Microwave Thermotherapy for Breast Cancer

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INSTRUCTIONS FOR USE: Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PLAN PRODUCT AND BENEFIT APPLICATION

☒ **Commercial** ☐ **Medicaid/OHP*** ☐ **Medicare****

*Medicaid/OHP Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

PHP follows Guideline Notes 172 and 173 of the OHP Prioritized List of Health Services for guidance on New and Emerging Technology. In the absence of OHP guidance, PHP will follow this policy.

**Medicare Members

This *Company* policy may be applied to Medicare Plan members only when directed by a separate *Medicare* policy. Note that investigational services are considered **"not medically necessary"** for Medicare members.

COVERAGE CRITERIA

I. Microwave thermotherapy for the treatment of breast cancer is considered **not medically necessary.**

Link to Evidence Summary

POLICY CROSS REFERENCES

None

The full Company portfolio of current Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

BACKGROUND

Microwave Thermotherapy

Microwave thermotherapy is a form of electromagnetic radiation that can be used to destroy tumor tissue through the application of heat. Microwave thermotherapy may also be referred to as microwave ablation, microwave coagulation or percutaneous microwave ablation/coagulation. This technique has been proposed as a minimally invasive technique to treat several tumors including hepatic tumors, various gynecological cancers and breast cancer. Tumors in the breast are thought to be potential candidates for microwave thermotherapy due to higher water content of the tumor relative to the surrounding fatty tissue, allowing for preferential heating of the tumor and minimal damage to healthy tissue.

Adaptive Phased Array Microwave Technology

A novel microwave thermotherapy technology known as "Adaptive Phased Array" (APA), currently marketed by Medifocus Inc. (previously by Celsion) as the APA 1000, is intended to destroy breast tumors. According to Medifocus, "this technology permits properly designed microwave devices to focus and concentrate energy targeted at diseased tissue areas deep within the body and to heat them selectively, without adverse impact on surrounding healthy tissue."[1] The APA 1000 breast cancer treatment system is intended to destroy localized breast tumors through the application of heat alone or in combination with chemotherapy.

According to Medifocus, to use the focused microwave technology, "a minimally invasive disposable catheter sensor is inserted into the breast under ultrasound guidance to provide feedback signals for microwave focusing and temperature measurement. The breast is then immobilized by compression, which also serves to reduce blood-flow and increase the efficiency of heat delivery for effective treatment, and microwave energy is applied to the breast via two parallel-opposed microwave applicators. A proprietary feedback, tracking, and control mechanism ensures that the microwave energy is focused on the center of the tumor, while a computer algorithm controls the amount of energy applied to the tumor, and monitors the temperature to ensure optimum effectiveness."[1]

The first indication of use of the APA 1000 focused microwave thermotherapy breast cancer treatment system is to treat locally advanced breast cancer (LABC), which involves tumors that are generally treated first with chemotherapy prior to surgical resection. According to Medifocus, the APA technology, "can significantly improve the efficacy of neo-adjuvant chemotherapy in shrinking large breast cancer tumors [3-8cm diameter], improving the chance of breast conservation, and decreasing the need for radical breast surgery."[1]

Medifocus intends to expand the indication of use for its APA breast cancer treatment system to include the treatment for medium size breast tumors (1-3 cm), ductal carcinoma in situ (DCIS) and benign breast tumors.

Locally Advanced Breast Cancer (LABC)

The current standard of care treatment for LABC is to use preoperative systemic therapy (chemotherapy and/or endocrine therapy, and in some cases radiation therapy) to induce tumor shrinkage to allow for inoperable tumors to become operable or for breast conservation surgery if the preoperative therapy results in clear surgical margins.[2] Microwave thermotherapy has the potential to be considered as a preoperative treatment option for LABC, to be used as an adjunct to current preoperative therapies or

on its own. In addition, microwave thermotherapy has been proposed as a potential stand-alone treatment to avoid breast surgery.

REGULATORY STATUS

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Approval or clearance by the Food and Drug Administration (FDA) does not in itself establish medical necessity or serve as a basis for coverage. Therefore, this section is provided for informational purposes only.

CLINICAL EVIDENCE AND LITERATURE REVIEW

EVIDENCE REVIEW

To determine the safety and efficacy of microwave thermotherapy as a treatment for locally advanced breast cancer (LABC), or other breast tumors, ideally studies comparing microwave thermotherapy to standard treatments in the form of randomized controlled trials are required. A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of microwave thermotherapy for breast cancer. Below is a summary of the available evidence identified through January 2025.

