Aetna considers cardiopulmonary exercise testing (CPET) medically necessary in any of the following conditions, after performance of standard testing, including echocardiography, and pulmonary function testing with measurement of diffusion capacity and measurement of oxygen desaturation (6-minute walk test):

- Development of exercise prescription to determine intensity of exercise training in cardiac or pulmonary rehabilitation programs in persons with cardiovascular disease or chronic pulmonary disease (see CPB 0021 - Cardiac Rehabilitation (../1_99/0021.html) and CPB 0032 - Pulmonary Rehabilitation (../1_99/0032.html)); or

- Differentiation of cardiac versus pulmonary limitations as a cause of exercise-induced dyspnea or impaired exercise capacity in persons with known or suspected cardiopulmonary disease when standard testing (e.g., echocardiography, electrocardiography, and resting pulmonary function tests) is inconclusive or non-diagnostic; or

- Evaluation of exercise capacity and response to therapy
in persons with chronic heart failure (CHF) who are being considered for heart transplantation or other advanced therapies; or

- Evaluation children and adolescents with congenital heart disease, to discriminate between pulmonary and cardiovascular causes of exercise limitation, and to evaluate improvements in exercise tolerance after surgery; or

- Evaluation of individuals presenting with heart failure to help determine whether heart failure is the cause of exercise limitations when the contribution of heart failure is uncertain; or

- Evaluation of exercise capacity in persons who are being considered for lung transplantation or lung resection surgery if predicted post-operative forced expiratory volume in 1 second (FEV1) or predicted post-operative diffusing capacity of the lung for carbon monoxide (DLCO) (or both) are less than 30 %, or when the performance of the stair-climbing test or the shuttle walk test is not satisfactory; or

- Evaluation of persons with mitochondrial myopathies; or

- Functional evaluation of persons with chronic obstructive pulmonary disease (COPD) when specific questions persist after consideration of basic clinical data, including history, physical examination, chest X-ray, pulmonary function tests (PFTs), and resting electrocardiogram (ECG); or

- Functional and prognostic evaluation of persons with interstitial lung disease when specific questions persist after consideration of basic clinical data, including history, physical examination, chest X-ray, pulmonary function tests (PFTs), and resting electrocardiogram (ECG).

Aetna considers CPET experimental and investigational for any of the following conditions (not an all-inclusive list):

- First-line diagnostic test of persons presenting with possible cardiac or pulmonary pathology (e.g., asthma, chest pain/early-stage ischemic heart disease, chronic fatigue syndrome, diabetes, fibromyalgia, hyperlipidemia, hypertension, obesity, pectus excavatum, polycystic ovary syndrome, and sickle cell disease; not an all-inclusive list); or
- Functional and prognostic evaluation of persons with cystic fibrosis; or
- Functional and prognostic evaluation of persons with dystrophinopathies (e.g., Becker muscular dystrophy and Duchenne muscular dystrophy) and multiple sclerosis, or
- Prediction of post-operative morbidity/survival in persons undergoing major surgery (e.g., abdominal aortic aneurysm repair, colorectal surgery, hepatic transplant and resection surgery, pancreatic surgery, renal transplant, and upper gastro-intestinal surgery); or
- Risk stratification of individuals undergoing vascular surgery; or
- Risk stratification of persons with asymptomatic valve diseases (e.g., aortic stenosis); or
- Routine assessment of persons' response to specific therapeutic interventions (e.g., bronchodilators, continuous positive airway pressure, and exercise training; not an all-inclusive list); or
- Routine pre-operative assessment (including evaluation of persons undergoing bariatric surgery); or
- Screening exercise testing.

**Background**
Cardiopulmonary exercise testing (CPET), also known as cardiopulmonary exercise stress testing, is a non-invasive tool that provides a comprehensive evaluation of exercise responses involving the cardiovascular, pulmonary, hematopoietic, neuropsychological, and musculoskeletal systems. Cardiopulmonary exercise testing entails measurements of oxygen uptake (VO2), carbon dioxide output (VCO2), minute ventilation (VE), and other variables in addition to a 12-lead electrocardiography (ECG), blood pressure (BP) monitoring and pulse oximetry. These data are gathered during a maximal symptom-limited incremental exercise test. In certain circumstances, an additional measurement of arterial blood gases may be used to assess pulmonary gas exchange. Measurement of expiratory gases during exercise allows estimation of functional capacity, grades the severity of the impairment, evaluates the response to
interventions, tracks disease progression, and assists in differentiating cardiac from pulmonary limitations in exercise tolerance. Cardiopulmonary exercise testing may be carried out on a treadmill or bicycle ergometer. Resting measurements are made for 3 to 5 minutes; followed by 3 minutes of unloaded cycling as a warm-up period. The workload is then increased at a rate designed to allow reaching maximum work capacity in 8 to 12 minutes. The test continues to symptom limitation (e.g., faintness, pallor, chest pain, severe dyspnea, and inability to continue pedaling or walking) or discontinuation by medical staff as a consequence of significant ECG abnormalities, drop in diastolic or systolic BP greater than 20 mm Hg below the resting value, rise in diastolic BP to greater than 120 mm Hg, rise in systolic BP to greater than 250 mm Hg, severe oxygen desaturation (less than 80 %), or achievement of maximum predicted heart rate (McCarthy and Dweik, 2006).

Cardiopulmonary exercise testing is not appropriate for use as a screening test or first line test. Guidelines from the American Thoracic Society state that “In practice, CPET is considered when specific questions persist after consideration of basic clinical data, including history, physical examination, chest X-ray, pulmonary function tests (PFTs), and resting electrocardiogram (ECG).”

