8.01.64	Non-Invasive Positive Airway Pressure for Chronic Obstructive Pulmonary Disease		
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Policy Statement

For patients with chronic obstructive pulmonary disease (COPD) without hypercapnia ($PaCO_2$ less than 52 mmHg) and with obstructive sleep apnea, see Blue Shield of California Medical Policy: Diagnosis and Medical Management of Obstructive Sleep Apnea.

Nocturnal bilevel positive airway pressure with backup rate may be considered **medically necessary** for patients with COPD and chronic respiratory failure who meet **either** of the following:

I. Chronic stable daytime (awake) hypercapnia ($PaCO_2$ greater than or equal to 52 mmHg)
II. Daytime (awake) hypercapnia ($PaCO_2$ greater than or equal to 52 mmHg) at least 2 weeks after discharge from the hospital for an acute exacerbation with decompensated acidosis

Individuals with COPD who are started on bilevel positive airway pressure at discharge from hospitalization may continue for up to 3 months to provide time to stabilize and complete reevaluation.

Non-invasive home mechanical ventilation may be considered **medically necessary** for patients with COPD who meet the following criteria:

I. Qualify for a bilevel positive airway pressure device **AND** meet at least **one** of the following:
   A. Higher pressure (e.g., greater than 25 cm H_2O) is needed to reduce hypercapnia than can be achieved with a bilevel device during titration
   B. Severe hypoxemia requiring FIO_2 greater than 40% or greater than 5 L/min
   C. Daytime use (battery operated unit) is required to reduce hypercapnia

Non-invasive positive airway pressure for COPD is considered **investigational** under all other conditions.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Respiratory failure in patients with COPD is characterized by the inability to sustain normal gas exchange, leading to low arterial blood oxygen (hypoxemia, PaO_2) and/or high arterial carbon dioxide (hypercapnia, $PaCO_2$). Assessment of hypoxemia would lead to supplemental oxygen administration. Stable clinical state is defined as free of exacerbations for at least 4 weeks with pH over 7.35.

Compliance with treatment of at least 4 hours per 24 hours should be documented after the first 3 months of use. There are limited data on which to base compliance assessment. Assessment could be further based on an average of at least 4 hours per 24 hours over a consecutive 30-day period or use of 4 hours per 24 hours for at least 65% of the days in a consecutive 30-day period.

The Centers for Medicare and Medicaid Services (CMS) classifies a respiratory assist device as a bilevel positive airway pressure device with (E0471) or without (E0470) backup respiratory rate capability. Treatment modalities that are reported with the E0471 code include BiPAP ST, ASV,

BiPAP AutoSV, iVAPS, AVAPS. Bi-level devices allow for higher inspiratory pressures with lower expiratory pressures that assist with the work of breathing. Backup rates allow the machine to deliver a breath when the patient does not initiate breathing frequently enough. BiPAP units with batteries have a battery life that is shorter than home mechanical ventilators and are infrequently used in the U.S.

CMS defines non-invasive mechanical ventilators (E0466) as life supporting/sustaining devices used in various settings, including home, hospital, and institutional settings. The non-invasive mechanical ventilators should have at least 6 pressure modes and 3 volume modes, and allow for both invasive (intubated) or non-invasive (mask) use. For examples, see the Regulatory Status section.

Although most patients with comorbid COPD and obstructive sleep apnea can be effectively treated with continuous or auto-adjusting positive airway pressure, approximately 10% of patients will need bilevel positive airway pressure to tolerate the required pressure. These devices are reviewed in Blue Shield of California Medical Policy: Diagnosis and Medical Management of Obstructive Sleep Apnea.

Respiratory therapy in the home may be provided for patients with COPD who are treated with E0466, E0470, or E0471 devices.

Coding

The following codes may be billed for this procedure:

- **E0466**: Home ventilator, any type, used with noninvasive interface, (e.g., mask, chest shell)
- **E0470**: Respiratory assist device, bi-level pressure capability, without backup rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
- **E0471**: Respiratory assist device, bi-level pressure capability, with back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
- **E0601**: Continuous positive airway pressure (CPAP) device

Description

Respiratory failure is characterized by low arterial blood oxygen (hypoxemia, PaO2) and/or high arterial carbon dioxide (hypercapnia, PaCO2 > 45 mmHg). Chronic respiratory insufficiency or failure can occur with chronic obstructive pulmonary disease (COPD) and may result in poor quality of life, sleepiness, hospital admission, intubation, and death. Non-invasive positive airway pressure ventilation (NPPV) including continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP) and home mechanical ventilators (HMV) that are pressure, rate and volume targeted are proposed for the treatment of COPD.

