Clinical Policy Title: Prophylactic mastectomy

Clinical Policy Number: 05.03.03

Effective Date: January 1, 2016
Initial Review Date: July 20, 2016
Most Recent Review Date: September 21, 2016
Next Review Date: September 2017

Related policies:

CP# 17.01.03 Breast cancer screening in women
CP# 16.03.05 Breast reduction surgery

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’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 Prestige Health Choice 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. Prestige Health Choice’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. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage Policy

Prestige Health Choice considers the use of prophylactic mastectomy to be clinically proven and therefore, medically necessary when the following criteria are met:

- Women diagnosed with breast cancer at 45 years of age or younger; or
- Women who are at increased risk for specific mutation(s) due to ethnic background (for instance: Ashkenazi Jewish descent) and who have 1 or more relatives with breast cancer or epithelial ovarian cancer at any age; or
- Women who carry a genetic mutation in the TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes); or
- Women who possess BRCA1 or BRCA2 mutations confirmed by molecular susceptibility testing for breast and/or epithelial ovarian cancer; or
- Women who received radiation treatment to the chest between ages of 10 and 30 years, such as for Hodgkin disease; or
Women with a 1st- or 2nd-degree male relative with breast cancer; or
Women with multiple primary or bilateral breast cancers in a 1st- or 2nd-degree blood relative; or
Women with multiple primary or bilateral breast cancers; or
Women with 1 or more cases of epithelial ovarian cancer AND 1 or more 1st- or 2nd-degree blood relatives on the same side of the family with breast cancer; or
Women with 3 or more affected 1st- or 2nd-degree blood relatives on the same side of the family, irrespective of age at diagnosis.

Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website can be accessed at http://ahca.myflorida.com/Medicaid/.

All other uses of prophylactic mastectomy are not medically necessary.

Alternative Covered Services:
None.

Background

For women in the U.S., breast cancer death rates are higher than those for any other cancer besides lung cancer. In 2016 an estimated 246,660 new cases of invasive breast cancer are expected in women in the U.S, along with 61,000 new cases of non-invasive breast cancer.

A woman can be at high risk if she has a strong family history of breast and/or ovarian cancer, a deleterious mutation in the BRCA1 gene or the BRCA2 gene, or a high-penetrance mutation in one of several other genes associated with breast cancer risk such as the ATM, BRIP1, CHEK2, and PTEN genes. The availability of improved means to identify high risk individuals intensifies the need to define the benefits and risks of early detection and protective measures for such women.

Women with a personal history of breast cancer are considered to be at high risk for developing contralateral breast cancer. The prevalence of synchronous cancer ranges from 1–3% to 10% and for this reason a woman may opt for prophylactic surgical removal of the breast. Data indicates that the use of contralateral prophylactic mastectomy (CPM) in women diagnosed with unilateral breast cancer has more than doubled in the last 10 years.

Bilateral prophylactic mastectomy (BPM) may involve complete removal of both breasts (total mastectomy), or it may involve removal of as much breast tissue as possible while leaving the nipples intact (subcutaneous or nipple-sparing mastectomy). Subcutaneous mastectomies preserve the nipple and allow for more natural-looking breasts if a woman chooses to have breast reconstruction surgery afterward.
Bilateral prophylactic mastectomy has been shown to reduce the risk for breast cancer by at least 95 percent in women who have a mutation in the BRCA1 gene or the BRCA2 gene, and by up to 90 percent in women who have a strong family history of breast cancer.

Total mastectomy provides the greatest breast cancer risk reduction because more breast tissue is removed; but, even with this procedure, not all breast tissue that may become cancerous in the future can be removed. With that being said, BPM is a major and irreversible elective surgery that may result in complications and adverse outcomes — from the surgical removal of both breasts and/or any subsequent reconstructive surgeries, a permanent change in a woman’s outward appearance, and the potential changes in her health-related quality of life (HRQOL). Decision-making requires full understanding of the benefits and risk of each approach. Although this applies to any surgical intervention, it is especially important when considering preference-sensitive care and where there is more than one clinically appropriate treatment option for the condition (Razdan 2015).