Cardiopulmonary exercise testing is performed in candidates for heart transplantation or other advanced therapies. In a prospective study, Myers et al (1998) examined clinical, hemodynamic, and CPET determinants of survival in patients with CHF. A total of 644 patients were included in this study. Age, cause of heart failure, body surface area, cardiac index, ejection fraction, pulmonary capillary wedge pressure, left ventricular dimensions, watts achieved during exercise, heart rate (HR), maximum systolic BP, and VO2 at the ventilatory threshold and at peak exercise were measured at baseline. Uni-variate and multi-variate analyses were carried out for clinical, hemodynamic, and exercise test predictors of death. A Cox hazards model was developed for time of death. During a mean follow-up period of 4 years, 187 patients (29 %) died and 101 underwent transplantation. Actuarial 1-year and 5-year
survival rates were 90.5% and 73.4%, respectively. Resting systolic BP, watts achieved, peak VO2, VO2 at the ventilatory threshold, and peak HR were greater among survivors than among non-survivors. Cause of heart failure (coronary artery disease or cardiomyopathy) was a strong determinant of death (relative risk for coronary artery disease, 1.73; p < 0.01). By multi-variate analysis, only peak VO2 was a significant predictor of death. Stratification of peak VO2 above and below 12, 14, and 16 ml/kg per minute demonstrated significant differences in risk for death, but each cut-point predicted risk to a similar degree. The authors concluded that peak VO2 outperforms clinical variables, right-heart catheterization data, exercise time, and other exercise test variables in predicting outcome in severe CHF. Direct measurement of VO2 should be included when clinical or surgical decisions are being made in patients referred for evaluation of CHF or those considered for heart transplantation. Oikawa and colleagues (2003) noted that patients with CHF frequently complain of fatigue and/or dyspnea during daily life. These exertional symptoms can be evaluated by the CPET. Peak VO2, anaerobic threshold, the ratio of the increase in VE to the increase in VCO2, the slope of the increase in VO2 relative to the increase in work rate, and the time constant of VO2 are reported to be useful in evaluating the severity and prognosis of patients with CHF. The information obtained from CPET can be used to select therapeutic option to improve both functional capacity and prognosis, as well as to identify patients with the greatest need for heart transplantation.

The American Thoracic Society (ATS)/American College of Chest Physicians (ACCP)'s statement on CPET (2003) noted that this approach has been used for over a decade as a standard assessment tool of CHF, especially to determine candidacy for heart transplantation. The ATS/ACCP (2003) also listed evaluation of undiagnosed exercise intolerance, prescription of pulmonary rehabilitation, as well as evaluation of lung, heart, and heart-lung transplantation as indications for CPET. Furthermore, Ingle (2008) stated that CPET is a well-established tool for stratifying cardiovascular risk in
patients with CHF. Important prognostic variables include a reduced peak VO2, which has a central use in the selection criteria of heart transplantation, as well as the abnormal relation between VE and VCO2, often referred to as the elevated VE/VCO2 slope.

Cardiopulmonary exercise testing has also been used for pre-operative evaluation for lung cancer resection surgery or lung volume reduction surgery. Beckles et al (2003) stated that the pre-operative physiologic assessment of patients being considered for surgical resection of lung cancer must consider the immediate peri-operative risks from co-morbid cardiopulmonary disease, the long-term risks of pulmonary disability, and the threat to survival due to inadequately treated lung cancer. As with any planned major surgery, especially in a population predisposed to atherosclerotic cardiovascular disease by cigarette smoking, a cardiovascular evaluation is an important component in assessing peri-operative risks. Measurements of the forced expiratory volume in 1 second (FEV1) and the diffusing capacity of the lung for carbon monoxide (DLCO) should be viewed as complementary physiologic tests for assessing risk related to pulmonary function. If there is evidence of interstitial lung disease on radiographical studies or undue dyspnea on exertion, even though the FEV1 may be adequate, a DLCO should be obtained. In patients with abnormalities in FEV1 or DLCO identified pre-operatively, it is essential to estimate the likely post-resection pulmonary reserve. The amount of lung function lost in lung cancer resection can be estimated by using either a perfusion scan or the number of segments removed. A predicted post-operative FEV1 or DLCO less than 40% indicates an increased risk for peri-operative complications, including death, from lung cancer resection. Exercise testing should be performed in these patients to further define the peri-operative risks prior to surgery. Formal CPET is a sophisticated tool that includes recording the exercise ECG, HR response to exercise, VE, and VO2 per minute, and allows calculation of maximal oxygen consumption (VO2max). Risk for peri-operative complications can generally be stratified by VO2max. Patients
with pre-operative VO2max greater than 20 ml/kg/min are not at increased risk of complications or death; VO2max less than 15 ml/kg/min indicates an increased risk of peri-operative complications; and patients with VO2max less than 10 ml/kg/min have a very high risk for post-operative complications. Alternative types of exercise testing include stair climbing, the shuttle walk, and the 6-min walk test (6MWT). Desaturation during an exercise test has been associated with an increased risk for peri-operative complications.

