RADIOEMBOLIZATION FOR PRIMARY AND METASTATIC TUMORS OF THE LIVER

- SIR-Spheres®
- TheraSphere®

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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RADIOEMBOLIZATION FOR PRIMARY AND METASTATIC TUMORS OF THE LIVER (cont.)

Description:

Radioembolization (RE) is also known as selective internal radiation therapy (SIRT). Small beads, called microspheres, embedded with Yttrium-90 (90Y) are delivered to the liver tumor by a catheter threaded through the femoral artery and into the hepatic artery.

The spheres become trapped in the tumor where they burn away the tumor from the inside. Currently, two commercial forms of 90Y microspheres are available: SIR-Spheres and TheraSphere. SIR-Spheres is used for the treatment of unresectable metastatic liver tumors from primary colorectal cancer. TheraSphere is used for radiation treatment or as a neoadjuvant to surgery or transplantation in individuals with unresectable hepatocellular carcinoma (HCC). TheraSphere treatments may be administered 1-2 times. SIR-Spheres is a single treatment for the whole liver or two separate lobar treatments.

Criteria:

All requests for treatment of hepatocellular carcinoma with radioembolization will be reviewed by the medical director(s) and/or clinical advisor(s).

- Radioembolization for the treatment of unresectable liver metastases due to colorectal carcinoma, melanoma (ocular or cutaneous), or breast cancer is considered medically necessary with documentation of ANY of the following:
  1. Disease is progressive and diffuse
  2. Liver-dominant disease refractory to chemotherapy
  3. Not a candidate for chemotherapy or other systemic therapy

- Radioembolization for the treatment of unresectable primary hepatocellular carcinoma that is limited to the liver is considered medically necessary.

- Radioembolization in primary hepatocellular carcinoma as a bridge to transplantation is considered medically necessary.

- Radioembolization for the treatment of primary intrahepatic cholangiocarcinoma in individuals with unresectable tumors is considered medically necessary.
RADIOEMBOLIZATION FOR PRIMARY AND METASTATIC TUMORS OF THE LIVER (cont.)

Criteria: (cont.)

- Radioembolization for the treatment of metastatic liver tumor(s) is considered medically necessary with documentation of All of the following:
  1. Liver metastasis is from ONE of the following neuroendocrine tumors:
     - Adrenal
     - Carcinoid (usually from the small intestine)
     - Pancreas (neuroendocrine tumors only)
     - Pituitary
     - Thyroid
  2. Disease is diffuse and symptomatic
  3. Systemic therapy has failed to control symptoms
  4. Child Pugh Classification (CPC) of liver dysfunction score is A or B (see CPC below)
  5. Eastern Cooperative Oncology Group (ECOG) Performance Status scale grade is no greater than 2 (see scale below)

- Radioembolization for all other indications not previously listed or if above criteria not met is considered experimental or investigational based upon:
  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

These indications include, but are not limited to:

- Resectable primary or metastatic hepatocellular carcinoma
- Liver metastasis for all other indications not previously listed
RADIOEMBOLIZATION FOR PRIMARY AND METASTATIC TUMORS OF THE LIVER (cont.)

Criteria: (cont.)

Child-Pugh Classification (CPC) of Liver Dysfunction:

CPC score is calculated from the sum of the points for each CPC criteria:

<table>
<thead>
<tr>
<th>CPC Classification</th>
<th>Level of Dysfunction</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Mild</td>
<td>5-6</td>
</tr>
<tr>
<td>B</td>
<td>Moderate</td>
<td>7-9</td>
</tr>
<tr>
<td>C</td>
<td>Severe</td>
<td>≥10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CPC Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy grade (see table below)</td>
<td>1</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
</tr>
<tr>
<td>Serum bilirubin, mg/dL</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Serum albumin, g/dL</td>
<td>&gt;3.5</td>
</tr>
<tr>
<td>Prothrombin time, sec prolonged</td>
<td>&lt;4</td>
</tr>
</tbody>
</table>

Encephalopathy Grade (EEG Required for Gr. 2, 3, 4)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal consciousness, personality, neurological exam</td>
</tr>
<tr>
<td>1</td>
<td>Restless, sleep disturbed, irritable/agitated, tremor, impaired handwriting</td>
</tr>
<tr>
<td>2</td>
<td>Lethargic, time-disoriented, inappropriate, asterixis, ataxia, slow triphasic waves on EEG</td>
</tr>
<tr>
<td>3</td>
<td>Somnolent, stuporous, place-disoriented, hyperactive reflexes, rigidity, slower waves on EEG</td>
</tr>
<tr>
<td>4</td>
<td>Unrousable coma, no personality/behavior, decerebrate, slow 2-3 cps delta activity on EEG</td>
</tr>
</tbody>
</table>

CPC should be calculated at baseline and prior to each treatment cycle.

Source: National Cancer Institute, Child Pugh Search, NCI Protocol #, "Specific Instructions for the Use of Organ Dysfunction Templates", Appendix A, accessed 01/15/08
RADIOEMBOLIZATION FOR PRIMARY AND METASTATIC TUMORS OF THE LIVER (cont.)

Criteria: (cont.)

Eastern Cooperative Oncology Group (ECOG) Performance Status¹:

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>

¹ As published in Am. J. Clin. Oncol.:


Source: Eastern Cooperative Oncology Group, Robert Comis M.D., Group Chair, accessed 01/15/08

Resources:

Literature reviewed through 08/15/17. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

Resources prior to 04/30/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ’s Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ’s Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kweé atah nílínígíí Blue Cross Blue Shield of Arizona haada yíł’éego bina’idilígíí doodago Háida bijá aniyeedígíí t’áadoo le’é yína’idilígíí beehaz’áannii hóó díí t’áá hazaad’ehí háká a’doowolgo bee ha’á doo baqáh ilínígóó. Ata’ halné’ítíí koj’ bich’é’ hodilíihíí 877-475-4799.

Chinese: 如果您，或是您正在协助的对象，有关于插入项目的名称 Blue Cross Blue Shield of Arizona 方面的问题，您有权免费以您的母语得到帮助和讯息。洽询一位翻译员，彼接电话。在此插入数字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو أدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والعلومات الضرورية بلغتك من دون أي تكلفة. للتحدث مع متجم كتصل ب 877-475-4799.
RADIOEMBOLIZATION FOR PRIMARY AND METASTATIC TUMORS OF THE LIVER (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang ilang tinutuuan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makaasap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역시와 매니지하기 위해서는 877-475-4799로 전화하십시오.

French: Si vous, ou quelqu’un que vous êtes en train d’aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d’obtenir de l’aide et l’information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi: 
اگر شما یا کسی که شما به او کمک می‌کنید، سوال در مورد اطلاعاتی که زبان خود را به طور رایگان دریافت نمایید 877-475-4799.

Assyrian: 
Blue Cross Blue Shield of Arizona, نین مادی و ضریب و خیره‌تاشین 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: ถ้าคุณหรือคนที่คุณช่วยเหลือมีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสามารถได้รับคำแนะนำและการช่วยเหลือโดยไม่เสียค่าใช้จ่าย โทร 877-475-4799