Bilateral prophylactic salpingo-oophorectomy, also known as prophylactic oophorectomy, involves the removal of both the fallopian tubes and the ovaries, and may be done alone or along with BPM in postmenopausal women who are at high risk of breast cancer (see Prestige Health Choice clinical policy on prophylactic salpingo-oophorectomy).

The American Cancer Society (ACS) recommends that the risks and benefits of PBM should be presented to BRCA1 and BRCA2 carriers, and may also be discussed on a case-by-case basis for other women. It also advocates that the surgery should be performed by a specialist in breast surgery and that preservation of the nipple and areola is desirable.

**Searches**

Prestige Health Choice 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.

Searches were conducted on June 20, 2016 using the terms “prophylactic mastectomy” and “risk-reducing mastectomy.”

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**

There is an increasing amount of research suggesting the value of prophylactic mastectomy as a preventative measure for women at risk of developing breast cancer. Much of the available medical evidence to date has focused on women with one or multiple risk factors for breast cancer. Risk factors include a strong family history of breast and/or ovarian cancer, a breast cancer susceptibility gene (BRCA1 or BRCA2 mutation), or the presence of lobular carcinoma in situ (LCIS). Prophylactic mastectomy is recommended for women with a strong family history of breast and/or ovarian cancer, only 10.39% of women with high hereditary risk have discussed genetic testing with a health professional, and 1.41% had undergone testing for cancer risk (Levy, 2009). Moreover, there may be some genetic mutations signaling high risk for breast cancer that have not yet been discovered.

The American Society of Clinical Oncology (ASCO) reported that after a woman with BRCA1 or BRCA2 mutation is diagnosed with unilateral breast cancer, the risk of contralateral breast cancer is approximately 3% per year (Metcalfe 2008). Bilateral mastectomy was shown to offer protection against contralateral breast cancer, and does not vary with age at diagnosis or time since surgery. In an earlier study that was conducted in 2004, one contralateral breast cancer occurred among 146 women with a CPM, compared with 97 contralateral breast cancers in 336 women who retained the contralateral breast. However, there were several limitations to this study: there was not enough information on breast cancer stage, and invasive breast cancers of all stages were included.

The National Comprehensive Cancer Network (NCCN) issued guidelines on assessing individuals at high risk for breast and ovarian cancer, the latest version released in 2016. The NCCN specified criteria for further genetic risk evaluation in otherwise healthy and asymptomatic women, based on factors including history of breast and ovarian cancer in first- and second-degree relatives. These criteria serve as the basis for whom prophylactic mastectomy might be medically necessary (NCCN, 2016a).

The NCCN 2016 *Clinical Practice Guidelines in Oncology for Breast Cancer Reduction* states that all options for risk reduction should be discussed with the patient in a shared decision making environment that includes genetic counseling if the woman is at high risk due to a strong family history or early onset breast or ovarian cancer. The NCCN guidelines advocate the use of total mastectomy for selected populations of women at high risk of breast cancer who elect to have surgery. The guidelines suggest that women considering CPM should undergo multidisciplinary consultations, clinical breast examination, and a bilateral mammogram if one has not been performed within the last 6 months (NCCNb).

The Journal of the National Cancer (JNCI 2001) also has produced recommendations for the use of prophylactic mastectomy, stating it is crucial to assess how preventative risk-reducing mastectomy (RRM) is relative to other breast cancer risk-reduction options, such as chemoprevention and bilateral prophylactic oophorectomy. Women and healthcare providers also need to weigh the potential benefits and risks of RRM against early-detection strategies, such as mammography and clinical breast examination.
In a meta-analysis conducted by the Cancer Epidemiology Biomarkers and Prevention Task Force it was shown that the greatest gains in life expectancy result from conducting prophylactic mastectomy immediately after BRCA1/2 mutation testing, but these gains vary with age at testing (Sigal 2012). Also, the study showed that by adding annual breast screening, life expectancy can be prolonged by 2 — 10 years for BRCA1 and 1.5 — 4.5 years for BRCA2. Delaying prophylactic surgery from age 30 years to 40 does not affect life expectancy as much as would a longer delay. More recent studies suggest that BRCA1 mutation carriers benefit more from prophylactic oophorectomy than prophylactic mastectomy, with the reverse finding for BRCA2 carriers.

