



CIGNA MEDICAL COVERAGE POLICY

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**Subject Brachytherapy Following
Femoropopliteal Percutaneous
Transluminal Angioplasty
(PTA)**

**Effective Date 6/15/2011
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Coverage Policy Number 0373**

Table of Contents

Coverage Policy	1
General Background	1
Coding/Billing Information	3
References	4
Policy History.....	6

Hyperlink to Related Coverage Policies

[Brachytherapy of the Coronary Arteries](#)

INSTRUCTIONS FOR USE

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Coverage Policy

CIGNA does not cover brachytherapy as an adjunct to femoropopliteal percutaneous transluminal angioplasty (PTA) because it is considered experimental, investigational or unproven.

General Background

Peripheral arterial disease (PAD), caused by atherosclerotic occlusion of leg arteries, is a sign of systemic atherosclerosis and is a major cause of morbidity and limb loss. Patients with peripheral arterial disease, even those with no history of myocardial infarction (MI) or ischemic stroke have the same relative risk of death from cardiovascular causes as patients who do have a history of MI or ischemic stroke. Most PAD of the lower extremities is caused by blockage in the femoropopliteal system. It is likely that the vessel size, flow velocity, the presence of vessel branch points and vessel wall morphology contribute to the prevalence of blockages in the femoropopliteal system. The major risk factors for PAD are persons over age 40, smoking, and diabetes. Additional risk factors include hyperlipidemia, hypertension, and high homocysteine levels. Approximately a third of patients with PAD have intermittent claudication, defined as pain in one or both legs (usually in the calf) when walking that does not diminish with further walking and is relieved by rest. More than half of the patients with PAD do not have intermittent claudication but have other types of leg pain on exertion that limit ambulation.

Medical treatment options used to modify risk factors and reduce the progression of PAD include smoking cessation, exercise programs that include walking, lipid lowering agents (statins) and antiplatelet therapy. Drugs

such as cilostazol (Pletal[®]) are commonly used to treat the symptoms of PAD and may increase functional status. When conservative treatment is not successful, revascularization of stenotic peripheral vessels may be considered. Bypass grafting using autologous saphenous veins is usually effective in restoring blood flow to ischemic areas. Femoropopliteal bypass is an open surgical procedure, however, with a lengthy recovery period. Percutaneous transluminal angioplasty (PTA) is a less invasive alternative and generally results in lower morbidity and a shorter recovery period. PTA of the femoropopliteal system, however, is associated with high rates of restenosis within six months of the procedure. The incidence of restenosis varies between 20–70%, depending on the length, degree and morphology of the lesions, the patency of runoff vessels, and length of time post-stenting. Because of the significant risk of late restenosis, PTA has generally been limited to patients with a partial stenosis that is discrete and short in length.

Intimal hyperplasia caused by proliferation of smooth muscle cells and matrix formation is a key factor in the development of restenosis. Negative remodeling may also occur, causing constriction of the vessel. Catheter-based endovascular irradiation (brachytherapy) has been investigated as an adjunctive procedure to prevent restenosis following femoropopliteal PTA. Coronary artery brachytherapy has been successfully used as an adjunct to percutaneous coronary intervention (PCI) to treat in-stent restenosis in native coronary arteries or saphenous vein grafts.

U.S. Food and Drug Administration (FDA)

Three brachytherapy devices have received Premarket Approval (PMA) from the U.S. Food and Drug Administration (FDA) for use in coronary arteries. The Novoste[™] Beta-Cath[™] System (Novoste Corp.) and the GALILEO[™] Intravascular Radiotherapy System (Guidant Corp.) deliver beta radiation, while the Cordis Checkmate[™] System delivers gamma radiation. There are no brachytherapy devices approved specifically for use in peripheral arteries.