Related Policies

- Diagnosis and Medical Management of Obstructive Sleep Apnea Syndrome

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Numerous CPAP and BPAP devices are available in the U.S. Examples of HMV devices that have both invasive and non-invasive interfaces and are available in the U.S. are described in Table 1.

Table 1. Select Home Mechanical Ventilators with Non-invasive Interface

Device	Manufacturer	FDA clearance	Date	FDA product code
Trilogy™ Evo Ventilator	Respironics	K181166	2019	NOU, CBK
Vivo 60	Breas	K160481	2016	NOU, CBK, DQA, CCK
Astral 100/150	ResMed	K152068	2016	NOU, CBK
Newport™	Medtronic	K121891	2012	NOU, CBK
iVent	GE Healthcare	K092135	2009	NOU, CBK
LTV	Cardinal Health	K083688	2009	CBK
Puritan Bennet 540	Covidien	K082966	2008	CBK

Rationale

Background

Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a common condition, affecting more than 5% of the population, and is associated with high morbidity and mortality. COPD is the fourth leading cause of death in the United States. It is a clinical syndrome with multiple etiologies that is characterized by chronic respiratory symptoms, structural pulmonary abnormalities, and/or lung function impairment. Chronic obstructive pulmonary disease is most frequently associated with cigarette smoking or other air pollutants, and a majority of patients with COPD in the United States have a history of cigarette smoking. Chronic obstructive pulmonary disease is progressive, with expiratory airflow limitation, air trapping/hyperinflation, and destruction of alveoli (emphysema). The Global Initiative for Chronic Obstructive Lung Disease (GOLD), defines COPD as "a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development".[1,2,]

Respiratory failure in patients with COPD is characterized by the inability to sustain normal gas exchange, leading to low arterial blood oxygen (hypoxemia, PaO_2) and/or high arterial carbon dioxide (hypercapnia, $PaCO_2$). Hypercapnia develops in about one-third of patients with COPD and is associated with poor quality of life, sleepiness, frequent hospital admissions due to exacerbations, and an increase in mortality compared to patients with COPD who are normocapnic. The hypercapnia is due in large part to poor lung biomechanics including low inspiratory muscle reserve, high CO_2 production, and a reduced ventilatory capability. [3,] The imbalance between the respiratory load and respiratory capability may in turn affect the ventilatory control center in the brain stem. Physiological changes in responsiveness to hypoxemia and hypercapnia during sleep can be particularly pronounced in patients with COPD, with overnight increases in $PaCO_2$ affecting daytime $PaCO_2$, possibly through bicarbonate retention or changes in cerebrospinal fluid.[4,] Patients with COPD may also have comorbid obstructive sleep apnea and/or obesity hypoventilation syndrome due to decreased ventilatory motor output and upper airway muscle activity during sleep.

Treatment With Non-invasive Positive Airway Pressure

Initial treatment is pharmacological with inhaled (e.g., bronchodilators and glucocorticoids) and oral medications. Long-term oxygen may also be used for patients who have severe hypoxemia.

A major goal of management of patients with COPD is to reduce hospitalizations and mortality. Long-term oxygen therapy is recommended for patients with poor clinical status and noninvasive positive airway pressure ventilation (NPPV) devices for patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure. Noninvasive positive airway pressure ventilation devices include nocturnal continuous positive airway pressure (CPAP) for individuals with hypercapnia due to obstructive sleep apnea or hypoventilation and bilevel positive airway pressure (BPAP) devices or non-invasive home mechanical ventilators that are pressure, rate, and volume targeted. The objective of this evidence review is to describe which features of NPPV are required to improve the net health outcome in patients with COPD. Benefits of nocturnal NPPV persist into the daytime with improved breathing patterns (lower frequencies and larger tidal volumes) and improved gas exchange. Explanations for the improvement in daytime respiration with nocturnal NPPV include increased respiratory drive, improved diaphragm function by unloading the respiratory muscles during sleep, increased CO_2 sensitivity, and reduction in air trapping and hyperinflation. It is not known which factors (e.g., muscle unloading, gas exchange normalization, decrease in hyperinflation) underlie the benefits of NPPV on health outcomes. It is also unclear if the reduction in $PaCO_2$ has an effect on health outcomes or if it is only a marker of effective ventilation.[4,]

Respiratory Assist Devices

The Centers for Medicare and Medicaid Services (CMS) defines respiratory assist devices (RADs) as bilevel devices with or without back-up respiratory rate capability. While CPAP devices provide continuous air at a pressure that prevents the collapse of the airway during inspiration, BPAP devices work by increasing pressure during inspiration and lowering it during expiration (pressure cycled). In some devices a backup respiratory rate is triggered when the patient's nocturnal respiratory rate decreases below a set threshold. The backup rate is typically set 2 breaths below the patient's spontaneous respiratory rate during wakefulness.