In a Cochrane systematic review, participants included women at risk for breast cancer in at least one breast, and interventions included all types of mastectomy with the purpose of preventing breast cancer. Based on the studies conducted in this review, only one out of 39 studies attempted to control for multiple differences between intervention groups, and that study showed no overall survival advantage for CPM at 15 years (Lostumbo 2010). Another study showed significantly improved survival following CPM but only after adjusting for bilateral oophorectomy. The CPM effect on all-cause mortality was not statistically significant.

A prospective study confirmed that bilateral RRM substantially reduces breast cancer occurrence in healthy BRCA1/2 mutation carriers (Gerritsen 2013). It is the first prospective observational study suggesting that bilateral RRM when compared with surveillance is associated with improved survival, although longer follow-up in combination with larger sample sizes are needed to confirm statistical significance.

In another Cochrane review, sixteen studies assessed psychological measures, and most reported high levels of satisfaction with the decision to have prophylactic mastectomy. Worry over breast cancer was significantly reduced after bilateral prophylactic mastectomy when compared both to baseline worry levels and to the groups who opted for surveillance rather than surgery.

A meta-analysis measured the contentment with quality of life, body image, sexual satisfaction, breast cancer concern, depression, and health promotion (Geiger 2006). Among 519 women who underwent contralateral prophylactic mastectomy, 86.5% were satisfied with their decision. Among all case subjects, less contentment with quality of life was not associated with contralateral prophylactic mastectomy, but was associated with poor or fair general health perception. Most women undergoing CPM report satisfaction with their decision and experience psychological outcomes similar to breast cancer survivors without the procedure.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Razdan (2015)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>Quality of Life Among Patients after Bilateral Prophylactic Mastectomy: A Systematic Review of</td>
<td>- Systematic review of 1082 studies, with 22 of them meeting the criteria that post Bilateral Prophylactic mastectomy patients are satisfied with the outcomes and report high psychosocial well-being and positive body image</td>
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</table>
### Patient Reported Outcomes

- 12 ad hoc questionnaires were used to measure psychological well-being and body image after BPM, sexual well-being, and somatosensory function
- Sexual well-being and somatosensory function were the HRQOL domains most negatively affected after BPM
- Found that psychological morbidity and anxiety decreased significantly at 6 and 18 months after BPM.

### Gerritsen, 2013

**Substantial Breast Cancer Risk Reduction and Potential Survival Benefit after Bilateral Mastectomy when Compared with Surveillance in Healthy BRCA1 and BRCA2 Mutation Carriers: A Prospective Analysis**

**Key points:**
- A meta-analysis of 570 healthy female mutation carriers (405 BRCA1, 165 BRCA2) were selected from the institutional Family Cancer Clinic Database; 156 BRCA1 and 56 BRCA2 mutation carriers underwent risk-reducing mastectomy
- Breast cancer was detected more often in BRCA1 than in BRCA2 mutation carriers (20% versus 7%; P <0.01), but the median age at breast cancer diagnosis was not different (43 versus 44 years)
- The prospective cohort study in healthy BRCA1/2 mutation carriers showed that after BRRM the breast cancer incidence rare was substantially reduced, compared with regular surveillance
- After bilateral risk-reducing mastectomy, no incident breast cancer cases were observed during 1379 person-year of observation (PYO), while during 2037 PYO 57 women in the surveillance group were diagnosed with breast cancer

### National Comprehensive Cancer Network (NCCN), 2013

**Key points:**
- The NCCN updated its Clinical Practice Guidelines in Oncology for Breast Cancer Risk Reduction in April 2013.
- The NCCN guidelines advocate the use of BRRM (total mastectomy) for selected populations of women at high risks
- Additional options include risk-reducing agents (i.e. tamoxifen, raloxifene, and exemestane); surgery (i.e. BRRM and/or bilateral salpingo-oophorectomy); participation in clinical research for screening, risk assessment, or risk-reduction interventions; and healthy lifestyle modifications
- The NCCN does not recommend BRRM for a majority of women with LCIS without additional risk factors, although it may remain an option.
- If invasive breast cancer is identified during BRRM, the guidelines recommend treatment for breast cancer as outlined in the NCCN Guidelines for breast cancer

