



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Transvaginal Ultrasound for Ovarian and Endometrial Cancer Screening or Surveillance

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Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	5
References	5
Policy History.....	8

Hyperlink to Related Coverage Policies

- Colorectal Cancer Screening and Surveillance
- Genetic Testing for Susceptibility to Breast and Ovarian Cancer (BRCA1 & BRCA2)
- Genetic Testing for Susceptibility to Colorectal Cancer
- Proteomic Pattern Analysis of Blood for the Early Detection of Ovarian Cancer (e.g., OvaCheck™)
- Prophylactic Oophorectomy With or Without Hysterectomy

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers periodic transvaginal ultrasound screening or surveillance as medically necessary for individuals at increased risk for ovarian and/or endometrial cancer with ANY of the following:

- known carrier of BRCA1 or BRCA2 mutation (hereditary breast/ovarian cancer syndrome) or hereditary nonpolyposis colorectal cancer (HNPCC)—associated genetic mutation (Lynch syndrome)
- high likelihood of being a carrier of hereditary breast/ovarian cancer syndrome mutation or Lynch syndrome mutation (e.g., a mutation is known to be present in a close blood relative*; or in the absence of genetic testing, there is suspicion of mutation carrier status due to close blood relative* with history of breast, ovarian, endometrial or HNPCC-associated cancer)
- personal history of breast, ovarian, endometrial, fallopian tube, primary peritoneal, or an HNPCC-associated cancer

*A close blood relative/close family member is defined as a first-, second-, or third-degree relative:

- A first-degree relative is defined as a blood relative with whom an individual shares approximately 50% of his/her genes, including the individual's parents, full siblings, and children.
- A second-degree relative is defined as a blood relative with whom an individual shares approximately 25% of his/her genes, including the individual's grandparents, grandchildren, aunts, uncles, nephews, nieces and half-siblings.
- A third-degree relative is defined as a blood relative with whom an individual shares approximately 12.5% of his/her genes, including the individual's great-grandparents and first-cousins.

CIGNA does not cover transvaginal ultrasound screening for ovarian and/or endometrial cancer for the general population because it is considered experimental, investigational or of unproven benefit.

General Background

Ultrasound imaging, also known as ultrasound scanning or sonography is a method of obtaining images from inside the human body through the use of high-frequency sound waves. The echoes of the sound waves are recorded and displayed as a real-time, visual image. One method used to perform pelvic ultrasound in females is transvaginally. A transvaginal ultrasound (TVU, TVUS), also known as transvaginal sonography (TVS), involves the insertion of the transducer into the vagina. The images are obtained from different orientations to get the best views of the uterus and ovaries. TVU is a standard gynecological imaging method. It can be used along with other testing, such as a blood test for CA-125, as a screening or surveillance tool in populations at high-risk for cancer.

U.S. Food and Drug Administration (FDA)

A number of ultrasound devices and probes have received FDA approval. The FDA notes that these devices are considered prescription devices and are to be used only with a physician's order.

Literature Review

Ovarian Cancer: Large clinical trials of average-risk populations have shown TVU to produce a high number of false-positives (Partridge, et al 2009; Van Nagell, et al., 2007; Lacey, et al., 2006; Buys, et al., 2005). The CA-125 blood test also has a high false-positive rate. Although combining the two tests and stratifying women into risk groups based on family history does increase the positive predictive value somewhat, studies fail to demonstrate a beneficial effect of screening on mortality (Evans, et al., 2009; Van Nagell, et al., 2007; Hermsen, et al., 2007; Woodward, et al., 2007; Lacey, et al., 2006; Bosse, et al., 2006). Additional trials are underway so the effect of screening on mortality can be determined (e.g., The Prostate, Lung, Colorectal and Ovarian [PLCO] Cancer Screening Trial).

Endometrial Cancer: Due to a low positive predictive value, TVU has not been proven to be an effective screening procedure for detection of endometrial abnormality in average-risk women (Fleischer, et al., 2001). In high-risk populations, studies indicated TVU failed to detect endometrial cancer; the efficacy of TVU screening for endometrial cancer in high-risk women remains unproven by clinical trials (Renkonen-Sinisalo, et al., 2007; Rijcken, et al., 2003; Dove-Edwin, et al., 2002).

Professional Societies/Organizations

American Cancer Society (ACS): The ACS Screening Guidelines (Smith, et al., 2010) do not address ovarian cancer. The ACS Detailed Guide to Ovarian Cancer states "In studies of women at average risk of ovarian cancer, transvaginal sonography and the CA-125 blood test did not lower the number of deaths caused by ovarian cancer. For this reason, these tests are not recommended for ovarian cancer screening of women without known strong risk factors. Even when these tests are used in women at high risk, it is not known how helpful they are" (ACS, 2009a).