Lung volume reduction surgery (LVRS) for patients with severe emphysema is a controversial procedure. Some reports document substantial improvements in lung function, exercise capability, and quality of life in highly selected patients with emphysema following LVRS. Case series of patients referred for LVRS indicate that perhaps 3 to 6% of these patients may have co-existing lung cancer. Anecdotal experience from these case series suggested that patients with extremely poor lung function can tolerate combined LVRS and resection of the lung cancer with an acceptable mortality rate and good post-operative outcomes. Combining LVRS and lung cancer resection should probably be limited to those patients with heterogeneous emphysema, particularly emphysema limited to the lobe containing the tumor (Beckles et al, 2003). DeCamp and colleagues (2008) stated that potential candidates for LVRS should undergo extensive evaluation and preparation to minimize peri-operative risks and optimize surgical outcomes. Initial screening includes spirometry, diffusion capacity, lung volumes by body plethysmography, and high-resolution computerized tomography scanning. Patients who have been successfully screened must complete a pre-operative pulmonary rehabilitation program of 6 to 10 weeks duration. During the pulmonary rehabilitation program, medical therapy should be maximized. Post-rehabilitation studies include CPET, arterial blood gas analysis, oxygen titration, 6MWT, and cardiac testing. The evaluation process aims at defining the severity and distribution of emphysema and attempts to eliminate those who do not meet criteria outlined by the National Emphysema Treatment Trial. Optimal
candidates have upper-lobe-predominant emphysema and acceptable operative risks.

The ACCP's practice guidelines on physiologic evaluation of the patient with lung cancer being considered for resectional surgery (Colice et al, 2007) stated that CPET for measuring VO2max should be performed to further define the peri-operative risk of surgery; a VO2max of less than 15 ml/kg/min indicates an increased risk of peri-operative complications. Alternative types of exercise testing (e.g., stair climbing, the shuttle walk, and the 6MWT) should be considered if CPET is unavailable.

Cardiopulmonary exercise testing is being used increasingly in a wide spectrum of clinical applications including pectus excavatum, polycystic ovary syndrome, and sickle cell disease (Malek and Coburn, 2008, Giallauria et al, 2008, and Das et al, 2008). However, there is insufficient evidence that CPET should be used as a screening tool or as a first-line test. The ATS/ACCP statement on CPET (2003) noted that this approach is generally not considered a first-line test, and is usually used when the diagnosis is still uncertain after standard work up with resting pulmonary function tests or ECG. Furthermore, the American Heart Association (AHA) Council on Clinical Cardiology's statement on exercise testing in asymptomatic adults (Lauer et al, 2005) noted that a wealth of data indicate that exercise testing can be used to evaluate and refine prognosis, especially when emphasis is placed on non-ECG measures (e.g., exercise capacity, chronotropic response, HR recovery, and ventricular ectopy). Nevertheless, randomized trial data on the clinical value of screening exercise testing are absent. It is unclear if a strategy of routine screening exercise testing in selected subjects reduces the risk for premature mortality or major cardiac morbidity. The writing group from the AHA believed that a large-scale randomized study of such a strategy should be carried out.

Forshaw and associates (2008) stated that CPET may identify patients at high risk of post-operative cardiopulmonary
morbidity and mortality. These investigators evaluated the utility of CPET before esophagectomy. A total of 78 consecutive patients (64 men) with a median age of 65 years (range of 40 to 81 years) underwent CPET before esophagectomy (50% transhiatal; 50% transthoracic). Measured variables included anaerobic threshold (AT) and VO2peak. Outcome measures were post-operative morbidity and mortality, length of hospital stay, and unplanned intensive therapy unit admission. Cardiopulmonary complications occurred in 33 (42%) patients and non-cardiopulmonary complications in 19 (24%). One in-hospital death (1.3%) occurred, and 13 patients (17%) required an unplanned intensive therapy unit admission. The level of VO2peak was significantly lower in patients with post-operative cardiopulmonary morbidity (p = 0.04). The area under a receiver operating characteristic curve was 0.63 (95% confidence interval [CI], 0.50 to 0.76) for the VO2peak and 0.62 (95% CI, 0.49 to 0.75) for AT. An AT cutoff of 11 ml/kg/min was a poor predictor of post-operative cardiopulmonary morbidity. The authors concluded that although the VO2peak was significantly lower in those patients who developed cardiopulmonary complications, CPET is of limited value in predicting post-operative cardiopulmonary morbidity in patients undergoing esophagectomy.

Brown and colleagues (2008) stated that 6MWT and CPET are used to evaluate impairment in emphysema. However, the extent of impairment in these tests as well as the correlation of these tests with each other and lung function in advanced emphysema is not well characterized. During screening for the National Emphysema Treatment Trial, maximum ergometer CPET and 6MWT were performed in 1218 individuals with severe COPD with an average FEV1 of 26.9 +/- 7.1% predicted. Predicted values for 6MWT and CPET were calculated from reference equations. Correlation coefficients and multi-variable regression models were used to determine the association between lung function, quality of life (QOL) scores, and exercise measures. The two forms of exercise testing were correlated with each other (r = 0.57, p < 0.0001). However, the impairment of performance on CPET was greater than on the
6MWT (27.6 +/− 16.8 versus 67.9 +/− 18.9 % predicted). Both exercise tests had similar correlation with measures of QOL, but maximum exercise capacity was better correlated with lung function measures than 6-min walk distance. After adjustment, 6-min walk distance had a slightly greater association with total St George’s Respiratory Questionnaire score than maximal exercise (effect size 0.37 +/− 0.04 versus 0.25 +/− 0.03 % predicted/unit). Despite advanced emphysema, patients are able to maintain 6-min walk distance to a greater degree than maximum exercise capacity. Moreover, the 6MWT may be a better test of functional capacity given its greater association with QOL measures whereas CPET is a better test of physiologic impairment.

Pulmonary arterial hypertension (PAH) is a debilitating chronic disorder of the pulmonary vasculature. It is characterized by a persistent elevation in pulmonary arterial pressure with normal left sided pressures, differentiating it from left sided heart disease. Symptoms progress from shortness of breath and decreasing exercise tolerance to right heart failure, with peripheral edema and marked functional limitation. Exercise-induced syncope, worsening symptoms at rest, and intractable right heart failure indicate critical disease. Pulmonary arterial hypertension may be idiopathic with no identifiable cause or associated with collagen vascular diseases, drugs, HIV, liver disease, and/or congenital heart disease. Familial or genetically mediated PAH accounts for a small percentage of cases. The 6MWT is the current standard to assess exercise capacity in patients with PAH (Traiger, 2007; Gomberg-Maitland et al, 2007).