Terminology on device features is described in Table 2.

Table 2. Device Features

Term	Definition	Description
Bilevel-S	Bilevel without a backup rate	Positive airway pressure that is higher during inspiration than expiration that is triggered by patient inspiration.
Bilevel-ST	Bilevel with a backup rate	Positive airway pressure that is higher during inspiration than expiration with a backup respiratory cycle length if the patient's breathing is slower than the preset rate.
VAPS	Volume-assured pressure support modes	Bilevel ST modes that use an algorithm to adjust inspiratory pressure support to meet a set tidal volume.
iVAPS	Intelligent volume-assured pressure support modes	Bilevel ST modes that use an algorithm to adjust inspiratory pressure support within a predetermined range to meet a set target ventilation.

Home Mechanical Ventilators

In some patients, nocturnal respiratory assist devices are insufficient to address the respiratory failure. Non-invasive home mechanical ventilators (HMV) are proposed for the treatment of chronic respiratory failure that is refractory to a respiratory assist device. Mechanical ventilators are devices that deliver more controlled breathing with bilevel ventilation at a higher pressure. The ventilators may also have additional features compared to BPAP machines such as alarms and battery backup power. Home mechanical ventilators can be used for patients with tracheostomy in the home, but may also be used with a non-invasive interface such as a mask or mouthpiece in patients who do not depend on 24 hour ventilation for survival. Current technology has decreased the size of home ventilators to around 10 pounds. In addition, some models may be wireless with battery backup, allowing greater mobility during the day.

Titration

Early studies with low intensity NPPV did not demonstrate health benefits in patients with hypercapnia. More recent studies have reinforced the importance of high-intensity NPPV (> 18 cm H_2O) that is titrated to decrease hypercapnia. A high respiratory backup rate that is increased to the level of spontaneous breathing has also been shown to be important to achieve positive health outcomes. Manually set, laboratory or hospital titration of NPPV with pressure control and backup rate have been recommended for stable hypercapnic COPD.[5,] The goal of titration of inspiratory positive airway pressure is to achieve normocapnia, a reduction in transcutaneous CO_2, or maximum tolerable inspiratory pressure. A fast rise in inspiratory pressure (rise time) allows enough time for expiration within the normal rate of breathing. In patients with air trapping and hyperinflation, use of positive end-expiratory pressure can also be beneficial.

A suggested protocol for in-laboratory titration of NPPV in patients with COPD in the U.S. is described by Orr et al (2020).[4,] Titration of NPPV is usually performed in a monitored environment after the patient has stabilized, as studies have not found an improvement in health outcomes when NPPV is started soon after an acute exacerbation. Polysomnography or respiratory monitoring may be used during titration to evaluate the presence of obstructive sleep apnea or hypoventilation. The inspiratory pressure is typically started at 6 to 8 cm H_2O of pressure support above the expiratory pressure and titrated to reduce hypercapnia. A Bilevel-ST (with backup rate) or a VAPS (volume assured) may be used if a Bilevel-S (without backup rate) fails to adequately reduce hypercapnia. Although titration in European studies has been performed with a hospital stay, this is not feasible in the U.S., and titration might be performed over several weeks in the patient's home by an external durable medical equipment (DME) provider.

Pulmonary Rehabilitation

Pulmonary rehabilitation is a personalized intervention that includes physical activity (e.g., activities of daily living, endurance exercises and muscle strengthening), health education, and psychological support. It may be performed in the hospital, outpatient clinic, or home, and has been shown to reduce mortality, exacerbation rate, intensive care admissions, and emergency department visits. Pulmonary rehabilitation is common in Europe but is less frequently provided in the U.S.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Continuous Positive Airway Pressure
Clinical Context and Therapy Purpose
Sleep-related breathing disorders are common in patients with chronic obstructive pulmonary disease (COPD). The coexistence of COPD and obstructive sleep apnea (OSA) is associated with more pronounced hypoxemia and hypercapnia than either condition individually, and patients are at greater risk of morbidity and mortality compared to patients who have either COPD or OSA alone. The purpose of continuous positive airway pressure (CPAP) in patients with overlap syndrome is to reduce morbidity and mortality in this population.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is patients with COPD who have clinically significant OSA. Obstructive sleep apnea is a partial or intermittent upper airway collapse that results in hypoxemia and arousal during sleep (see Blue Shield of California Medical Policy: Diagnosis and Medical Management of Obstructive Sleep Apnea).

