolonged progression-free and overall survival (OS) in patients with no other treatment options (ie, those with chemotherapy refractory liver-dominant disease). Other uses include palliation of symptoms from tumor bulk. Therefore, the available evidence is sufficient to determine that RE is associated with improved outcomes for the treatment of CRC liver metastases with liver dominant disease.

Radioembolization for Primary and Metastatic Tumors of the Liver

For the use of RE for the treatment of intrahepatic cholangiocarcinoma, the evidence consists of retrospective and prospective observational studies, some of which compare RE with alternative therapies. Although no randomized trials are available, there is some suggestion that RE for primary intrahepatic cholangiocarcinoma has response rates similar to those seen with standard chemotherapy. RE may play a role patients with unresectable tumors that are chemorefractory or unable to tolerate systemic chemotherapy. Clinical input in 2015 supported the use of RE for intrahepatic cholangiocarcinoma. Given the low likelihood of large-scale clinical trials for this rare tumor, the available evidence is sufficient to conclude that RE is associated with improved outcomes for patients with primary intrahepatic cholangiocarcinoma.

Similarly, for other tumors metastatic to the liver, including breast cancer and melanoma, the evidence consists of observational studies. In 2015, clinical input supported the use of RE for the treatment of liver-dominant metastases from breast cancer and melanoma in patients who are not candidates for or who have not responded to systemic therapies. Given the clinical input, the available evidence is sufficient to conclude that RE is associated with improved outcomes for patients with hepatic metastases from breast cancer and melanoma with liver-dominant disease.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 37243, 75894, 77778, 79445, S2095

Diagnoses: 153.0, 153.1, 155.0, 155.1, 155.2, 197.7, 573.8, 573.9

ICD-10 diagnosis codes: C18.3, C18.4, C22.0, C22.1, C22.2, C22.3, C22.4, C22.7, C22.8, C22.9, C78.7, K76.1, K76.5, K76.89, K76.9

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 10/9/2003.

Specialty Matched Consultant Advisory Panel - 5/2004

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 12/15/2005.

Specialty Matched Consultant Advisory Panel - 3/2006

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 4/17/07

Specialty Matched Consultant Advisory Panel - 3/2008

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 7/9/09

National Cancer Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. V.2.2009. Hepatobiliary Cancers. Accessed 8/27/09 at http://www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf.

Senior Medical Director Review - 9/2009

Specialty Matched Consultant Advisory Panel - 5/2010

Radioembolization for Primary and Metastatic Tumors of the Liver

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 8/12/10
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 3/10/11
Specialty Matched Consultant Advisory Panel- 5/2011
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 3/8/12
Specialty Matched Consultant Advisory Panel- 5/2012
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 3/14/13
Specialty Matched Consultant Advisory Panel 5/2013
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 3/13/14
Specialty Matched Consultant Advisory Panel 6/2014
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 3/12/15
Specialty Matched Consultant Advisory Panel 5/2015
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 6/11/15
Specialty Matched Consultant Advisory Panel 5/2016
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 7/14/16
Specialty Matched Consultant Advisory Panel 5/2017
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 7/13/17
Specialty Matched Consultant Advisory Panel 5/2018
Medical Director review 5/2018
BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.43, 7/12/18
Specialty Matched Consultant Advisory Panel 5/2019

Policy Implementation/Update Information

For policy named: Selective Internal Radiation Therapy for Tumors of the Liver

- 6/10/04 New policy originated. Specialty Matched Consultant Advisory Panel review. Selective Internal Radiation Therapy for Tumors of the Liver is considered investigational. References added. Notification date 6/10/2004. Effective date 8/12/2004.
- 1/20/05 Added brachytherapy and policy number to Key Words section.
- 4/07/05 New HCPCS codes Q9955, Q9956, Q9957 added to Billing/Coding section of policy.
- 8/4/05 Removed HCPCS codes Q9955, Q9956, Q9957 from Billing/Coding section as they do not apply to this policy.
- 12/15/05 Added 79445 to "Billing/Coding" section.
- 4/10/06 Specialty Matched Consultant Advisory Panel review 3/15/06. Referenced medical policy, "Clinical Trial Services for Life-Threatening Conditions, MED1093" in the "Description" section. Added the following statement to the "Policy" section; "Some patients may be eligible for coverage under Clinical Trials. Refer to the policy on Clinical Trial Services for Life-Threatening Conditions." Rationale added to the "Policy Guidelines" section. References added.