Cardiopulmonary exercise testing has also been used in the management of patients with PAH, especially in assessing exercise tolerance. Guazzi and Opasich (2005) noted that the importance of studying the pathophysiological bases and clinical correlates of exercise limitation in patients with PAH is well-established. Two modes of exercise testing, the 6MWT and CPET, are currently proposed for diagnostic, therapeutic, as well as prognostic finalities. The 6MWT is inexpensive, feasible
and is thought to better reproduce daily life activities and to reliably detect therapeutic benefits. On the other hand, CPET requires the patients' maximal effort and does not provide a reliable quality of life measure. However, it is highly reproducible and provides insights into the pathophysiological mechanisms that lead to exercise intolerance.

The ACCP’s clinical practice guidelines on prognosis of PAH (McLaughlin et al, 2004) stated that in patients with idiopathic PAH, low VO2max and low peak exercise systolic BP and diastolic BP as determined by CPET may be used to predict a worse prognosis. Furthermore, the European Respiratory Society (ERS)’s Task Force (Palange et al, 2007) recommended the use of CPET for functional and prognostic evaluation of patients with primary pulmonary hypertension.

In a case report on the utility of CPET to detect and track early-stage ischemic heart disease, Chaudhry and colleagues (2010) concluded that "this study illustrates the potential value of CPET in the primary prevention setting to detect and track early-stage ischemic heart disease .... Research in this area should continue to more firmly establish the clinical role of CPET in the evaluation of ischemic heart disease (macrovascular or microvascular) for the purpose of improving preventive cardiac care and thus reducing long-term health care costs".

The American College of Cardiology (ACC)/AHA Task Force on Practice Guidelines guidelines for exercise testing (Gibbons et al, 1997) stated that ventilatory gas exchange analysis during exercise testing is a useful adjunctive tool in assessment of patients with cardiovascular and pulmonary disease. Measures of gas exchange primarily include VO2, VCO2, VE, and ventilatory/anaerobic threshold. VO2 at maximal exercise is considered the best index of aerobic capacity and cardiorespiratory function. Estimation of maximal aerobic capacity using published formulas without direct measurement is limited by physiological and methodological inaccuracies. Data derived from exercise testing with ventilatory gas analysis have proved to be reliable and important in evaluation of
patients with heart failure. Such data are only partly influenced by resting left ventricular dysfunction. Maximal exercise capacity does not necessarily reflect the daily activities of patients with heart failure. Use of this technique in stratification of ambulatory heart failure patients has improved ability to identify those with the poorest prognosis, who should be considered for heart transplantation. The ACC/AHA published a partial update to these guidelines (Gibbons et al, 2002), however, there was no change in regard to CPET.

The European Respiratory Society (ERS)'s Task Force (Palange et al, 2007) also provided the following recommendations (ranging from "A", the highest, to "D", the lowest) regarding the clinical use of CPET:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommendation grade</th>
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<tbody>
<tr>
<td>Detection of exercise-induced bronchoconstriction</td>
<td>A</td>
</tr>
<tr>
<td>Detection of exercise-induced arterial oxygen desaturation</td>
<td>B</td>
</tr>
<tr>
<td>Functional evaluation of subjects with unexplained exertional dyspnea and/or exercise intolerance and normal resting lung and heart function</td>
<td>D</td>
</tr>
<tr>
<td>To recognize specific disease exercise response patterns that may help in the differential diagnosis of ventilatory versus circulatory causes of exercise limitation</td>
<td>C</td>
</tr>
<tr>
<td>Functional and prognostic evaluation of patients with COPD</td>
<td>B, C</td>
</tr>
<tr>
<td>Functional and prognostic evaluation of patients with ILD</td>
<td>B, B</td>
</tr>
<tr>
<td>Functional and prognostic evaluation of patients with CF</td>
<td>C, C</td>
</tr>
<tr>
<td>Functional and prognostic evaluation of patients with PPH</td>
<td>B, B</td>
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<td>----------------------------------------------------------</td>
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<tr>
<td>Functional and prognostic evaluation of patients with CHF</td>
<td>B, B</td>
</tr>
<tr>
<td>Evaluation of interventions (Maximal incremental test)</td>
<td>C</td>
</tr>
<tr>
<td>Evaluation of interventions (High-intensity constant work-rate “endurance” tests)</td>
<td>B</td>
</tr>
<tr>
<td>Prescription of exercise training</td>
<td>B</td>
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The authors stated that with the use of this rigorous grading system, "A" is relatively rare and "B" is usually considered the best achievable. The low power recommendation grades are reflective not so much of well-powered statistical judgments as they are of weakness in the density of the relevant evidence base. Such areas should be regarded as important priorities for future investigation.

The American Heart Association (AHA)’s scientific statement on CPET in adults (Balady et al, 2010) stated that CPET has been studied and found to be useful in the following clinical applications (not an all-inclusive list):

- Development of the exercise prescription in patients with cardiovascular disease or stroke
- Evaluation of disability in patients with cardiac or pulmonary disease
- Evaluation of patients with heart failure
- Evaluation of patients with mitochondrial myopathies
- Evaluation of patients with unexplained dyspnea.

