Clinical Policy Title: Brachytherapy of coronary arteries

Clinical Policy Number: 04.02.04

Effective Date: January 1, 2016
Initial Review Date: September 16, 2015
Most Recent Review Date: October 19, 2016
Next Review Date: October 2017

Policy contains:
- Brachytherapy of coronary arteries.
- Percutaneous coronary intervention.
- Saphenous vein grafts.

Related policies:

CP# 05.02.02 Brachytherapy for localized prostate cancer
CP# 05.02.07 Brachytherapy for cancers other than prostate

ABOUT THIS POLICY: AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania’s clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas Pennsylvania considers the use of brachytherapy for coronary arteries intervention to be clinically proven and, therefore, medically necessary when the following criteria are met:

- When used as an adjunct to percutaneous coronary intervention (PCI) for treatment of in-stent restenosis in a native coronary artery bare-metal stent (BMS).
- To treat in-stent restenosis in grafted coronary vessels — that is, saphenous vein grafts (SVGs).

Limitations:

All other uses of brachytherapy for coronary arteries intervention are not medically necessary, including the use of drug-eluting stents (DES), because they are considered experimental, investigational, or unproven, including, but not limited to:
Managing initial lesions or treating restenosis in native or grafted coronary vessels without stents.
As an alternative to stent placement to reduce the risk of or treat restenosis of native vessels or SVG at an unstented site of a prior PCI.
Treating in-stent restenosis in SVG grafts using radioactive sources, excluding those that emit gamma radiation.

Alternative covered services:

Repeat PCI without brachytherapy surgery.

Background

Intracoronary brachytherapy involves inserting a special catheter to radiate a local area in an artery. The procedure is needed to reduce recurrence of arterial obstruction or narrowing after stent placement (restenosis) during most angioplasty procedures. Restenosis occurs in 10 percent and 27 percent of patients with balloon angioplasty (van Werkum 2009). The radiation used in brachytherapy inhibits the growth of certain cells that cause restenosis.

Several drug-eluting stents (DES) have been developed to minimize the incidence of restenosis, and represent approximately 70–90 percent of stent implantations. The choice of stent (bare metal versus drug-eluting) depends on various factors, including lesion location and morphology, patient characteristics, and the patient’s ability to adhere to the extended period of dual antiplatelet therapy, required for DES.

There are two devices approved by the FDA for in-stent restenosis. The Checkmate System™ (Cordis Corporation) employs gamma radiation, and the Beta-Cath System™ (Novosite Corporation) employs beta radiation. Both are used for previously implanted stents.

In-stent restenosis continues to be a significant problem with bare metal stents (BMS), and is thought to be caused by neointimal hyperplasia within the stent. Several mechanical treatments of in-stent restenosis were attempted, including balloon re-dilation, removal of in-stent hyperplasia by atherectomy, and repeated bare metal stenting. Brachytherapy was introduced as a method to treat in-stent restenosis by the delivery of gamma or beta radiotherapy via a catheter-based system. Brachytherapy affects the proliferation of smooth muscle cells that are responsible for restenosis, and may be used to treat in-stent restenosis of native coronary arteries and SVGs. The role of brachytherapy has diminished, however, and DES has emerged as the preferred method of treatment for in-stent restenosis. Nonetheless, brachytherapy may still play a role in the treatment of selected members.

Searches

AmeriHealth Caritas Pennsylvania searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on September 16, 2016. Search terms were: “brachytherapy, cardiac disease, DES, percutaneous transluminal coronary angioplasty, in-stent restenosis.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

A guideline update published by the American College of Cardiology (ACC), American Heart Association (AHA), and the Society for Cardiovascular Angiography and Interventions (SCAI) (Smith 2006), states that vascular brachytherapy is a successful treatment for restenosis occurring within stents, while other adjunctive therapies, such as the cutting balloon, rotary ablation, excimer laser, and re-stenting show mixed results.

The ACC/AHA/SCAI guideline states that brachytherapy is a safe and effective treatment for in-stent restenosis (Class IIa recommendation). A Class IIa recommendation indicates that there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment, but that the weight of evidence is in favor of usefulness/efficacy. No changes to this recommendation occurred in focused updates to the PCI guideline, published in 2007 (King 2008) and 2009 (Kushner 2009).