### Sigal, 2012

**A Simulation Model to Predict the Impact of Prophylactic Surgery and Screening on the Life Expectancy of BRCA1 and BRCA2 Mutation Carriers**

**Key points:**
- To determine age-specific breast cancer incidence in the absence of prophylactic oophorectomy, which is an input to the simulation model, and provide sensitivity analysis on related
- Life expectancy is greatest in gains when a prophylactic mastectomy and prophylactic oophorectomy is conducted immediately after BRCA1/2 mutation testing; these gains vary with age at testing, from 6.8 to 10.3 years for BRCA1 and 3.4 to 4.4 years for BRCA2 mutation carriers and depends on the timing of prophylactic surgery
- Adding annual breast screening provides gains of 2.0 to 9.9 years for BRCA1 and 1.5 to 4.3 years for BRCA2
- More recent studies suggest that BRCA1 mutation carriers benefit more from prophylactic oophorectomy than prophylactic mastectomy, with the reverse finding for BRCA2 carriers
- It is assumed that an asymptomatic patient is detected with a malignant breast tumor at the time of prophylactic mastectomy if the tumor diameter is greater than 2 mm; if the tumor
| Lostumbo, 2010 | **Key points:** |
| Prophylactic Mastectomy for the Prevention of Breast Cancer |
| 7,384 women with a wide range of risk factors for breast cancer who underwent prophylactic mastectomy were included in 39 observational studies |
| Sixteen of these studies assessed psychological measures, while most reported high levels of satisfaction with the decision to have prophylactic mastectomy |
| Published observations studies demonstrated that BPM was effective in reducing both the incidence of, and death from, breast cancer, but more randomized trials are needed |
| There is insufficient literature that CPM improves survival and studies that control for multiple confounding variables are needed |
| After BPM, most women are satisfied with their decision, but are less satisfied with cosmetic results and body image |

| Domchek, 2010 | **Key points:** |
| Association of Risk-Reducing Surgery in BRCA1 or BRCA2 Mutation Carriers with Cancer Risk and Mortality |
| A systematic review of 2482 women with BRCA1 or BRCA2 mutations ascertained between 1974 and 2008. The study conducted 22 clinical and research genetics centers in Europe and North America to assess the relationship between risk reducing mastectomy or salpingo-oophorectomy with cancer outcomes. The women were followed until the end of 2009. |
| No breast cancers were diagnosed in the 247 women with risk-reducing mastectomy compared with 98 women of 1372 diagnosed with breast cancer who did not have risk-reducing mastectomy. |
| Among a cohort of women with BRCA1 and BRCA2 mutations, the use of risk-reducing mastectomy was associated with a lower risk of breast cancer, risk reducing salpingo-oophorectomy was associated with a lower risk of ovarian cancer. |
| No breast cancer events were seen in women who underwent risk-reducing mastectomy over a similar follow-up period were diagnosed with breast cancer |
| Women who have inherited mutations in the BRCA1 and BRCA2 genes have substantially elevated risks of breast cancer and ovarian cancer, with a lifetime risk of breast cancer of 56% to 84% |

| Metcalfe, 2008 | **Key points:** |
| Predictors of Contralateral Prophylactic Mastectomy in Women with BRCA1 or BRCA2 Mutation: The Hereditary Breast Cancer Clinical Study Group |
| The study included 1,022 women from 8 different countries (Austria, Canada, France, Israel, Italy, Norway, Poland, and the United States) was conducted to evaluate the rate of prophylactic contralateral mastectomy in an international cohort of women with hereditary breast cancer and to evaluate the predictors of uptake of preventative surgery |
| Women with a BRCA1 or BRCA2 mutation who had been diagnosed with unilateral breast cancer, were between 25 and 80 years old, and were known to be a BRCA1/2 mutation carrier, and had no reported diagnosis of unilateral invasive breast cancer were eligible and were followed for a minimum of 1.5 years |
| A subgroup of nine hundred twenty-seven women was included in the study to evaluate predictors of contralateral mastectomy and was followed for at least 1.5 years; of these, 253 women (27.3%) underwent a contralateral prophylactic mastectomy after the initial diagnosis of breast cancer. |
| Participants were eligible for this study if they were known to be a BRCA1 or BRCA2 mutation carrier, were between 25 and 80 years old, reported a diagnosis of unilateral invasive breast cancer and had no previous history of another cancer. |
| All of the women included in the study had been diagnosed with the initial breast cancer before genetic testing for BRCA1 or BRCA2 |
**Society of Surgical Oncology (SSO), 2007**