The AHA’s scientific statement on CPET in adults (Balady et al,
2010) also listed the following emerging and less well-studied clinical applications of CPET (not an all-inclusive list):

- Evaluation of patients with congenital heart disease
- Evaluation of patients with cardiac arrhythmias and pacemakers
- Evaluation of patients with ischemic heart disease
- Evaluation of patients with pulmonary hypertension
- Pre-operative evaluation of patients undergoing pulmonary resection or bariatric surgery.

The AHA scientific statement (Balady et al, 2010) also stated that more studies are needed to rigorously evaluate if CPET provides additional discriminatory diagnostic and prognostic value over and above that provided by standard exercise tests and other clinical variables. In addition, more studies are needed to assess the increasing number of variables that can be derived from CPET, as well as their utility in many conditions that affect the cardiovascular and pulmonary systems.

Young and colleagues (2012) performed a systematic review of CPET in the pre-operative evaluation of patients with abdominal aortic aneurysm or peripheral vascular disease requiring surgery. Review methods and reporting were according to the PRISMA guidelines. Studies were eligible if they reported CPET-derived physiological parameters in patients undergoing abdominal aortic aneurysm repair or lower extremity arterial bypass. Data were extracted regarding patient populations and correlation between CPET and surgical outcomes including mortality, morbidity, critical care bed usage and length of hospital stay. These researchers identified a total of 1,301 articles. Although 53 abstracts referred to the index vascular procedures, only 7 articles met inclusion criteria. There were no data from randomized controlled trials. Data from prospective studies did not comprehensively correlate CPET and surgical outcomes in patients with abdominal aortic aneurysms. There were no studies reporting CPET in patients undergoing lower extremity arterial bypass. Major limitations included small sample sizes, lack of blinding, and an absence of
reporting standards. The authors concluded that the paucity of robust data precludes routine adoption of CPET in risk-stratifying patients undergoing major vascular surgery. They stated that the use of CPET should be restricted to clinical trials and experimental registries, reporting to consensus-defined standards.

Marzolini et al (2012) noted that despite the importance of exercise training in mitigating cardiovascular risk, the development of exercise programs for people post-stroke has been limited by lack of feasibility data concerning CPET to inform the exercise prescription. These researches examined the feasibility of CPETs for developing an exercise prescription in people greater than or equal to 3 months post-stroke. Cardiopulmonary exercise testing results from 98 consecutively enrolled patients post-stroke with motor impairments and 98 age- and sex-matched patients with coronary artery disease were examined at baseline and after 6 months of exercise training. The proportion of patients with stroke and coronary artery disease attaining an intensity sufficient for prescribing exercise at baseline was 68.4 % versus 82.7 %, respectively (p = 0.02) and 84.7 % versus 83.8 % (p = 0.9) at 6 months. Women were less likely than men post-stroke to achieve a sufficient intensity at baseline (40 % versus 80.9 %, p < 0.001) but not at 6 months (78.3 % versus 87.1, p = 0.3). A clinically relevant abnormality occurred in 11.2 % of stroke and 12.2 % of patients with coronary artery disease on baseline CPETs (p = 0.8) and 10.6 % of stroke and 5.9 % of patients with coronary artery disease on the 6-month CPET (p = 0.4). No serious cardiovascular events occurred during 349 CPETs. The authors concluded that most patients after stroke achieved a level of exertion during the CPET sufficient to inform an exercise prescription. At least 1 of 10 patients post-stroke developed a clinically relevant abnormality on baseline and post-program CPETs with no serious cardiovascular events. Moreover, they state that these data supported the feasibility and safety of CPETs for prescribing exercise post-stroke; and strategies to improve use of baseline CPETs for women post-stroke require further investigation. The clinical value of CPET for prescribing
exercise to people after stroke needs to be ascertained in well-designed studies.

The 3rd edition of the American College of Chest Physicians' evidence-based clinical practice guidelines on “Physiologic evaluation of the patient with lung cancer being considered for resectional surgery” (Brunelli et al, 2013) states that “The preoperative physiologic assessment should begin with a cardiovascular evaluation and spirometry to measure the FEV1 and the diffusing capacity for carbon monoxide (DLCO). Predicted post-operative (PPO) lung functions should be calculated. If the % PPO FEV1 and % PPO DLCO values are both > 60 %, the patient is considered at low risk of anatomic lung resection, and no further tests are indicated. If either the % PPO FEV1 or % PPO DLCO are within 60 % and 30 % predicted, a low technology exercise test should be performed as a screening test. If performance on the low technology exercise test is satisfactory (stair climbing altitude > 22 m or shuttle walk distance > 400 m), patients are regarded as at low risk of anatomic resection. A cardiopulmonary exercise test is indicated when the PPO FEV1 or PPO DLCO (or both) are < 30 % or when the performance of the stair-climbing test or the shuttle walk test is not satisfactory. A peak oxygen consumption (V'O2 peak) < 10 ml/kg/min or 35 % predicted indicates a high risk of mortality and long-term disability for major anatomic resection. Conversely, a V'O2 peak > 20 mL/kg/min or 75 % predicted indicates a low risk”. The authors concluded that a careful pre-operative physiologic assessment is useful for identifying those patients at increased risk with standard lung cancer resection and for enabling an informed decision by the patient about the appropriate therapeutic approach to treating his or her lung cancer. This pre-operative risk assessment must be placed in the context that surgery for early-stage lung cancer is the most effective currently available treatment of this disease.

A European Respiratory Society Task Force (2007) stated that clear evidence now exists for the utility of CPET in children and adolescents with congenital heart diseases. The guidelines cite
evidence that CPET may help to discriminate between pulmonary, cardiovascular and deconditioning causes of exercise limitation in congenital heart diseases. The authors state that CPET has been used to evaluate improvements in exercise tolerance after heart surgery. The guidelines note that the use of exercise testing to assess the long-term prognosis of children with CHD have not been reported.