Literature Review

Wolfram et al. reported five-year results from the Vienna 2 trial (2006), a prospective randomized controlled trial to evaluate the efficacy of adjunctive endovascular brachytherapy compared to no further treatment following revascularization in patients with long-segment femoropopliteal lesions (n=102). Following PTA, patients were assigned to receive endovascular brachytherapy (n=51) using an iridium 192 source or no further treatment (n=51). After six months, the restenosis rate for the 102 patients who completed five-year follow-up was significantly reduced for the PTA plus brachytherapy group compared to the PTA-alone group. During follow-up, the researchers noted a “catch-up phenomenon”, and at five years, the recurrence rate was comparable in both groups. The authors concluded that PTA followed by gamma radiation brachytherapy with a dose of 12 Gy resulted in a delay, but not an inhibition of restenosis, compared to PTA alone.

The Vienna 3 trial (Pokrajac, et al., 2005), a prospective multicenter, double-blind controlled trial, randomized 134 patients following PTA to receive brachytherapy (n=67) or sham irradiation (n=67). There were 38 patients excluded from as-treated analysis because of residual stenosis after PTA, complete lack of follow-up data, or early recurrence within one month. These patients were considered as treatment failures. Based on an intention to treat analysis, the cumulative patency rates after 24 months were 54% in the brachytherapy group and 27% in the placebo group. The corresponding as-treated analysis showed patency rates of 77% in the brachytherapy group and 39% in the placebo group. Target lesion revascularization was required in 14 patients in the placebo group and five in the brachytherapy group. The authors concluded that endovascular brachytherapy can lower restenosis rates after femoropopliteal PTA in high-risk patients, and that use of a centering device and escalated dose further reduces restenosis. This study is limited by small numbers and a relatively large number of patients lost to follow-up. In addition, angiographic follow-up was obtained in only 81% of patients.

The Vienna-5 trial (Wolfram, et al., 2005), a double-blind randomized controlled trial, evaluated the effectiveness of endovascular brachytherapy in the prevention of restenosis after femoropopliteal stent implantation in high-risk patients (n=88). Patients underwent PTA and stent implantation for femoropopliteal lesions and were randomized to gamma brachytherapy with an iridium 192 source or treatment with nonradioactive seeds. Revascularization and brachytherapy were accomplished successfully in all patients. The overall six-month recurrence rate was 35% in patients who underwent only stent implantation and 33% in patients who underwent both stent implantation and brachytherapy. Nine patients developed early reocclusion in the segment treated with a stent (two patients in the stent group and seven in the stent plus brachytherapy group). Of these patients, three in the stent plus brachytherapy group experienced reocclusion within 24 hours of the procedure. Late occlusion (i.e., > 30 days after the procedure) occurred in three patients in the stent plus brachytherapy group.

The authors concluded that brachytherapy does not improve six-month patency after femoropopliteal stent implantation in high-risk patients because of a high rate of early and late thrombotic occlusion.

Diehm et al. (2005) conducted a randomized controlled trial to determine if the short-term efficacy of adjunctive endovascular brachytherapy is maintained over time in patients undergoing balloon angioplasty of femoropopliteal atherosclerotic lesions. Patients were randomized to balloon angioplasty with adjunctive endovascular brachytherapy (n=72) or to balloon angioplasty alone (n=75). Mean clinical follow-up was 32.3 ± 21.5 months. Cumulative clinical success rates at one, two and three years, respectively, were 84.3%, 82.1%, and 76.4% in the balloon angioplasty group compared to 82.4%, 69.8%, 67.5% in the balloon angioplasty plus brachytherapy group. Angiographic follow-up was available for 42 patients in the angioplasty group and 41 in the angioplasty plus brachytherapy group. The freedom from angiographic restenosis at one, two and three years was 70.7%, 63.1%, and 47.1% after balloon angioplasty compared to 82.7%, 64.3%, and 64.3% in the balloon angioplasty plus brachytherapy group. No difference was found in outcomes in patients with de novo versus recurrent femoropopliteal lesions. The authors concluded that the seemingly beneficial short-term effects of brachytherapy are not sustained in the longer term.