Current ACS Screening Guidelines (Smith, et al., 2010) note there is insufficient evidence to recommend screening for endometrial cancer in women at average risk, or those at an increased risk due to a history of unopposed estrogen therapy, tamoxifen therapy, late menopause, nulliparity, infertility or failure to ovulate, obesity, diabetes, or hypertension. The ACS recommends that women at average and increased risk should be informed about the risks and symptoms (in particular, unexpected bleeding and spotting) of endometrial cancer at the onset of menopause, and should be strongly encouraged to immediately report these symptoms to their

physician. Women at very high risk for endometrial cancer due to 1) known HNPCC genetic mutation carrier status; 2) a substantial likelihood of being a mutation carrier (i.e., a mutation is known to be present in the family); or 3) the absence of genetic testing results in families with a suspected autosomal dominant predisposition to colon cancer should consider beginning annual testing for the detection of early endometrial cancer at age 35 years. The ACS states that these women should be informed that the recommendation for screening is based on expert opinion and they should be informed about potential benefits, risks, and limitations of testing for early endometrial cancer detection. The ACS Detailed Guide to Endometrial Cancer states that TVU is often done before an endometrial biopsy (ACS, 2009b). TVU was not mentioned re screening or surveillance of women at high-risk for endometrial cancer.

National Comprehensive Cancer Network® (NCCN®): The NCCN publishes Clinical Practice Guidelines in Oncology™. The Genetic/Familial High-Risk Assessment: Breast and Ovarian guideline (v.1.2010) recommends at-risk patients who have not elected ovarian cancer risk reducing surgery to consider concurrent transvaginal ultrasound + CA 125, every six months starting at age 35 or 5–10 years earlier than the earliest age of first diagnosis of ovarian cancer in the family, and preferably day 1–10 of cycle for premenopausal women for the early detection of ovarian cancer. The NCCN states that one or more of the following criteria are suggestive of hereditary breast/ovarian cancer (HBOC) syndrome that warrants further professional evaluation:

- Individual from a family with a known BRCA1/BRCA2 mutation
- Personal history of breast cancer¹ plus one or more of the following:
 - diagnosed at age ≤45 years
 - diagnosed at age ≤50 years with one or more close blood relative with breast cancer at ≤50 years and/or one or more close blood relative with epithelial ovarian/fallopian tube/primary peritoneal cancer
 - two breast primaries², when first breast cancer diagnosis occurred prior to age 50
 - diagnosed at any age, with two or more close blood relatives with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
 - close male blood relative with breast cancer
 - personal history of epithelial ovarian³/fallopian tube/primary peritoneal cancer
 - for an individual of ethnicity associated with higher mutation frequency (e.g., founder populations of Ashkenazi Jewish, Icelandic, Swedish, Hungarian or Dutch), no additional family history may be required⁴
- Personal history of epithelial ovarian³/fallopian tube/primary peritoneal cancer
- Personal history of male breast cancer
- Family history only with one of the following:
 - First- or second-degree blood relative meeting any of the above criteria
 - Third-degree blood relative with ≥2 close relatives with breast and/or ovarian cancer (at least one close blood relative with breast cancer ≤50 years)

1) for purposes of the guidelines, invasive and ductal carcinoma in situ breast cancers should be included.

2) two breast primaries including bilateral disease or cases where there are two or more clearly separate ipsilateral primary tumors

3) ovarian cancer is a component tumor of or hereditary nonpolyposis colorectal cancer (HNPCC)/Lynch syndrome, be attentive for clinical evidence of this syndrome.

4) testing for founder-specific mutation(s), if available, should be performed first. Full sequencing may be considered if other hereditary breast and/or ovarian cancer criteria met.

The NCCN also notes that individuals with limited family history, such as fewer than two first- or second- degree female relatives or female relatives surviving beyond 45 years in either lineage, may have an underestimated probability of familial mutation. When investigating family histories, the maternal and paternal sides should be considered independently. Close relatives are considered to include first-, second-, and third-degree relatives. A first-degree relative is defined as a blood relative with whom an individual shares approximately 50% of his/her genes, including the individual's parents, full siblings, and children. A second-degree relative is defined as a blood relative with whom an individual shares approximately 25% of his/her genes, including the individual's grandparents, grandchildren, aunts, uncles, nephews, nieces and half-siblings. A third-degree relative is defined as a blood relative with whom an individual shares approximately 12.5% of his/her genes, including the individual's great-grandparents and first-cousins. The early onset of breast or epithelial

ovarian/fallopian tube/primary peritoneal cancers at any age also increases suspicion of HBOC. Other malignancies reported in some families with hereditary breast and ovarian cancer includes prostate, pancreatic, and melanoma.