Systematic Reviews

- In 2010, Zhao and Wu published the results of a systematic review of minimally invasive thermal ablation techniques for early-stage breast cancer, including microwave ablation.[3] The reviewers stated that all three studies included were nonrandomized feasibility studies that were published by the same group of investigators and were conducted in research settings for the assessment of technical safety and feasibility.[4-6] The key studies from this group are described below. The reviewers reported that complete tumor ablation could be achieved in 0-8% of patients using microwave ablation. They concluded that large, randomized control studies were required to assess the long-term advantages of minimally-invasive thermal ablation techniques such as microwave thermotherapy compared to the current breast conserving therapies.

- In 2016, Peek et al. published the results of a systematic review of minimally invasive techniques in the treatment of breast cancer, including six studies (N=144 patients) on microwave ablation.[7] Although ultrasound guidance was reported in three studies, in the remaining three included studies the imaging modality was not known. In adjusted analyses microwave ablation achieved the second highest rate of complete ablation (83.2 ± 11.6%, 89 /107 patients), behind radiofrequency ablation (87.1%, 491/564 patients). No local recurrences were reported with microwave ablation, (0/144). However, microwave ablation resulted in the most complications (14.6%, 21/144). Limitations of the included studies for MWA included lack of blinding in RCTs, lack of follow up and no information on withdrawal rate. The reviewers concluded that while

minimally invasive techniques are promising, that adequately powered and prospectively conducted cohort trials are required.

- In 2017, Mauri et al. published the results of a systematic review that assessed the technical success, technique efficacy and complications of five minimally-invasive imaging-guided percutaneous ablation procedures of breast cancer, including microwave ablation.[8] Three studies (n= 78 lesions) (7%) were included in the review which addressed microwave ablation.[6,9,10] The pooled technical success of microwave ablation was reported as 93% (range 81-98%). Pooled technique efficacy was not reported for microwave ablation, since only one of the three studies had reported this outcome, which was 90%. The rate of major complications for microwave ablation was lower than other minimally invasive techniques (4%, 95% CI 1–17%), compared to 10% for high-intensity focused ultrasound and 6% for radiofrequency ablation. The reviewers concluded that although imaging-guided ablation techniques for breast cancer have a high rate of technical success and a low complication rate, efficacy remains suboptimal.

Randomized Controlled Trials (RCTs)

- In 2007, Vargas et al. published the results of a small, prospective, multicenter, un-blinded, RCT that investigated whether focused microwave thermotherapy in combination with neoadjuvant anthracycline-based chemotherapy (thermochemotherapy) could increase local tumor response in patients with invasive (T2, T3) breast cancer when compared with neoadjuvant anthracycline-based chemotherapy alone. [11] Fifteen patients were randomized to receive thermochemotherapy and thirteen patients were assigned to a control group that received chemotherapy alone. Although it was unclear what the follow-up time was, the investigators reported a weakly significant reduction in tumor volume in the thermochemotherapy group compared with the control group (88% vs. 59%, p=0.048). However, there was no significant difference between treatment groups in terms of tumor necrosis by volume. In addition, the investigators indicated that there was a lack of clinical efficacy of the experimental treatment, since the percentage of women in each group eligible for breast conserving surgery (BCS) due to treatment was similar between treatments. The impact of microwave thermotherapy on primary health outcomes such as survival was not reported in this study.

- In 2008, Dooley et al. published the results of a multi-center RCT that assessed whether preoperative focused microwave thermotherapy (FMT) killed breast carcinomas prior to surgery and reduced the incidence of positive margins compared to no treatment prior to surgery, including 75 patients with early stage breast cancer receiving BCS.[12] Thirty four patients were randomized to an experimental group who received thermotherapy prior to surgery while 41 patients were assigned to the control group who received surgery only. Post-treatment there was a nonsignificant difference in positive margin reduction between groups (0 of 34 [0%] patients in the thermotherapy arm had positive margins versus 4 of 41 [9.8%] in the surgery-alone; p=0.13).