**Position Statement on Prophylactic Mastectomy**

**Key points:**

- The SSO recommends that consideration of a bilateral risk-reducing mastectomy (BRRM) is best undertaken by a multidisciplinary team that includes surgeons, oncologists, pathologists, and genetic counselors.
- In women with a history of or current breast cancer diagnosis, the SSO states that potential indications for contralateral risk-reducing mastectomy (CRRM) include further risk reduction in patients at high risk of developing contralateral breast cancer, difficulty conducting surveillance of remaining breast, and/or reconstructive tissues.
- The SSO states that patients who have undergone therapeutic mastectomy may elect to have a CRRM to increase symmetry and/or reduce contralateral breast cancer risk.
- The SSO states that potential indications for bilateral BRRM in patients without a breast cancer diagnosis include: breast cancer susceptibility gene (BRCA) mutations or other genetic susceptibility genes; a strong family history with no demonstrable mutation; or histological risk factors, including atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), and lobular carcinoma in situ (LCIS).

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**Geiger, 2006**

**Contentment with Quality of Life Among Breast Cancer Survivors with and without Contralateral Prophylactic Mastectomy**

**Key points:**

- A meta-analysis of women ages 18-80 years of age with contralateral prophylactic mastectomy after breast cancer diagnosis between 1979 and 1999 at six health care delivery, which included 519 women.
- The goal was to determine the psychological outcomes after prophylactic removal of the contralateral breast in women with unilateral breast cancer.
- The response rate was 72.6%; 86.5% were satisfied with their decision; 76.3% reported high contentment with quality of life compared with 75.4% of 61 women who did not undergo the procedure.
- Among all case subjects, less contentment with quality of life was not associated with contralateral prophylactic mastectomy or demographic characteristics.

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**Glossary**

**American Cancer Society (ACS)** — nationwide voluntary health organization dedicated to eliminating cancer.

**BRCA1 and BRCA2** — genes involved in the repair of breaks in DNA.

**Contralateral prophylactic mastectomy** — a risk reducing mastectomy performed in a clinical setting for the patient diagnosed with an invasive or noninvasive breast cancer.

**Prophylactic mastectomy** — surgery to remove one or both breasts to reduce the risk of developing breast cancer.

**Subcutaneous mastectomy** — a surgical procedure which removes the mammary glandular tissue.

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


Sigal, B. (2012). A Simulation Model to Predict the Impact of Prophylactic Surgery and Screening on the Life Expectancy of BRCA1 and BRCA2 Mutation Carriers. Cancer Epidemiology, Biomarkers and Prevention. [http://cebp.aacrjournals.org/content/21/7/1066.full](http://cebp.aacrjournals.org/content/21/7/1066.full)

**Clinical trials:**

Searched clinicaltrials.gov on June 20, 2016, using the terms “prophylactic mastectomy” and “risk-reducing mastectomy”. Open studies. 9 studies found, 4 relevant.


NCT00496288. Prophylactic Irradiation to the Contralateral Breast for BRCA Mutation Carriers Undergoing Treatment for Breast Cancer.

CMS National Coverage Determination (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 in accordance with those manuals.

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<td>19303</td>
<td>Mastectomy, simple, complete</td>
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<td>19304</td>
<td>Mastectomy, subcutaneous</td>
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<tr>
<td>19305</td>
<td>Mastectomy, radical, including pectoris muscles, axillary lymph nodes</td>
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<tr>
<td>19306</td>
<td>Mastectomy, radical, including pectoris muscles, axillary and internal mammary lymph nodes (Urban type operation)</td>
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<tr>
<td>19307</td>
<td>Mastectomy, modified radical, including axillary lymph nodes, with or without pectoralis minor muscle, but excluding pectoralis major muscle</td>
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