Cigna Medical Coverage Policy

Subject: Low-Dose Computed Tomography for Lung Cancer Screening

Effective Date: 2/15/2014
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Coverage Policy

In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna covers annual screening for lung cancer with low-dose computed tomography (LDCT) as medically necessary in an adult age 55 to 80 that has a 30 pack-year smoking history and either currently smokes or has quit within the past 15 years.

Cigna does not cover annual screening for lung cancer with low-dose computed tomography in an adult age 55 to 80 with a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery because it is considered not medically necessary.

Cigna does not cover annual screening for lung cancer with low-dose computed tomography for any other indication including screening in an individual who has not smoked for 15 years because it is considered experimental, investigational, or unproven.

General Background

In the United States, lung cancer is the most commonly occurring noncutaneous cancer in men and a woman combined, and is the leading cause of cancer deaths. The most important risk factor for lung cancer is tobacco use. Other risk factors are small compared with cigarette smoking—these causal factors include exposures to environmental and occupational substances and family history of lung cancer. Most lung cancer patients are diagnosed when their disease is advanced. Due to the prevalence and the mortality associated with lung cancer, there has been much interest in developing screening tests for lung cancer, in particular, for at-risk
individuals and at an earlier and more curable stage. Chest x-ray (CXR) and sputum cytology have been the most common methods used for screening for lung cancer.

More recently, low-dose CT has been proposed as a method of screening asymptomatic, high-risk individuals for lung cancer. It has been suggested that spiral CT may be an improved early lung cancer detection tool based on the advantages it appears to have over CXR and sputum cytology to detect lung cancer at an earlier stage. However, questions remain as to whether screening with spiral CT can reduce lung cancer mortality. This is the subject of ongoing randomized controlled clinical trials. Potential disadvantages associated with this test include false-positive results and over-diagnosis.

U.S. Food and Drug Administration (FDA)
Low-dose CT scanners are categorized as Class II devices by the FDA. Several spiral CT scanner systems have been approved by the FDA under the 510(k) approval process.

Literature Review – Randomized Controlled Trials
The National Lung Screening Trial Research Team reported on findings from the National Lung Screening Trial (NLST) which was conducted to determine whether screening with low-dose CT, as compared with chest radiography, could reduce mortality from lung cancer in high-risk patients (NLST, 2011). The study included 53,454 participants at high risk for lung cancer at 33 U.S. medical centers. The participants were between 55 and 74 years of age at the time of randomization, with a history of cigarette smoking of at least 30 pack-years, and, if former smokers, had quit within the previous 15 years. Individuals who had previously received a diagnosis of lung cancer, had undergone chest CT within 18 months before enrollment, had hemoptysis, or had an unexplained weight loss of more than 6.8 kg (15 lb) in the preceding year were excluded. The participants were randomly assigned to undergo three annual screenings with either low-dose CT (26,722) or single-view posteroanterior chest radiography (26,732). Data was collected on cases of lung cancer and deaths from lung cancer that occurred through December 31, 2009. There was a rate of adherence to screening of more than 90%. It was found that the rate of positive screening tests was 24.2% with low-dose CT and 6.9% with radiography over all three rounds. A total of 96.4% of the positive screening results in the low-dose CT group and 94.5% in the radiography group were false positive results. The study found the incidence of lung cancer was 645 cases per 100,000 person-years (1060 cancers) in the low-dose CT group, as compared with 572 cases per 100,000 person-years (941 cancers) in the radiography group (rate ratio, 1.13; 95% confidence interval [CI], 1.03 to 1.23). There were 247 deaths from lung cancer per 100,000 person-years in the low-dose CT group and 309 deaths per 100,000 person-years in the radiography group, that represented a relative reduction in mortality from lung cancer with low-dose CT screening of 20.0% (95% CI, 6.8 to 26.7; p=0.004). The rate of death from any cause was reduced in the low-dose CT group, as compared with the radiography group, by 6.7% (95% CI, 1.2 to 13.6; p=0.02). The study included a specific population, it is not known if this will apply to other populations. The author’s note that based on findings of the NSLT are not sufficient to fully inform decisions in lung-screening recommendations. Adverse events from the actual screening examinations were few and minor.