American Heart Association/ American College of Cardiology Foundation’s scientific statement on “The evaluation of syncope” (Strickberger et al, 2006) did not mention cardiopulmonary exercise testing for evaluating patients with syncope.

**Evaluation of Dystrophinopathies (e.g., Becker Muscular Dystrophy and Duchenne Muscular Dystrophy):**

In a pilot study, Bartels et al (2015) determined exercise response during CPET in children and adolescents with dystrophinopathies. Exercise response on CPET was compared with a standard care test protocol. A total of 9 boys (aged 10.8 ± 4.7 years) with Becker muscular dystrophy (n = 6) and Duchenne muscular dystrophy (n = 3) were included. The feasibility of the CPET was similar to a standard care test protocol, and no serious adverse events occurred. In 67% of the subjects with normal or only mildly impaired functional capacity, the CPET could be used to detect moderate-to-severe cardiopulmonary exercise limitations. The authors concluded that CPET appeared to be a promising outcome measure for cardiopulmonary exercise limitations in youth with mild functional limitations. They stated that further research with larger samples is needed to confirm current findings and investigate the additional value of the CPET to longitudinal follow-up of cardiomyopathy and the development of safe exercise programs for youth with dystrophinopathies.

**Evaluation of Multiple Sclerosis:**

van den Akker and colleagues (2015) examined the feasibility
and safety of CPET in patients with multiple sclerosis (MS). PubMed, EMBASE, CINAHL, SPORTDiscus, PsycINFO, ERIC, and the Psychology and Behavioral Sciences Collection were searched up to October 2014. References from retrieved articles were examined to identify additional relevant studies. Inclusion of original studies was on the basis of performance of maximal CPET, description of the protocol, and participants with definite MS aged greater than or equal to 18 years. No language restrictions were applied. The quality of CPET reporting in included studies was scored according to a structured checklist considering 10 feasibility (e.g., test abnormalities) and 12 safety quality criteria (e.g., adverse events). Structured data extraction was performed for these feasibility and safety features of CPET. A total of 46 studies were included, comprising 1,483 patients with MS, with a mean age ± SD of 42.0 ± 5.8 years and a median Expanded Disability Status Scale (EDSS) score of 2.8 (first quartile = 2.1; third quartile = 3.9; range of average EDSS scores, 0.75 to 5.8). Quality of reporting on CPET varied from 3 to 13 out of a possible 22 quality points. The percentage of test abnormalities (feasibility) was 10.0 %, primarily because of an inability to maintain pedaling at a specific resistance. The percentage of adverse events (safety) was 2.1 %; all adverse events were temporary. The authors concluded that CPET is feasible provided that the CPET modality is tailored to the physical abilities of the patient. Furthermore, CPET is safe when recommended precautions and safety measures are implemented. Moreover, they stated that future optimization of CPET will require protocolized testing and the implementation of standard reporting procedures.

van den Akker and associates (2015) examined the feasibility and safety of CPET in patients with MS. PubMed, Embase, CINAHL, SPORTDiscus, PsycINFO, ERIC, and the Psychology and Behavioral Sciences Collection were searched up to October 2014. References from retrieved articles were examined to identify additional relevant studies. Inclusion of original studies was on the basis of performance of maximal CPET, description of the protocol, and participants with definite MS aged greater than or equal to 18 years. No language restrictions were
applied. The quality of CPET reporting in included studies was scored according to a structured checklist considering 10 feasibility (e.g., test abnormalities) and 12 safety quality criteria (e.g., adverse events). Structured data extraction was performed for these feasibility and safety features of CPET. A total of 46 studies were included, comprising 1,483 patients with MS, with a mean age ± SD of 42.0 ± 5.8 years and a median EDSS score of 2.8 (1st quartile = 2.1; 3rd quartile = 3.9; range of average EDSS scores, 0.75 to 5.8). Quality of reporting on CPET varied from 3 to 13 out of a possible 22 quality points. The percentage of test abnormalities (feasibility) was 10.0 %, primarily because of an inability to maintain pedaling at a specific resistance. The percentage of adverse events (safety) was 2.1 %. All adverse events were temporary. The authors concluded that based on the available data, CPET is feasible provided that the CPET modality is tailored to the physical abilities of the patient. Furthermore, CPET is safe when recommended precautions and safety measures are implemented. However, they stated that future optimization of CPET will require protocolized testing and the implementation of standard reporting procedures.

Prediction of Post-Operative Morbidity/Survival in Persons Undergoing Major Surgery:

Kasivisvanathan et al (2015) examined if CPET may predict which patients are at risk for adverse outcomes after undergoing hepatic resection surgery. High-risk patients undergoing elective, 1-stage, open hepatic resection were pre-operatively assessed using CPET. Morbidity, as defined by the post-operative morbidity survey (POMS), was assessed on post-operative day 3. A total of 104 patients underwent pre-operative CPET and were included in the analysis. Of these, 73 patients (70.2 %) experienced post-operative morbidity. Oxygen consumption at anaerobic threshold (\(V'\text{O}_2\) at AT, ml/kg/min) was the only CPET predictor of post-operative morbidity on multi-variable analysis, with an area under the curve (AUC) of 0.66 [95 % CI: 0.55 to 0.76]. In patients requiring a major hepatic resection (3 or more segments), a \(V'\text{O}_2\) at AT of
less than 10.2 ml/kg/min gave an AUC of 0.79 (95 % CI: 0.68 to 0.86) with 83.9 % sensitivity and 52.0 % specificity, 80.6 % positive predictive value (PPV) and 62.5 % negative predictive value (NPV). The authors concluded that the application of a cut-off value for V’O2 at AT of less than 10.2 ml/kg/min in patients undergoing major hepatic resection may be useful for predicting which patients will experience morbidity. These findings need to be validated by well-designed studies.