Clinically significant OSA in adults that is indicated for treatment is defined as:
- An Apnea/Hypopnea Index or Respiratory Disturbance Index of at least 15 events per hour, OR
- An Apnea/Hypopnea Index or Respiratory Disturbance Index of at least 5 events per hour in a patient with 1 or more signs or symptoms associated with OSA (e.g., excessive daytime sleepiness, hypertension, cardiovascular heart disease, or stroke);

The criterion standard for a diagnosis of sleep disorders is a polysomnogram performed in a sleep laboratory. A standard polysomnogram includes electroencephalogram, submental electromyogram, and electrooculogram (to detect rapid eye movement sleep) for sleep staging. Polysomnography also typically includes electrocardiography and monitoring of respiratory airflow, effort, snoring, oxygen desaturation, and sleep position. A variety of devices have been developed specifically to evaluate OSA at home. They range from portable full polysomnography systems to single-channel oximeters. Available devices evaluate different parameters, which may include oximetry, respiratory and cardiac monitoring, and sleep/wake activity.

A definition of terms and scoring criteria for OSA are described in Table 3.

Table 3. Definitions of Terms and Scoring Criteria for Obstructive Sleep Apnea

Terms	Definition
Respiratory event	
Apnea	The frequency of apneas is measured from channels assessing oxygen desaturation, respiratory airflow, and respiratory effort. In adults, apnea is defined as a drop in airflow by 90% or more of pre-event baseline for at least 10 seconds.
Hypopnea	Hypopnea in adults is scored when the peak airflow drops by at least 30% of pre-event baseline for at least 10 seconds in association with either at least 3% or 4% arterial oxygen desaturation (depending on criteria) or an arousal.
Positive airway pressure	
APAP	Auto-adjusting positive airway pressure may be used either to provide treatment or to determine the most effective pressure for CPAP.
BPAP	Bilevel positive airway pressure that is higher on inspiration than expiration.
CPAP	Continuous positive airway pressure provides the same pressure throughout the breathing cycle.
PAP	Positive airway pressure that may be continuous (CPAP), auto-adjusting (APAP), or bilevel (BPAP).

Comparators
The following therapies are currently being used to make decisions about patients with overlap of COPD and OSA: medical treatment for COPD without treatment for OSA.

Outcomes
The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. These are measured with a variety of tools as shown in Table 4.

Table 4. Health Outcome Measures Relevant to Patients with COPD

Outcome	Measure (Units)	Description
Readmission	Measured as readmission-free survival or time to readmission	May be part of a composite of readmission or death
Mortality	Measured as time to death or percent mortality within a set period	May be specific to chronic obstructive pulmonary disease or overall
PaO_2	Partial pressure of oxygen (kPa or mmHg)	The level of arterial oxygen.
$PaCO_2$	Partial pressure of carbon dioxide (kPa or mmHg)	The level of arterial carbon dioxide. Some studies have used a threshold of 45 mmHg. Severe hypercapnia is $PaCo_2$ > 7.3 kPa or > 52 mmHg.
6MWD	Six-minute walking distance (meters)	The distance that can be walked in 6 minutes.
HRQL	Health-related quality of life	Severe Respiratory Insufficiency Questionnaire (SRI) or the St George's Respiratory Questionnaire (SGRQ)

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Systematic Reviews
A 2021 evidence review by the American Thoracic Society found several studies suggesting that identification and treatment with CPAP in patients with overlap syndrome improves outcomes.[2,] However, no trials were identified that compared an OSA screening strategy with no screening strategy in patients with stable hypercapnic COPD or with use of CPAP in patients already on other modes of positive airway pressure (PAP).

Observational Studies
Marin et al (2010) evaluated outcomes of patients who have both COPD and OSA from a prospective database of patients referred to a university sleep clinic.[6,] The authors analyzed 3 groups of patients; those with overlap syndrome who were started on CPAP (n=228), those with overlap syndrome not treated with CPAP (n=213), and patients with COPD who did not have OSA (n=210). Patients were seen at least once a year or until death, and the primary outcome was time to death from any cause. The secondary outcome was the time to first severe COPD exacerbation requiring hospitalization. There were 589 patients with overlap syndrome and 210 with COPD and simple snoring. Positive pressure was recommended for 468 patients, another 121 patients did not qualify for CPAP and were given other options for treatment.

Of the 468 patients with overlap syndrome who received a recommendation for PAP, 228 were treated with CPAP, 27 were treated with bilevel positive airway pressure (BPAP), and 213 did not accept treatment. The apnea/hypopnea index (AHI) was similar (35 vs. 34) in the 2 groups; these patients would have received a recommendation for treatment based on presence of clinically significant OSA. Median follow-up was 9.4 years (range, 3.3 to 12.7). When compared to patients with COPD only, patients with overlap syndrome who were not treated with PAP had a higher

mortality risk (42.2% vs. 24.2%; relative risk [RR] 1.79; 95% confidence interval [CI]: 1.16 to 2.77) and were more likely to suffer a severe COPD exacerbation leading to hospitalization (RR 1.70; 95% CI: 1.21 to 2.38). Patients with overlap syndrome treated with CPAP did not have a statistically significant increased risk for death from any cause (31.6%) compared to patients with COPD only (24.2%). There were a number of baseline differences between the COPD only and the overlap syndrome groups which may impact mortality, but the 2 overlap groups were well matched for baseline characteristics. The main conclusion of the study was that patients with COPD should be screened for OSA and offered treatment.