Infante et al. (2008) presented the baseline results of a prospective, randomized trial that compared screening for lung cancer with annual spiral computed tomography (CT) as compared to a yearly clinical review (DANTE trial). Secondary endpoints in the study include incidence, stage at diagnosis, and resectability. The study was started in 2001 and includes 2472 subjects, age 60–74 years old, that were smokers of at least 20 pack-years. All of the participants received a baseline medical examination, CXR and sputum cytology. The spiral CT group (n=1276) received a spiral CT scan at baseline, then yearly for the following 4 years. For the control group (n=1196), a yearly clinical examination was scheduled for the following 4 years. In the spiral CT group, 28 lung cancers were detected, 13 of which were visible in the baseline chest X-rays (overall prevalence 2.2%). Sixteen out of 28 tumors (57%) were stage I, and 19 (68%) were resectable. In the control group, eight cases were detected by the baseline chest X-rays (prevalence rate 0.67%), four (50%) were stage I, and six (75%) were resectable. There was further investigation with high-resolution CT and with PET performed in 128 (10.0%) and 35 (2.7%) patients in the spiral CT group and in 20 (1.8%) and 2 (0.2%) patients in the control group, respectively with a significant difference (p<0.05) for both of these tests. In addition, a significant increase in invasive procedures was observed in the CT group compared with the control arm (52 versus 12; p<0.05). Six patients in the control group underwent thoracotomy for lung cancer. In the CT group, 22 of the 32 thoracotomies were performed for lung cancer, while four patients had other disease—six of the 32 thoracotomies were performed for benign pulmonary nodules. Longer follow-up is needed to clarify the role of lung cancer screening and the impact on reducing mortality.
In 2009, Infante et al. reported on interim three year results (33 months) of the Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays (DANTE) Trial. This trial included two Italian centers of the same hospital network. A total of 2,472 males participated aged 60 to 75 years without significant comorbid conditions, smokers of 20 or more pack-years. A total of 1,276 were randomized to CT and 1,196 randomized to controls. All participants had a baseline clinical interview and examination, chest radiography, and 3-day sputum cytology; those in the intervention group also received CT. All participants were followed annually with clinical interviews and physical examinations focused on detecting lung cancer; the intervention group also received 4 annual CTs. Controls had the same yearly medical interview and physical examination as the screening-arm subjects, but if no abnormalities were detected clinically, they did not undergo further evaluation. After median follow-up of almost three years, 60 (4.7%) patients were diagnosed with lung cancer in the low-dose CT (LDCT) group and 34 (2.8%) (p=0.016) in the control group. There were more patients with stage 1 disease in the LDCT group (54 vs. 34%; p=0.06). It was noted that the number of advanced lung cancer cases was the same in both groups. Twenty patients in the LDCT group (1.6%) and 20 controls (1.7%) died of lung cancer, while 26 and 25 respectively have died of other causes. A significant number of surgical procedures (13%) were performed for pulmonary lesions that ultimately turned out to be benign. There was a small stage-shift in favor of the screening arm was observed; however, resection rates, advanced case rates and disease-specific mortality were similar. The authors recommend that lung cancer screening by spiral CT should not be proposed outside research programs.

The Danish Lung Cancer Screening Trial (DLCST) (Saghir, et al., 2012) is a single Danish center randomized controlled trial. A total of 4104 healthy men and women aged 50 to 70 years who were current or former smokers (220 pack-years) and were able to walk at least 36 steps without stopping, were included. Former smokers must have quit after age 50 years and less than 10 years before enrollment. The control group received no screening. The CT group received five annual screening rounds. Results after 4.8 years demonstrated significantly more lung cancers were diagnosed in the screening group (p=0.001) and more were low stage (p=0.002). At the end of screening, 103 of 4104 participants had died. Sixty-one (2.97%) died in the screening group, while 42 (2.05%) died in the control group (log-rank test, all-cause mortality (p=0.059). Fifteen (0.73%) died of lung cancer in the screening group compared with 11 (0.54%) in the control group (lung cancer specific mortality: p=0.428). Therefore, no differences in mortality were found. The authors concluded that CT screening for lung cancer brings forward early disease, while at this point no stage shift or reduction in mortality was observed.