Levett and Grocott (2015) evaluated the current and future role of CPET in the context of enhanced recovery after surgery (ERAS) programs. There is substantial literature confirming the relationship between physical fitness and peri-operative outcome in general. The few small studies in patients undergoing surgery within an ERAS program described less fit individuals having a greater incidence of morbidity and mortality. There is evidence of increasing adoption of peri-operative CPET, particularly in the United Kingdom. Although CPET-derived variables have been used to guide clinical decisions about choice of surgical procedure and level of peri-operative care as well as to screen for uncommon co-morbidities, the ability of CPET-derived variables to guide therapy and thereby improve outcome remains uncertain. Recent studies have reported a reduction in CPET-defined physical fitness following neoadjuvant therapies (chemo- and radio-therapy) prior to surgery. Preliminary data suggested that this effect may be associated with an adverse effect on clinical outcomes in less fit patients. Early reports suggested that CPET-derived variables can be used to guide the prescription of exercise training interventions and thereby improve physical fitness in patients prior to surgery (i.e., pre-habilitation). The impact of such interventions on clinical outcomes remains uncertain. The authors concluded that peri-operative CPET is finding an increasing spectrum of roles, including risk evaluation, collaborative decision-making, personalized care, monitoring interventions, and guiding prescription of pre-habilitation. They stated that these indications are potentially of importance to patients having surgery within an ERAS program, but there are currently few publications specific
Grant et al (2015) examined if CPET can identify patients at risk of reduced survival after abdominal aortic aneurysm (AAA) repair. Prospectively collected data from consecutive patients who underwent CPET before elective open or endovascular AAA repair (EVAR) at 2 tertiary vascular centers between January 2007 and October 2012 were analyzed. A symptom-limited maximal CPET was performed on each patient. Multivariable Cox proportional hazards regression modelling was used to identify risk factors associated with reduced survival. The study included 506 patients with a mean age of 73.4 (range of 44 to 90) years; 82.6 % were men and 64.6 % underwent EVAR. The in-hospital mortality was 2.6 %. The median follow-up was 26 months. The 3-year survival for patients with 0 or 1 sub-threshold CPET value was 86.4 % compared with 59.9 % for patients with 3 sub-threshold CPET values. Risk factors independently associated with survival were female sex [hazard ratio = 0.44, 95 % CI: 0.22 to 0.85, p = 0.015], diabetes (hazard ratio = 1.95, 95 % CI: 1.04 to 3.69, p = 0.039), pre-operative statins (hazard ratio = 0.58, 95 % CI: 0.38 to 0.90, p = 0.016), hemoglobin g/dL (hazard ratio = 0.84, 95 % CI: 0.74 to 0.95, p = 0.006), peak VO2 (less than 15 ml/kg/min) (hazard ratio = 1.63, 95 % CI: 1.01 to 2.63, p = 0.046), and at anaerobic threshold greater than 42 (hazard ratio = 1.68, 95 % CI: 1.00 to 2.80, p = 0.049). The authors concluded that CPET variables are independent predictors of reduced survival after elective AAA repair and can identify a cohort of patients with reduced survival at 3 years post-procedure. Moreover, they stated that CPET is a potentially useful adjunct for clinical decision-making in patients with AAA.

In a systematic review, Moran and colleagues (2016) evaluated the ability of CPET to predict post-operative outcome. The following databases were searched: PubMed, Embase, PEDro, the Cochrane Library, Cinahl, and AMED. A total of 37 full-text articles were included. Data extraction included the following: author, patient characteristics, setting, surgery type, post-operative outcome measure, and CPET outcomes.
Surgeries reviewed were hepatic transplant and resection \( (n = 7) \), abdominal aortic aneurysm (AAA) repair \( (n = 5) \), colorectal \( (n = 6) \), pancreatic \( (n = 4) \), renal transplant \( (n = 2) \), upper gastrointestinal (GI) \( (n = 4) \), bariatric \( (n = 2) \), and general intra-abdominal surgery \( (n = 12) \). Cardio-pulmonary exercise testing-derived cut-points, peak oxygen consumption and anaerobic threshold (AT) predicted the following post-operative outcomes: 90-day to 3-year survival \( (AT 9 \text{ to } 11 \text{ ml/kg/min}) \) and intensive care unit (ICU) admission \( (AT \text{ less than } 9.9 \text{ to } 11 \text{ ml/kg/min}) \) after hepatic transplant and resection, 90-day survival after AAA repair \( (15 \text{ ml/kg/min}) \), LOS and morbidity after pancreatic surgery \( (AT \text{ less than } 10 \text{ to } 10.1 \text{ ml/kg/min}) \), and mortality and morbidity after intra-abdominal surgery \( (AT 10.9 \text{ and less than } 10.1 \text{ ml/kg/min}, \text{ respectively}) \). The authors concluded that CPET is a useful pre-operative risk-stratification tool that can predict post-operative outcome. Moreover, they stated that further research is needed to justify the ability of CPET to predict post-operative outcome in renal transplant, colorectal, upper GI, and bariatric surgery.