Similar findings were reported by Machado et al (2010), who reported a prospective comparative study of 95 patients with moderate to severe OSA and hypoxemic COPD who were offered CPAP treatment.[7] Of the 95 patients, 61 (64%) accepted CPAP and were adherent while 34 did not accept or were not adherent. After adjusting for confounders, patients treated with CPAP had a significantly lower risk of death (hazard ratio of 0.19; 95% CI: 0.08 to 0.48).

Other studies have evaluated the patient characteristics that show most benefit from PAP.

Jaoude et al (2014) evaluated 271 consecutive patients with overlap syndrome who were seen at a Veterans Administration sleep center.[8] Of the 271 overlap patients identified, 104 were considered hypercapnic (mean $PaCO_2$ = 51.6 $\pm$ 4.3 mmHg), indicating that the level of hypercapnia was lower than in other studies that had a threshold of 52 mmHg. The normocapnic and hypercapnic patients had similar AHI (29.3 $\pm$ 23.8 and 35.2 $\pm$ 29.2 events per hour, respectively; p=.07) and similar adherences rates to CPAP (43% and 42%, respectively). During a median follow-up of 71 months, mortality was higher in patients who were hypercapnic (35%) compared to patients who were normocapnic (17%, p=.001). Mortality in patients who were hypercapnic was lower in those who were adherent to CPAP compared to those who were not (p=.04), but adherence to CPAP had little impact on mortality in normocapnic patients (p=.42).

Singh et al (2019) evaluated the impact of PAP therapy on emergency room visits and hospitalization rates in Medicare beneficiaries with overlap syndrome.[9] Using a 5% Medicare sample of claims data from 2010 to 2012, they identified 319 patients with overlap syndrome who were new users of PAP therapy in 2011. Subjects were categorized by age (66-74, 75-84, >85), gender, race, socioeconomic status, CMS geographic region, comorbidity score, COPD complexity, tobacco use, and selected comorbidities. Comorbidities included hypertension (84%), diabetes (42%), and congestive heart failure (32%); 63% of individuals had 3 or more comorbidities. COPD complexity was based on pulmonary and non-pulmonary comorbid conditions and the prevalence of exacerbations and utilization of healthcare services; 26.0% of individuals were considered low complexity, 57.7% moderate complexity, and 16.3% high complexity. When compared with the year before PAP initiation, hospitalization for COPD-related conditions was significantly reduced (19.4% vs. 25.4%, p=.03). Rates of emergency room visits and hospitalization for any cause were not significantly different for the pre- and post-initiation periods. Although the benefit was seen primarily in patients who were considered to be of higher complexity, no information could be obtained from the claims data on the severity of COPD and OSA.

Section Summary: Continuous Positive Airway Pressure

The evidence on use of CPAP in patients with COPD includes observational studies of patients with both COPD and OSA who do or do not use CPAP and a systematic review of those studies. Studies show a mortality benefit in patients with overlap syndrome who are treated with PAP. The greatest benefits occur in patients with COPD and hypercapnia and in older adults, and individuals with more comorbid conditions and higher complexity ratings. It should be noted that the mean $PaCO_2$ was 51.6 $\pm$ 4.3 mmHg in at least one study, indicating that the threshold for what was considered hypercapnia was lower than the threshold for hypercapnia in other studies (see below). Although the literature indicates that patients with COPD should be screened for OSA due to increased mortality in overlap syndrome, no studies were identified to indicate that

CPAP would be prescribed in any manner other than would typically be recommended for patients with clinically significant OSA (see Blue Shield of California Medical Policy: Diagnosis and Medical Management of Obstructive Sleep Apnea).

Bilevel Positive Airway Pressure

Clinical Context and Therapy Purpose

Morbidity and mortality are high in patients with COPD and chronic respiratory failure. Despite maximal medical therapy, the occurrence of acute exacerbations requiring hospitalizations is high, and a substantial percentage of patients will die within 1 year. The purpose of bilevel non-invasive positive airway pressure ventilation (NPPV) in patients who have COPD and chronic respiratory failure is to improve function and quality of life and to reduce acute exacerbations and death.

The following PICO was used to select literature to inform this review.

Populations

The relevant populations of interest are patients with COPD who have chronic respiratory failure or who have had an acute exacerbation.