Radioembolization for Primary and Metastatic Tumors of the Liver

- 5/19/08 Specialty Matched Consultant Advisory Panel review 3/2008. Revised "Policy" section as follows: "BCBSNC will provide coverage for Selective Internal Radiation Therapy to treat unresectable hepatocellular carcinoma." **and** "BCBSNC will not provide coverage for Selective Internal Radiation Therapy to treat metastatic liver tumors because it is considered investigational. BCBSNC does not cover investigational services." Under "When Covered" section, added "Selective internal radiation therapy may be considered medically necessary for treatment of unresectable hepatocellular carcinoma." Under "When not covered" section, revised statement to read "BCBSNC will not provide coverage for selective internal radiation therapy for metastatic liver tumors because it is considered investigational. BCBSNC does not cover investigational services." Policy Guidelines revised to indicate that SIRT is considered investigational for the treatment of metastatic tumors of the liver. References added. (pmo)
- 9/28/09 Reviewed with Senior Medical Director 9/1/09. "Description" section revised. "Policy" statement changed to indicate "BCBSNC will not provide coverage for selective internal radiation therapy using intra-arterial injection of radiolabeled microspheres to treat primary or metastatic liver tumors because it is considered investigational." Removed coverage statement in the "When Covered" section that stated; "Selective internal radiation therapy may be considered medically necessary for treatment of unresectable hepatocellular carcinoma." and replaced with "Not applicable." Under the "When Not Covered" section revised non coverage statement to indicate; "BCBSNC will not provide coverage for selective internal radiation therapy using intra-arterial injection of radiolabeled microspheres to treat primary or metastatic tumors of the liver because it is considered investigational." Updated rationale in the "Policy Guidelines" section. Added CPT codes "75894 and 77778" to "Billing/Coding" section. References added. Notice given 9/28/09. Policy effective 1/5/2010. (btw)
- 6/22/10 Specialty Matched Consultant Advisory Panel review 5/24/10. Medical Policy number removed. Applicable diagnoses added to "Billing/Coding" section. (lr)

For Policy Renamed: Radioembolization for Primary and Metastatic Tumors of the Liver

- 11/9/10 Description section extensively revised. Policy statement changed to indicate that selective cases of hepatocellular carcinoma and metastatic neuroendocrine tumors may be considered medically necessary. Under "When Covered" section: added Radioembolization may be considered medically necessary for the following: to treat primary hepatocellular carcinoma that is unresectable and limited to the liver, in primary hepatocellular carcinoma as a bridge to liver transplantation, to treat hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and symptomatic disease when systemic therapy has failed to control symptoms. Under "When Not Covered" section added Radioembolization is considered investigational to treat unresectable hepatic metastases from colorectal carcinoma and Radioembolization is considered investigational for all other hepatic metastases except for metastatic neuroendocrine tumors as noted above. Policy name changed from Selective Internal Radiation Therapy for Tumors of the Liver to Radioembolization for Primary and Metastatic Tumors of the Liver for consistency with BCBSA policy. References added. Reviewed with medical director. (lpr)
- 6/7/11 "Description" section revised. Under "When Covered" section added medical necessity statement: "to treat unresectable hepatic metastases from colorectal carcinoma that are both progressive and diffuse, in patients with liver-dominant disease who are refractory to chemotherapy or are not candidates for chemotherapy." Specialty Matched Consultant Advisory Panel review 5/2011. References added. (lpr)
- 11/22/11 Removed the x from the ICD-9 codes 153.0, 153.1, 155.0, 155.1, 155.2, 197.7, 573.8, 573.9 in the Billing/Coding section since there are no 5th digits for these codes. (lpr)
- 5/29/12 Specialty Matched Consultant Advisory Panel review 5/16/2012. No change to policy statement. Reference added. (lpr)

Radioembolization for Primary and Metastatic Tumors of the Liver

- 4/30/13 Policy Guidelines and Description sections revised. Under When Not Covered section added investigational indication “Radioembolization is considered investigational to treat primary intrahepatic cholangiocarcinoma.” Reference added. Medical director review 3/2013. Notification given 4/30/13 for effective date 7/30/13. (lpr)
- 7/1/13 ICD-10 diagnosis codes added to “Billing/Coding” section. Policy remains on notification for effective date July 30, 2013. (lpr)
- 8/13/13 Policy effective 7/30/13. Web link was corrected. (lpr)
- 12/31/13 Added CPT code 37210 to the Billing/Coding section for 2014 code update and deleted CPT 37204. (lpr)
- 7/29/14 Removed ICD-10 effective date 10/1/2014 from Billing/Coding section. Specialty matched consultant advisory panel review meeting 6/24/2014. No change to policy statement. Reference added. (lpr)
- 3/10/15 Deleted CPT code 37210 from Billing/Coding section and added CPT code 37243. (lpr)
- 7/28/15 Specialty Matched Consultant Advisory Panel review 5/27/2015. Reference added. Updated Description and Policy Guideline sections. Medically necessary statements added for unresectable metastatic breast cancer and melanoma with liver dominant disease and unresectable intrahepatic cholangiocarcinoma. Under “When Covered” section added bullet #4 and bullet #5: to treat unresectable hepatic metastases from colorectal carcinoma, melanoma (ocular or cutaneous), or breast cancer that are both progressive and diffuse, in patients with liver-dominant disease who are refractory to chemotherapy or are not candidates for chemotherapy or other systemic therapies and to treat primary intrahepatic cholangiocarcinoma in patients with unresectable tumors. Under “When Not Covered” section, deleted the statement “Radioembolization is considered investigational to treat primary intrahepatic cholangiocarcinoma”; and added the statements “Radioembolization is considered investigational for all other indications not described above” and “Radioembolization is considered investigational for all other hepatic metastases, except as noted above. Senior medical director review 6/2015. (lpr)
- 7/1/16 Specialty Matched Consultant Advisory Panel review 5/25/2016. No change to policy statement. (lpr)
- 10/25/16 Reference added. No change to policy statement. (lpr)
- 6/30/17 Specialty Matched Consultant Advisory Panel review 5/31/2017. No change to policy statement. (lpr)
- 8/25/17 Reference added. No change to policy statement. (lpr)
- 6/8/18 Specialty Matched Consultant Advisory Panel review 5/2018. No changes to policy statements. Medical Director review 5/2018. (mco)
- 5/28/19 Specialty Matched Consultant Advisory Panel review 5/15/2019. No change to policy intent. Reference added. (lpr)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.