The Multicentric Italian Lung Detection (MILD) study (Pastorino, et al., 2012) is an ongoing randomized controlled trial including a total of 4099 participants with 1723 were randomized to the control group and 2376 to the LDCT group: 1190 were assigned to screening with annual LDCT and 1186 with biennial LDCT. The median duration of follow-up was 4.4 years. Forty-nine lung cancers were detected by LDCT (20 in biennial and 29 in the annual arm), of which 17 were identified at baseline examination; 63% were of stage I and 84% were surgically resectable. Stage distribution and resection rates were similar in the two LDCT arms. The cumulative 5-year lung cancer incidence rate was 311/100 000 in the control group, 457 in the biennial, and 620 in the annual LDCT group (p=0.036); lung cancer mortality rates were 109, 109, and 216/100 000. There was no evidence of a protective effect of annual or biennial LDCT screening.

Literature review – Systematic Reviews

Bach et al. (2012) conducted a systematic review of the evidence regarding benefits and harms of lung cancer screening using LDCT. Eight randomized trials and 13 cohort studies of LDCT screening met the inclusion criteria. Primary outcomes were lung cancer mortality and all-cause mortality, and secondary outcomes included nodule detection, invasive procedures, follow-up tests, and smoking cessation. Three randomized studies provided evidence on the effect of LDCT screening on lung cancer mortality—of which the National Lung Screening Trial (NLST) was the most informative, demonstrating that among 53,454 participants, screening resulted in significantly fewer lung cancer deaths (356 vs 443 deaths; lung cancer–specific mortality, 274 vs 309 events per 100,000 person-years for LDCT and control groups, respectively; relative risk, 0.80; 95% CI, 0.73-0.93; absolute risk reduction, 0.33%; p=004). The other two smaller studies demonstrated no such benefit (Danish Lung Cancer Screening Trial [DLCST]; Dante trial). In terms of potential harms of LDCT screening, across all trials and cohorts, approximately 20% of individuals in each round of screening had positive results requiring some degree of follow-up, while approximately 1% had lung cancer. A marked heterogeneity was noted in this finding and in the frequency of follow-up investigations, biopsies, and percentage of surgical
procedures performed in patients with benign lesions. Major complications in those with benign conditions were rare. The overdiagnosis rate for LDCT screening cannot yet be estimated; NLST data show a persistent gap of about 120 excess lung cancers in the LDCT group compared to the chest radiographs group, but further follow-up is needed. The effective dose of radiation of LDCT is estimated to be 1.5 mSv per examination; however, there is substantial variation in actual clinical practice. It is thought that diagnostic chest CT or PET CT that are performed to further investigate detected lesions rapidly increases the exposure and accounts for most of the radiation exposure in screening studies. The effect of LDCT screening on quality of life is uncertain—there are also potential detriments due to anxiety, costs, and harms from the evaluation of both false-positive scans and overdiagnosed cancers. The authors concluded that low-dose computed tomography screening may benefit individuals at an increased risk for lung cancer, but uncertainty exists about the potential harms of screening and the generalizability of the results.

The California Technology Assessment Forum (CTAF, 2011) conducted an assessment for LDCT screening as a modality for lung cancer screening. The assessment noted that with the publication of the National Lung Screening Trial (NLST) has demonstrated that lung cancer mortality and total mortality can be reduced with LDCT screening of high risk individuals. However, the assessment notes that there is a very high rate of false positive tests. Many of the test results require additional evaluation and procedures and the potential risks and benefits of the additional procedures is not known. There are questions that remain regarding whom to target for screening and also the appropriate interval for screening. In addition, the extent of risk of the cumulative radiation exposure attributable to the LDCT is not known. The assessment notes that the use of LDCT screening cannot be currently recommended outside of the investigational setting. The recommendation of the CTAF assessment is: It is recommended that the use of LDCT as a screening test for lung cancer in high risk individuals at specialized centers meets CTAF criteria.

Gopal et al. (2010) reported on a systematic review and a meta-analysis of the baseline results of randomized controlled trials so far published, which included six studies and 14,055 patients. The studies were analyzed to determine whether data was for or against the screening of lung cancers using low-dose computed tomography (LDCT). The results indicated that screening for lung cancer using LDCT resulted in a significantly higher number of stage I lung cancers (odds ratio 3.9, 95% confidence interval [CI] 2.0 –7.4), higher number of total non-small cell lung cancers (odds ratio 5.5, 95% CI 3.1–9.6), and higher total lung cancers (odds ratio 4.1, 95% CI 2.4 –7.1). Screening resulted in increased detection of false-positive nodules (odds ratio 3.1, 95% CI 2.6 –3.7) and more unnecessary thoracotomies for benign lesions (event rate 3.7 per 1000, 95% CI 3.5–3.8). It was found that for every 1,000 individuals screened for lung cancer, nine stage I non-small cell lung cancer and 235 false-positive nodules were found, and four thoracotomies for benign lesions were performed. The authors concluded that the baseline data from six randomized controlled trials offer no compelling data in favor or against the use of LDCT screening for lung cancer.