Interventions

The therapy being considered is bilevel NPPV with or without a backup rate.

Comparators

The following therapies are currently being used to treat COPD with chronic respiratory failure: medications and home oxygen therapy.

Outcomes

The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. These are measured with a variety of tools as shown in Table 4. This is a chronic treatment in a patient population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 months to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

An updated Cochrane review by Raveling et al (2021) evaluated the evidence for nocturnal NPPV for the treatment of either stable COPD or COPD after an acute exacerbation.[10,] The primary outcomes were arterial blood gas and exercise capacity measured with the 6-minute walk distance (6MWD) as well as readmissions for acute exacerbations. Where available, the meta-analysis included individual patient data (chronic: n=778; acute exacerbation: n=364) along with missing data from the primary RCTs. Criteria for inclusion were RCT, NPPV prescribed for at least 4 hours per night, and use for greater than 3 weeks; trials that allowed daytime use

were excluded from the review. Most of the trials were conducted in Europe and excluded patients with OSA or high body mass index (BMI).

The update included 17 trials on stable COPD and 4 trials on NPPV after an acute exacerbation of COPD. Bilevel positive airway pressure with a backup rate was used in 3 studies, including the trials by Kohnlein et al (2014), Murphy et al (2017) and Struik et al (2014) described below. Eight studies were judged to be at low risk of bias, including the 3 by Kohnlein et al, Murphy et al and Struik et al. Sources of heterogeneity were baseline hypercapnia ($PaCO_2$ < 7.3 kPa vs. ≥ 7.3 kPa) and the mean inspiratory pressure of NPPV (< 18 cm H_2O vs. ≥ 18 cm H_2O). Sensitivity analysis removing studies with high or unclear risk of bias in the chronic COPD cohort increased the treatment effects for PaO_2, $PaCO_2$, 6MWD, and health related quality of life (HRQL). The authors concluded that the addition of chronic NPPV to standard treatment improves diurnal hypercapnia (high certainty), and there was evidence that NPPV improved PaO_2 and all cause mortality (moderate certainty) and HRQL (very low certainty). In patients with stable COPD, the effect on gas exchange seemed to be larger in people with more severe hypercapnia ($PaCO_2$ ≥ 7.3 kPa), better treatment compliance (> 5 hours per night), and treated with a high inspiratory pressure (IPAP ≥ 18 cm H_2O). The uncertain contribution of improvements in gas exchange, along with possible mechanisms, for an improvement in health outcomes were discussed.

Wilson et al (2020) published a meta-analysis that included 21 RCTs and 12 observational studies (N=51,085) on patients with COPD and hypercapnia treated with NPPV.[11,]. Of these, 15 RCTs and 6 observational studies evaluated BPAP compared with no device. The BPAP modes were spontaneous/timed, volume-assured pressure support, pressure-controlled ventilation, or the mode was not specified. The primary outcomes were mortality, all-cause hospital admissions, intubation, and quality of life. Analysis indicated that overall, use of BPAP, compared with no device, was significantly associated with a lower risk of mortality (odds ratio [OR] 0.66), fewer patients with hospital admissions (OR 0.22), and lower need for intubation (OR 0.34). There was no significant difference in quality of life, and sensitivity analysis indicated that observational studies were driving the significant results. Further analysis of subgroups evaluated the timing of the initiation of NPPV (stable vs. recent exacerbation) and separated the $PaCO_2$ threshold categories as 45 to 49 mmHg, 50 to 51 mmHg, and at least 52 mmHg. Post-hoc subgroup analysis found no significant differences in mortality or all-cause hospital admissions based on $PaCO_2$ levels, but improved quality of life in patients with higher $PaCO_2$ levels.

A 2020 evidence review by the American Thoracic Society evaluated NPPV on health outcomes in patients with stable hypercapnic COPD (Table 5).[2,] Studies varied in the severity of baseline hypercapnia and lung disease, mode of ventilation, pressure settings, and comparator, all of which may have contributed to the imprecision of the studies.

Table 5. Effect of Non-invasive Positive Pressure Ventilation on Health Outcomes in Patients With Stable Hypercapnic COPD

Outcome	Effect	Level of Certainty
Mortality	RR: 0.86 (0.58 to 2.27)	Low
Hospitalizations	MD: -1.26 (-2.59 to 0.08)	Low
Quality of Life	MD: 0.48 (0.09 to 0.88)	Low
Dyspnea	SMD: -0.51 (-0.95 to -0.06)	Moderate