The 2011 and 2015 American College of Cardiology Foundation (ACCF)/AHA/SCAI PCI guidelines (Levine 2011 and 2016), do not include recommendations for brachytherapy. The guidelines reference studies demonstrating the superiority of DES over brachytherapy.

Guidelines on Myocardial Revascularization developed by The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), state that intracoronary brachytherapy is currently of very limited use (Kolh 2014): restenosis rates have declined and in-stent restenosis after BMS are treated by DES or coronary artery bypass graft (CABG).
The recent introduction of DES contributes a major breakthrough to interventional cardiology. Many large randomized clinical trials (RCTs) using DES show a remarkable reduction in angiographic restenosis and target vessel revascularization, when compared with BMS. The results of these trials appear to be supported by evidence from everyday practice and non-controlled clinical trials. However, the expanded applications of DES, especially in treating complex lesions such as left main trunk, bifurcation, SVG, or in-stent restenosis, are still under evaluation with ongoing studies. With the availability of different types of DES in the market, the issue of cost should not be a deterrent and DES will eventually be an economically viable option for all members. The adoption of DES in all PCI may become a reality in the near future.

Prior to the widespread use of DES, in-stent restenosis following PCI was a significant clinical problem, frequently resulting in the need for repeat revascularization procedures. Intracoronary brachytherapy was shown to be an effective treatment for in-stent restenosis of native coronary arteries or SVG.

In recent years, brachytherapy procedures have decreased in frequency and DES emerged as the treatment of choice, in the majority of cases. However, brachytherapy may still play a role in the treatment of in-stent restenosis in selected members. A recent article citing 186 patients concluded that intravascular brachytherapy is a safe treatment for recurrent DES in-stent restenosis, with a low recurrence rate at 12 months (Negi 2016).

A recent meta-analysis comparing DES with vascular brachytherapy covered a 2 – 5 year followup of five studies with 1,375 patients. There was no difference between the two groups for myocardial infarction, stent thrombosis, cardiovascular mortality, and overall mortality. However, target lesion and target vessel revascularization rates were elevated in the brachytherapy group (Benjo 2016). Another recent meta analysis of 31 studies found that brachytherapy had similar target vessel revascularization rates to balloon angioplasty, cutting balloon, excimer laser, and rotational atherectomy, but had higher rates than paclitaxel-eluting cutting balloon, everolimus-eluting stent, and paclitaxel-eluting balloon in patients with at least two restenosis treatments (Sethi 2015). A third meta-analysis of percent diameter stenosis found brachytherapy to be higher than some treatments and lower than others (Siontis 2015).

There is insufficient evidence in the published medical literature to demonstrate the safety and efficacy of brachytherapy for expanded indications, including treatment for new stenosis of native coronary arteries and SVGs, restenosis of native coronary arteries and SVGs at the unstented site of a previous PCI, or as primary prevention of restenosis after stent implantation for de novo lesions. The use of brachytherapy for treatment of restenosis in a DES also remains investigational, as medical efficacy has not yet been demonstrated.

SVGs are commonly used conduits for surgical revascularization of coronary arteries; however, they are associated with poor long-term patency rates. Percutaneous revascularization of SVGs is associated with worse clinical outcomes, including higher rates of in-stent restenosis, target vessel revascularization, myocardial infarction, and death compared with PCI of native coronary arteries. Use of embolic protection devices is a Class I indication according to the ACC/AHA guidelines to decrease the risk of distal embolization, no-reflow and periprocedural myocardial infarction. Nonetheless, these devices are underused in clinical practice.
Policy updates:

An additional six practice guidelines and six peer-reviewed references were added to this policy. Most are recent publications (2015 or 2016).