National Cancer Institute (NCI): The NCI states that there is “inadequate evidence to determine whether routine screening for ovarian cancer with serum markers such as CA125 levels, TVU, or pelvic examinations would result in a decrease in mortality from ovarian cancer. Based on solid evidence, routine screening for ovarian cancer would result in more diagnostic laparoscopies and laparotomies than new ovarian cancers found” (NCI, 2009b).

The NCI states that there is inadequate evidence that screening by ultrasonography (e.g., endovaginal ultrasound or transvaginal ultrasound) reduces mortality from endometrial cancer. Most cases of endometrial cancer (85%) are diagnosed at low stage because of symptoms, and survival rates are high. Based on solid evidence, screening asymptomatic women will result in unnecessary additional biopsies because of false-positive test results. Risks associated with false-positive tests include anxiety and complications from biopsies (NCI, 2009a).

The NCI states that routine screening for endometrial cancer has not been shown to be beneficial in the general population, but expert consensus suggests that it be considered in women who are members of high-risk Lynch syndrome (i.e., HNPCC) families. Some studies suggest that women with a clinical or genetic diagnosis of Lynch syndrome do not universally adopt intensive gynecologic screening (Yang, et al., 2006; Collins, et al., 2007). Despite absence of a survival advantage, a task force organized by the National Institutes of Health (NIH) has suggested annual endometrial sampling beginning at age 30 to 35 years. TVUS can also be considered annually to evaluate the ovaries (Lindor, et al., 2006; Vasen, et al., 2007) (NCI, 2010).

American College of Obstetricians and Gynecologists (ACOG): The ACOG Practice Bulletin on Hereditary Breast and Ovarian Cancer Syndrome (April, 2009) states “Available screening procedures have a limited ability to detect ovarian cancer at an early, more curable stage of disease, and patients should be informed that there is no evidence that screening has reduced the mortality or improved the survival associated with ovarian cancer in high-risk populations. Nevertheless, given the extremely high risk for ovarian cancer and fallopian tube cancer in women with mutations in BRCA1 or BRCA2, consensus groups have recommended periodic screening with CA 125 and transvaginal ultrasonography, beginning between the ages of 30 years and 35 years or 5–10 years earlier than the earliest age of first diagnosis of ovarian cancer in the family (Burke, et al., 1997; NCCN, 2008)”.

American College of Radiology (ACR): The American College of Radiology Practice Guideline for the Performance of Pelvic Ultrasound in Females addresses transvaginal ultrasound. One of the indications listed is “screening for malignancy in patients with an increased risk” (ACR, 2009). The ACR Appropriateness Criteria® For Ovarian Cancer Screening (2007) states that there is currently no sufficiently accurate screening test for ovarian cancer in women at average risk.

U.S. Preventive Services Task Force (USPSTF): The USPSTF recommends against routine screening for ovarian cancer (May 2004). The USPSTF found fair evidence that screening with serum CA125 level or TVU can detect ovarian cancer at an earlier stage than it can be detected in the absence of screening; however, the USPSTF found fair evidence that earlier detection would likely have a small effect, at best, on mortality from ovarian cancer. Because of the low prevalence of ovarian cancer and the invasive nature of diagnostic testing after a positive screening test, there is fair evidence that screening could likely lead to important harms. The USPSTF concluded that the potential harms outweigh the potential benefits.

Summary

Evidence in the published, peer-reviewed scientific literature indicates the clinical utility of transvaginal ultrasound (TVU) for ovarian and endometrial cancer screening in asymptomatic women in the general population is unknown. There is concern that high false-positive rates may cause unnecessary invasive procedures. Although clinical trials have not demonstrated any survival advantage, TVU may be used as a screening tool in high-risk populations and as a surveillance tool in women with a personal history of breast, ovarian, endometrial, fallopian tube, primary peritoneal, or Lynch syndrome-associated cancer.

Coding/Billing Information

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

Covered when medically necessary:

CPT ^{®*} Codes	Description
76830	Ultrasound, transvaginal

ICD-9-CM Diagnosis Codes	Description
183.0	Malignant neoplasm of ovary
198.6	Secondary neoplasm of ovary
V10.05	Personal history of malignant neoplasm of large intestine
V10.3	Personal history of malignant neoplasm of breast
V10.41	Personal history of malignant neoplasm of cervix uteri
V10.43	Personal history of malignant neoplasm of ovary
V10.44	Personal history of malignant neoplasm of other female genital organs
V16.0	Family history of malignant neoplasm of gastrointestinal tract
V16.3	Family history of malignant neoplasm of breast
V16.41	Family history of malignant neoplasm, ovary

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

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2. American Cancer Society. Detailed Guide: Endometrial Cancer. How Is Endometrial Cancer Diagnosed? Last Revised: 10/22/2009b. Accessed June 2010. Available at URL address: http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?rnav=cridg&dt=11
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Policy History

<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	8/15/2008	0398	Transvaginal Ultrasound for Ovarian and Endometrial Cancer Screening or Surveillance

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