**Risk Stratification of Persons with Asymptomatic Valve Diseases:**

Levy and colleagues stated that risk stratification in asymptomatic patients with severe aortic stenosis (AS) is based on exercise test results. However, differentiating between pathological and physiological breathlessness during exercise is sometimes challenging. Cardiopulmonary exercise testing may improve quantification of cardiopulmonary exercise capacity in patients with valve diseases. In a pilot study, these researchers evaluated the ability of CPET to detect abnormal responses to exercise and a clinical end-point (occurrence of European Society of Cardiology guidelines surgical class I triggers). A total of 43 consecutive patients (mean age of 69 ± 13 years; 31 men) with no reported symptoms and severe AS (aortic valve surface area less than 1 cm² or indexed aortic valve surface area less than or equal to 0.6 cm²/m²) prospectively underwent symptom-limited CPET. Twelve (28 %) patients had an abnormal exercise test (AET) with symptoms (abnormal dyspnea \( n = 11 \); angina \( n = 1 \)). Both VE/VCO2 slope greater than 34 (hazard ratio
= 5.76, 95% CI: 1.086 to 30.587; p = 0.04) and peak VO2 less than or equal to 14 ml/kg/min (hazard ratio 6.01, 95% CI: 1.153 to 31.275; p = 0.03) were independently associated with an AET. Furthermore, VE/VCO2 slope greater than 34 (hazard ratio 3.681, 95% CI: 1.318 to 10.286; p = 0.013) and peak VO2 less than or equal to 14 ml/kg/min (hazard ratio 3.058, 95% CI: 1.74 to 8.713; p = 0.036) were independent predictors of reaching the clinical end-point. The authors concluded that CPET is a useful tool for characterizing breathlessness during an exercise test in apparently asymptomatic patients with AS. Peak VO2 less than or equal to 14 ml/kg/min and VE/VCO2 slope greater than 34 were associated with an AET and the occurrence of European Society of Cardiology guideline surgical class I triggers. The findings of this pilot study need to be validated by well-designed studies.

In a review on “Exercise testing in asymptomatic severe aortic stenosis”, Magne et al (2014) stated that exercise stress test is now recommended by current guidelines in asymptomatic patients and may provide incremental prognostic value. Indeed, the development of symptoms during exercise or an abnormal BP response are associated with poor outcome and should be considered as an indication for surgery, as suggested by the most recently updated European Society of Cardiology 2012 guidelines. Exercise stress echocardiography may also improve the risk stratification and identify asymptomatic patients at higher risk of a cardiac event. When the test is combined with imaging, echocardiography during exercise should be recommended rather than post-exercise echocardiography. During exercise, an increase greater than 18 to 20 mm Hg in mean pressure gradient, absence of improvement in left ventricular ejection fraction (i.e., absence of contractile reserve), and/or a systolic pulmonary arterial pressure greater than 60 mm Hg (i.e., exercise pulmonary hypertension) are suggestive signs of advanced stages of the disease and impaired prognosis. Hence, exercise stress test may identify resting asymptomatic patients who develop exercise abnormalities and in whom surgery is recommended according to current guidelines. Exercise stress echocardiography may further
unmask a subset of asymptomatic patients (i.e., without exercise stress test abnormalities) who are at high risk of reduced cardiac event free survival. In these patients, early surgery could be beneficial, whereas regular follow-up seems more appropriate in patients without echocardiographic abnormalities during exercise. This review does not mention the use of CPET.

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<tr>
<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
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<td>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;:</td>
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<td>ICD-10 codes will become effective as of October 1, 2015:</td>
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<td>CPT codes covered if selection criteria are met:</td>
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<td>94621 Pulmonary stress testing; complex (including measurements of CO2 production, O2 uptake, and electrocardiographic recordings)</td>
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<td>ICD-10 codes covered if selection criteria are met:</td>
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<tr>
<td>C34.00 - C34.92 Malignant neoplasm of bronchus and lung</td>
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<td>I42.0 - I43 Cardiomyopathy</td>
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<tr>
<td>I50.1 - I50.9 Heart Failure</td>
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<tr>
<td>J40 - J44.9 Chronic bronchitis, emphysema and other chronic obstructive pulmonary disease</td>
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<td>J47.0 - J47.9 Bronchiectasis</td>
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<tr>
<td>J67.0 - J67.9 Hypersensitivity pneumonitis due to organic dust</td>
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<tr>
<td>J84.111 - J84.117 Idiopathic interstitial pneumonia</td>
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<td>Q20.0 - Q28.9 Congenital malformations of the circulatory system</td>
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<td>Q67.6 Pectus excavatum</td>
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<td>R06.02 Shortness of breath</td>
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<td>Z76.82 Awaiting organ transplant status [lung]</td>
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The above policy is based on the following references:


8. Lauer M, Froelicher ES, Williams M, Kligfield P; American Heart Association Council on Clinical Cardiology, Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention. Exercise testing in asymptomatic adults: A


29. Strickberger SA, Benson DW, Biaggioni I, et al; American Heart Association Councils on Clinical Cardiology, Cardiovascular Nursing, Cardiovascular Disease in the Young, and Stroke; Quality of Care and Outcomes Research Interdisciplinary Working Group; American College of Cardiology Foundation; Heart Rhythm Society. AHA/ACCF scientific statement on the evaluation of syncope: From the American Heart Association Councils on Clinical Cardiology, Cardiovascular Nursing, Cardiovascular Disease in the Young, and Stroke, and the Quality of Care and Outcomes Research Interdisciplinary Working Group; and the American College of Cardiology Foundation In Collaboration With The Heart Rhythm Society. J Am Coll Cardiol. 2006;47(2):473-484.


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aortic aneurysm repair. Br J Anaesth. 2015;114(3):430-
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Feasibility and safety of cardiopulmonary exercise testing

Feasibility and safety of cardiopulmonary exercise testing

38. Moran J, Wilson F, Guinan E, et al. Role of
cardiopulmonary exercise testing as a risk-assessment
method in patients undergoing intra-abdominal surgery:
Amendment to Aetna Clinical Policy Bulletin Number: 0825 Cardiopulmonary Exercise Testing

There are no amendments for Medicaid.