MD: mean difference; RR: relative risk; SMD: standardized mean difference

Randomized Controlled Trials

Chronic Hypercapnic Respiratory Failure

Kohnlein et al (2014) conducted a multicenter RCT to determine whether BPAP would improve survival in patients with COPD and stable hypercapnic respiratory failure when ventilator settings were targeted to reduce hypercapnia.[12,] Patients (N=195) with GOLD stage IV COPD, $PaCO_2$ 51.9 mmHg or higher, and pH higher than 7.35 were randomized into treatment as usual (including O_2), or BPAP plus treatment as usual. Excluded were patients with BMI of 35 kg/m2 or greater, abnormalities of the lung or thorax other than COPD, or other conditions resulting in

hypercapnia. Titration was performed in the hospital over a mean of 5.6 days with pressure targeted to reduce the baseline $PaCO_2$ by at least 20% or to achieve $PaCO_2$ < 48.1 mmHg. The mean inspiratory pressure in the NPPV group was 21.6 cm H_2O with a backup rate of 16.1. Patients in both groups were admitted to the hospital at 3, 6, 9, and 12 months after randomization to ensure optimized treatment and additionally contacted by telephone every 4 weeks to ensure adherence to therapy. At 12 months, the $PaCO_2$ was 48.8 mmHg in the NPPV group (mean use of 5.9 hours per day) compared to 55.5 in the control group. The primary outcome of 1-year all cause mortality was 12% in the NPPV group compared to 33% in the control group, with a hazard ratio of 0.24 (95% CI: 0.11 to 0.49; p=.004). Emergency hospital admissions were limited to 3 patients (3%) in the control group. The study utilized intention-to-treat analysis with blinded outcomes assessors. Previous studies that had not shown a significant improvement in survival with NPPV included patients with mild hypercapnia who did not have reduced hypercapnia or improved blood gases with treatment.[13,]

Post-Acute Hypercapnic Respiratory Failure

Murphy et al (2017) reported an RCT on the use of BPAP in addition to home oxygen therapy in patients with persistent hypercapnia following acute respiratory failure in the Home Oxygen Therapy Home Mechanical Ventilation (HOT-HMV) trial.[14,] Patients (N=116) who had persistent hypercapnia following hospitalization for an acute exacerbation of COPD were randomized to a BPAP device with home oxygen therapy (NPPV+O_2) or to oxygen therapy alone (O_2). Randomization occurred between 2 to 4 weeks after resolution of decompensated acidosis (arterial pH > 7.30) in patients who had persistent hypercapnia ($PaCO_2$ > 53 mmHg) and hypoxemia (PaO_2 < 55 mmHg or < 60 mmHg; ≥ 1 of polycythemia, pulmonary hypertension, or cor pulmonale; > 30% of sleep time with oxygen saturation < 90% as measured by pulse oximetry) and arterial pH greater than 7.30 while breathing room air. Patients were admitted for inpatient titration with either the Harmony 2 ST (Philips-Respironics) or VPAP IIIST (ResMed) with pressure support and backup rate. Settings were adjusted during overnight sleep studies to control hypoventilation and hypoxemia with a median inspiratory positive airway pressure of 24 cm H_2O. Respiratory failure was attributed to COPD if FEV_1 was less than 50% predicted, the FEV_1/FVC ratio was less than 60%, and the patient had a smoking history in the absence of 1) obesity (BMI > 35), 2) clinically significant obstructive sleep apnea, or 3) neuromuscular or chest wall disease. $PaCO_2$ levels improved significantly more in the NPPV group at 6 weeks (between group difference of -5.0; 95% CI: -9.0 to -1.3) and 3 months (-4.0; 95% CI:-7.1 to -0.8) but not at 6 or 12 months. Improvements in PaO_2 levels were not significantly different in the 2 groups. There was a significant reduction in the composite endpoint of readmission or death within 12 months (63.4% in the NPPV+O_2 group vs. 80.4% in the O_2 alone group), with an adjusted hazard ratio of 0.49 (95% CI: 0.31 to 0.77; p=.002) and a number needed to treat of 5.8 to prevent 1 readmission or death. The median time to readmission or death was 4.3 months in the NPPV+O_2 group and 1.4 months in patients receiving oxygen alone, and the exacerbation rate in 12 months was reduced to 3.8 for the NPPV+O2 group compared to 5.1 with O_2 alone (adjusted rate ratio 0.66; 95% CI: 0.46 to 0.95, p=.02). Twelve month mortality was not significantly different between the groups. The study utilized intention-to-treat analysis with blinded outcomes assessors.