A systematic review was performed by the National Coordinating Centre for Health Technology Assessment (Black, et al., 2006) to examine the clinical- and cost-effectiveness of screening for lung cancer using CT. Twelve studies of CT screening for lung cancer were included in the study, with two randomized controlled trials and ten studies without a control group. The randomized controlled trials were less than one year’s duration. The conclusion noted that there was currently no evidence that screening improves survival or reduces mortality. The review contained the recommendations that evidence with randomized controlled trials is needed regarding the effect of CT screening on mortality.

A Cochrane review was performed (Manser, et al., 2004) for the purpose of assessing the evidence regarding the ability of various methods to reduce lung cancer mortality and to evaluate the possible harms and costs associated with screening. Seven trials (six randomized controlled trials and one non-randomized controlled trial) with a total of 245,610 subjects were included in the review. The review noted that there were no studies with an unscreened controlled group, and there were no controlled studies of spiral CT. The reviewers concluded that the current evidence does not support regular screening for lung cancer. It is noted that the review found early detection methods such as CXR, testing sputum or CT scan do not appear to have much impact on either treatment or number of deaths from lung cancer. In addition, it is noted that the review found frequent CXR may be associated with harm. The authors concluded that there is insufficient evidence to support screening for lung cancer with any screening modality including CXR, sputum cytology, or helical CT. Further randomized controlled studies of screening methods for lung cancer are indicated.

**Literature Review - Other**
The International Early Lung Cancer Action Program Investigators (I-ELCAP) reported on a large, non-randomized study that involved 31,567 asymptomatic persons who were at risk for lung cancer (2006). The participants were 40 years of age and older, and were at risk of lung cancer due to a history of cigarette smoking, occupational exposure, or exposure to secondhand smoke. The participants underwent baseline CT screening, with repeat screening performed seven to 18 months after the previous screening. The 10-year lung cancer-specific survival rate was estimated for participants with clinical stage I lung cancer that was detected on CT screening and diagnosed by biopsy. The screening resulted in a diagnosis of lung cancer in 484 participants. Of these, 412 (85%) were found to have clinical stage I lung cancer with an estimated 10-year survival rate of 88%. Among participants with stage I lung cancer who underwent surgical resection within one month after diagnosis, the survival rate was 92%. The eight participants who did not receive treatment died within five years of diagnosis. The authors concluded that annual spiral CT screening can detect lung cancer that is curable. While the results of this trial are promising, this study 1) focused on high-risk individuals, 2) was not a randomized controlled trial and did not contain a comparison group, and 3) relied on specialty centers for follow-up and treatment.

Professional Societies/Organizations

United States Preventive Services Task Force (USPSTF): The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30-pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery (B recommendation). (Note: Grade B - The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.)

American Cancer Society: The American Cancer Society lung cancer screening guidelines (Wender, et al., 2013) state these recommendations:

Clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should initiate a discussion about lung cancer screening with patients aged 55 years to 74 years who have at least a 30-pack-year smoking history, currently smoke, or have quit within the past 15 years, and who are in relatively good health. Core elements of this discussion should include the following benefits, uncertainties, and harms of screening:

- **Benefit:** Screening with LDCT has been shown to substantially reduce the risk of dying from lung cancer.
- **Limitations:** LDCT will not detect all lung cancers or all lung cancers early, and not all patients who have a lung cancer detected by LDCT will avoid death from lung cancer.
- **Harms:** There is a significant chance of a false-positive result, which will require additional periodic testing and, in some instances, an invasive procedure to determine whether or not an abnormality is lung cancer or some nonlung cancer-related incidental finding. Less than 1 in 1000 patients with a false-positive result experience a major complication resulting from a diagnostic workup. Death within 60 days of a diagnostic evaluation has been documented, but is rare and most often occurs in patients with lung cancer.

Smoking cessation counseling constitutes a high priority for clinical attention for patients who are currently smoking. Current smokers should be informed of their continuing risk of lung cancer, and referred to smoking cessation programs. Screening should not be viewed as an alternative to smoking cessation.