Nonrandomized Studies

- In 2010, Dooley et al. published a review that summarized the results of four clinical studies performed by their group, including the two RCTs described above as well as two nonrandomized studies that evaluated FMT for preoperative treatment of invasive breast

cancer.[4,6,11-13] All clinical studies were published between 2002 and 2007, and the RCTs are described in detail above. In the initial phase I study, eight of 10 (80%) participants receiving one low dose of focused microwave thermotherapy prior to mastectomy had a partial tumor response after 5-18 days post-treatment and significant reduction in tumor size in six out of 10 (60%) of patients.[4] In the phase II study, the focused microwave thermotherapy dose was increased to stimulate 100% pathologic tumor cell kill for invasive carcinoma prior to BCS.[6] In this study, tumor size was unchanged after thermotherapy but pathologic necrosis was achieved in 17 (68%) patients, with complete necrosis achieved in two patients. Adverse events reported in these clinical studies include severe pain, erythema, edema, second- and third-degree burns, skin blistering, flap necrosis and nipple retraction. The authors concluded that the clinical studies performed by their group suggested FMT elicited both a reduction in positive tumor margins as a heat-alone treatment for early-stage breast cancer and a reduction in tumor volume when used in combination with anthracycline-based chemotherapy for patients with large breast cancer tumors, but larger RCTs were required to verify these conclusions.

- In 2012, Zhou et al. published the results a case series of 41 patients with small breast cancer treated with microwave thermotherapy, which they referred to as "percutaneous microwave coagulation (PMC)".[9] The group reported that 37 of 41 cases (90%; 95% confidence interval [CI]: 76.9% - 97.3%) showed complete tumor coagulation, as observed by using α-NADH-diaphorase staining. Of 38 cases diagnosed with invasive ductal carcinoma, 36 cases (95%; 95% CI: 82.3%, 99.4%) showed complete tumor coagulation. Adverse events reported included thermal injuries to the skin and pectoralis major muscle in three cases. The authors concluded that although the treatment was feasible, larger-scale clinical trials were needed to validate PMC for adoption into a standard clinical practice.

- In 2014, Zhou et al. reported on a second smaller pilot study to evaluate the effects of microwave ablation (MWA) by assessing the ablation zone by magnetic resonance (MR) imaging as well as pathological changes after MWA in twelve women with non-operable LABC.[10] All women were treated by MWA and then neoadjuvant chemotherapy, followed by surgery. At 24-hours post-ablation the ablation zones had a mean diameter between 2.23- 2.98 cm, and the ablated area became gradually smaller in MR imaging. No adverse effects related to MWA were noted in all 12 patients during and after MWA. Pathological evaluation confirmed the effect about three months after MWA. However, the investigators noted that long-term effect of MWA in the treatment of small breast cancer is needed.

CLINICAL PRACTICE GUIDELINES

No clinical practice guidelines, including those published by the National Comprehensive Cancer Network (NCCN)[2] and the American Society of Clinical Oncology (ASCO)[14] address microwave thermotherapy as a treatment for breast cancer.

EVIDENCE SUMMARY

There is insufficient evidence regarding the safety and efficacy of focused microwave thermotherapy as a treatment for breast tumors. The limited number of studies comparing microwave thermotherapy to current standard of care preoperative treatments, prior to breast surgery, are small in sample size and

are mainly published by one group of investigators. Additional independent randomized controlled studies are needed to evaluate the long-term safety and effectiveness of this treatment, whether used as an adjunct to other therapies or as a stand-alone treatment prior to surgical resection and breast conserving surgery. In addition, there is a lack of support from clinical practice guidelines for microwave thermotherapy to treat breast tumors.

HEALTH EQUITY CONSIDERATIONS

The Centers for Disease Control and Prevention (CDC) defines health equity as the state in which everyone has a fair and just opportunity to attain their highest level of health. Achieving health equity requires addressing health disparities and social determinants of health. A health disparity is the occurrence of diseases at greater levels among certain population groups more than among others. Health disparities are linked to social determinants of health which are non-medical factors that influence health outcomes such as the conditions in which people are born, grow, work, live, age, and the wider set of forces and systems shaping the conditions of daily life. Social determinants of health include unequal access to health care, lack of education, poverty, stigma, and racism.

The U.S. Department of Health and Human Services Office of Minority Health calls out unique areas where health disparities are noted based on race and ethnicity. Providence Health Plan (PHP) regularly reviews these areas of opportunity to see if any changes can be made to our medical or pharmacy policies to support our members obtaining their highest level of health. Upon review, PHP creates a Coverage Recommendation (CORE) form detailing which groups are impacted by the disparity, the research surrounding the disparity, and recommendations from professional organizations. PHP Health Equity COREs are updated regularly and can be found online here.

BILLING GUIDELINES AND CODING

CODES*		
CPT	19499	Unlisted procedure, breast
HCPCS	None	

***Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for

Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

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POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.
4/2023	Annual review. Policy now specific to commercial lines of business.
4/2024	Annual review. Policy name change. No change to policy criteria.
4/2025	Annual review. No changes.