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tbody>
<tr>
<td>Benjo (2016)</td>
<td><strong>Key points:</strong></td>
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</tbody>
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| Long term outcomes of vascular brachytherapy vs. DES | - Meta-analysis of five studies (n=1375), 2 – 5 years after brachytherapy or DES.  
- No differences between two groups in myocardial infarction, stent thrombosis, cardiovascular mortality, and overall mortality.  
- Brachytherapy group had significantly higher target lesion and target vessel revascularization. |
| Sethi (2015) | **Key points:** |
| Comparison of re-stenosis interventions — target vessel revascularization rates | - Meta analysis of 31 studies (8157 patient years), patients with at least two treatments for in-stent restenosis.  
- Brachytherapy has similar rate to balloon angioplasty, cutting balloon, excimer laser, rotational atherectomy.  
- Brachytherapy has higher rates than paclitaxel-eluting balloon, paclitaxel-eluting stent, and sirolius-eluting stent. |
| Siontis (2015) | **Key points:** |
| Comparison of re-stenosis interventions – percent diameter stenosis at angiographic follow-up | - Meta-analysis of 27 studies, n=5923, followup 6 – 60 months.  
- Most effective treatment was everolimus-eluting stents; brachytherapy 19.2% less.  
- Brachytherapy not as effective as drugcoated balloons (-9.0%), sirolimus eluging stents (-9.4%), paclitaxel-eluting stents (-10.2%).  
- Brachytherapy more effective than bare metal stents (-24.2%) and rotablation (-31.8%). |
| Alli, et al. (2012) | **Key points:** |
| Five year follow up of Sirolimus-Eluting Coronary Stent Trial | - No differences in safety/efficacy for treatment of BMS restenosis with SES vs. VBT.  
- No differences in survival free from TLR, TVR or major adverse cardiac events between groups. |
| C. Holmes, et al. (2008) | **Key points:** |
| Randomized trial to evaluate safety and efficacy of sirolimus-eluting stents (SES) and vascular brachytherapy (VBT) | - SES =259, VBT=125, 3-5 year follow-up.  
- SES (vs. TLR or TVR) had superior survival at three years.  
- SES and TVR had greater freedom from TLR than did brachytherapy.  
- No differences in target vessel failure and major adverse cardiac events.  
- No differences in definite or probable stent thrombosis.  
- No differences in safety or efficacy of BMS restenosis with SES vs. VBT (five years).  
- No differences in survival free from TLR, TVR or major adverse cardiac events. |
| Oliver, et al. (2008) | **Key points:** |
Outcomes of brachytherapy and DES for in-stent restenosis

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<th>Content, Methods, Recommendations</th>
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|          | • Meta analysis of 14 studies/3103 patients.  
|          | • Neither treatment had any effect on mortality or rate of myocardial infarction.  
|          | • At intermediate follow-up, brachytherapy reduced the rate of revascularization, binary restenosis, and late loss vs. balloon angioplasty and selective bare metal stents alone. |

**Glossary**

**Brachytherapy of coronary arteries** — Treatment for coronary in-stent restenosis, in which a catheter is placed inside blood vessels and sources are inserted and removed. Also known as interstitial radiation, intracavitary radiation, or internal radiation therapy.

Coronary artery bypass graft – See saphenous vein graft.

**Coronary restenosis** — Recurrent narrowing or constriction of a coronary artery following surgical procedures, performed to alleviate a prior obstruction.

**Drug-eluting stent (DES)** — A peripheral or coronary stent (a scaffold) placed into narrowed, diseased peripheral or coronary arteries that slowly releases a drug to block cell proliferation. This prevents fibrosis that, together with clots (thrombi), could otherwise block the stented artery, a process called restenosis.

**Percutaneous coronary intervention (PCI)** — A non-surgical procedure used to treat the stenotic (narrowed) coronary arteries of the heart found in coronary heart disease; also known as coronary angioplasty or simply angioplasty, during which a balloon is inserted into the artery to open arteries.

**Restenosis** — Pertains to an artery or other large blood vessel that has become narrowed, received treatment to clear the blockage and subsequently become renarrowed.

Saphenous vein graft – a procedure that involves using the saphenous veins from the leg and grafting them to (blocked) coronary arteries; also known as coronary artery bypass graft)

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


**Clinical trials:**

Searched clinicaltrials.gov on September 19, 2016 using terms brachytherapy and cardiac. | Open Studies. Four studies found, none relevant.

**CMS National Coverage Determinations (NCDs):**

No NCDs identified as of the writing of this policy.

**Local Coverage Determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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