Eligible patients should make the screening decision together with their health care provider. Helping individuals to clarify their personal values can facilitate effective decision-making:

- Individuals who value the opportunity to reduce their risk of dying from lung cancer and who are willing to accept the risks and costs associated with having a LDCT and the relatively high likelihood of the need for further tests, even tests that have the rare but real risk of complications and death, may opt to be screened with LDCT every year.
- Individuals who place greater value on avoiding testing that carries a high risk of false-positive results and a small risk of complications, and who understand and accept that they are at a much higher risk of death from lung cancer than from screening complications, may opt not to be screened with LDCT.
Clinicians should not discuss lung cancer screening with LDCT with patients who do not meet the above criteria. If lung cancer screening is requested, these patients should be informed that at this time, there is too much uncertainty regarding the balance of benefits and harms for individuals at younger or older ages and/or with less lifetime exposure to tobacco smoke and/or with sufficiently severe lung damage to require oxygen (or other health-related NLST exclusion criteria), and therefore screening is not recommended.

Adults who choose to be screened should follow the NLST protocol of annual LDCT screening until they reach age 74 years.

**National Comprehensive Cancer Network (NCCN):** NCCN has published guidelines (National Comprehensive Cancer Network Guidelines™ [NCCN Guidelines™]) for lung cancer screening. The guidelines state that an Update is in Progress and include the following recommendation for lung cancer screening (NCCN, 1.2014):

- A baseline low-dose CT (LDCT) is recommended for high risk individuals that includes either of the following conditions:
  - All of the following (category 1):
    - Age 55–74 years
    - ≥ 30 pack year history of smoking
    - Smoking cessation of < 15 years
  - All of the following (category 2B):
    - Age ≥ 50 years
    - ≥ 20 pack year history of smoking
    - One additional risk factor (other than second-hand smoke)*

- When no lung nodule is found on LDCT: annual LDCT for two years (category 1) and consider annual LDCT until patient no longer eligible for definitive treatment

- Guidelines include specific recommendations for follow-up of screening findings

*Additional risk factors include:
- radon exposure (documented high radon exposure)
- Occupational exposure agents that are identified specifically as carcinogens targeting the lungs: silica, cadmium, asbestos, arsenic, beryllium, chromium, diesel fumes, nickel, coal smoke, and soot
- Cancer history: there is increased risk of developing new primary lung cancer among survivors of lung cancer, lymphomas, cancers of the head and neck, or smoking-related cancers
- Family history of lung cancer
- Disease history that includes COPD or pulmonary fibrosis

Category 1: based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2B: based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate

**American College of Chest Physicians (ACCP):** The ACCP published evidenced-based practice guidelines regarding the role of CT screening for lung cancer (Detterbeck, et al., 2013). The guideline makes two major recommendations related to LDCT screening for lung cancer:

- **Recommendation 1:** For smokers and former smokers aged 55 to 74 years who have smoked for 30 pack-years or more and either continue to smoke or have quit within the past 15 years, we suggest that annual screening with low-dose computed tomography (LDCT) should be offered over both annual screening with chest radiograph or no screening, but only in settings that can deliver the comprehensive care provided to National Lung Screening Trial (NLST) participants. (Grade of recommendation: 2B*)

- **Recommendation 2:** For individuals who have accumulated fewer than 30 pack years of smoking or are either younger than 55 years or older than 74 years, or individuals who quit smoking more than 15 years ago, and for individuals with severe comorbidities that would preclude potentially curative treatment, limit life expectancy, or both, we suggest that CT screening should not be performed. (Grade of recommendation: 2C*)
Use Outside of the US
The United Kingdom began the United Kingdom Lung Cancer Screening Trial (UKLS) in April 2011.

Summary
The United States Preventive Services Task Force (USPSTF) recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Covered when used to report low-dose computed tomography (CT) for lung cancer screening:

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<th>Description</th>
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<td>71250</td>
<td>Computed tomography, thorax; without contrast material</td>
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<tr>
<td>76497</td>
<td>Unlisted computed tomography procedure (eg, diagnostic, interventional)</td>
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<tr>
<td>S8032</td>
<td>Low-dose computed tomography for lung cancer screening</td>
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<tr>
<td>S8092</td>
<td>Electron beam computed tomography (also known as Ultrafast CT, Cine CT)</td>
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References


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