Krueger et al. published a follow-up study in 2004, evaluating 24-month outcomes of a randomized single-blinded controlled trial (n=30) to determine whether endovascular brachytherapy immediately following PTA of de novo femoropopliteal stenoses lowers the stenosis rate. At 24 months, the rate of target lesion re-treatment, including interventional and surgical procedures for revascularization, was similar between the two groups. It was unclear whether the new stenoses in the irradiation group were "candy-wrapper" or edge stenoses or were due to atherosclerotic progression. The candy-wrapper or edge effect has been seen with coronary artery brachytherapy, but develops earlier in the coronary arteries. The authors concluded that, although endovascular irradiation results in significantly reduced degrees of stenosis, the benefit is more significant immediately following PTA and is reduced at the 24-month follow-up.

Professional Societies/Organizations

The American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Management of Patients with Peripheral Arterial Disease 2006 update states that investigational randomized trials suggest that endovascular brachytherapy may reduce restenosis rates of PTA and stenting in the femoral-popliteal arteries. The ACC/AHA Guideline, however, does not include brachytherapy in recommendations for the treatment of PAD in the lower extremity.

Summary

Although brachytherapy has been successfully used as an adjunct to percutaneous coronary intervention (PCI) to treat in-stent restenosis in coronary arteries, similar success has not been achieved in treating femoropopliteal arteries. This is thought to be due in part to the greater anatomic variability in length, diameter and curvature seen in systemic arteries as compared to coronary arteries. Clinical studies published to date have demonstrated that adjunctive use of brachytherapy can provide short-term inhibition of restenosis in selected patients for whom PTA is clinically indicated. It is not clear, however, whether brachytherapy prevents restenosis or simply delays it, or whether brachytherapy is linked to subsequent thrombotic occlusion. In addition, the long-term effects of intravascular radiation are unknown. There are currently no U.S. Food and Drug Administration (FDA)-approved devices for brachytherapy of the femoropopliteal system. The safety and efficacy of this procedure have not been established in the published medical literature.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Experimental/Investigational/Unproven/Not Covered when used to report brachytherapy following femoropopliteal percutaneous transluminal angioplasty (PTA):

CPT* Codes	Description
77326	Brachytherapy isodose plan; simple (calculation made from single plane, one to four sources/ribbon application, remote afterloading brachytherapy, 1 to 8 sources)

77327	Brachytherapy isodose plan; intermediate (multiplane dosage calculations, application involving 5 to 10 sources/ribbons, remote afterloading brachytherapy, 9 to 12 sources)
77328	Brachytherapy isodose plan; complex (multiplane isodose plan, volume implant calculations, over 10 sources/ribbons used, special spatial reconstruction, remote afterloading brachytherapy, over 12 sources)
77785	Remote afterloading high dose rate radionuclide brachytherapy 1 channel
77786	Remote afterloading high dose rate radionuclide brachytherapy; 2-12 channels
77787	Remote afterloading high dose rate radionuclide brachytherapy; over 12 channels
93799†	Unlisted cardiovascular service or procedure

†**Note: Experimental/Investigational/Unproven/Not Covered when used to report transcatheter placement of radiation delivery device for subsequent peripheral artery brachytherapy.**

ICD-9-CM Diagnosis Codes	Description
440.20	Atherosclerosis of native arteries of the extremities, unspecified
440.21	Atherosclerosis of native arteries of the extremities, with intermittent claudication
440.22	Atherosclerosis of native arteries of the extremities, with rest pain
440.23	Atherosclerosis of native arteries of the extremities, with ulceration
440.24	Atherosclerosis of native arteries of the extremities, with gangrene
440.29	Atherosclerosis of native arteries of the extremities, other
440.4	Chronic total occlusion of artery of the extremities
440.9	Generalized and unspecified atherosclerosis
443.9	Peripheral vascular disease, unspecified
444.22	Embolism and thrombosis of arteries of lower extremities
444.81	Arterial embolism and thrombosis of other specified artery; iliac artery
444.81	Arterial embolism and thrombosis of other specified artery; other
447.1	Stricture of artery

*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	06/15/2008	0373	Brachytherapy Following Femoropopliteal Percutaneous Transluminal Angioplasty (PTA)

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