Several differences were noted between the results of the HOT-HMV trial and the RESCUE trial, which failed to demonstrate an improvement in hospitalizations or mortality.[15,]In the RESCUE trial there was less stringent $PaCO_2$ criteria (>45 mmHg) and treatment began immediately following cessation of acute ventilation rather than after a 2 week stabilization period, so that patients with spontaneously reversible hypercapnia would have been included in the study. For example, in the HOT-HMV trial 21% of potential patients were excluded due to not meeting the $PaCO_2$ criteria 2 weeks after the acute exacerbation. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) notes that several factors may account for discrepancies in study results, including differences in patient selection, underpowered studies, NPPV settings, and poor adherence.[1,]

Section Summary: Bilevel Positive Airway Pressure
The evidence on bilevel NPPV includes RCTs and systematic reviews of those RCTs. The primary limitation of the evidence base is the heterogeneity of patient selection criteria and treatment parameters. The most recent trials indicate that bilevel NPPV improves hypercapnia in both patients with stable hypercapnia and in patients who have stabilized following an acute exacerbation. There is evidence that some health outcomes including function, readmissions, and death are improved, although the strength of evidence is low. Notable differences between the results of the HOT-HMV trial and the RESCUE trial, which failed to demonstrate an improvement in hospitalizations or mortality, are that in the RESCUE trial there was less stringent $PaCO_2$ criteria (> 45 mmHg) and treatment began immediately following cessation of acute ventilation, so that patients with spontaneously reversible hypercapnia may have been included in the study. Meta-analysis of individual patient data supports the importance of the level of hypercapnia and intensity of the pressure on outcomes in patients with COPD. Other factors that are reported to be important to achieve benefit of NPPV include use for at least 5 hours per night, and for patients with hypercapnia following an acute exacerbation, titration should occur at least 2 weeks after hospitalization when hypercapnia has stabilized.

Home Mechanical Ventilation
Clinical Context and Therapy Purpose
The purpose of non-invasive home mechanical ventilation (HMV) in patients who have COPD is to provide a treatment option that is an improvement over high flow oxygen or BPAP.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is patients with COPD and chronic respiratory failure that is refractory to pharmacologic management, oxygen, and BPAP.

Interventions
The therapy being considered is HMV. Mechanical ventilators are devices that deliver more controlled breathing with bilevel ventilation. They can be used either invasively with tracheostomy or non-invasively with a mask. Compared to BPAP, HMVs have additional ventilatory modes and ventilatory control along with features such as alarms and battery backup power for patients who require backup at night or daytime use with mobility. HMVs are classified by the U.S. Food and Drug Administration as life support devices.

Comparators
BPAP with high flow oxygen may be used to treat patients with COPD and chronic respiratory failure.

Outcomes
The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. These are measured with a variety of tools as shown in Table 4. This is a chronic treatment in a patient population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

A technology assessment by the Agency for Healthcare Research and Quality (AHRQ, 2019) for the Centers for Medicare and Medicaid Services identified 5 studies on the initiation of HMV.[16,] No studies were identified that compared initiation criteria for HMV versus BPAP. The AHRQ systematic review found low quality evidence that HMV compared to BPAP, CPAP, or no device was associated with significantly fewer hospital admissions. This was based on 2 observational studies that compared HMV to no device and a large study of administrative claims data (Vasquez et al, 2017, described below) that compared HMV, BPAP, and CPAP.
In 2020 the AHRQ authors published a meta-analysis of RCTs and comparative observational studies of patients with COPD and hypercapnia treated with BPAP or HMV.[11,]. The primary outcomes were mortality, all-cause hospital admissions, intubation, and quality of life. Based on 2 observational studies, HMV was significantly associated with fewer all-cause hospital admissions (rate ratio, 0.50; 95% CI, 0.35 to 0.71) compared with no device, but there was not a statistically significant difference in mortality (21.84% vs. 34.09%; OR, 0.56 (0.29 to 1.08). However, the evidence was low to moderate in quality and based on small numbers of studies.

Observational Studies

Vasquez et al (2017) performed a retrospective analysis of claims data of hospitalization in patients with COPD who did or did not receive therapy with CPAP, BPAP, or HMV.[17,] Differences in COPD-related hospitalization were compared from 6 months before the prescription of a device to 6 months after prescription of a device across the device types. Models were stratified by sleep disordered breathing, congestive heart failure, age less than or greater than 65 years, and chronic respiratory failure. There were 1,881,652 enrollees with at least 2 COPD-related claims; 28,774 were on BPAP, 112,119 on CPAP, and 1011 enrolled on HMV. After exclusion criteria (health plan coverage for 12 month before and 6 months after the index date) were applied, there were 39,385 patients on CPAP, 9,156 patients on BPAP, and 315 patients on HMV who were included in the analysis. Propensity matching was used to compare the NPPV groups to medication groups. Most patients (92.5%) were not receiving any form of NPPV. Continuous positive airway pressure was prescribed for 5.6% of patients, BPAP for 1.5% of patients, and HMV in less than 1% of patients. Most patients prescribed HMV were older and there was high geographic variability; a majority (59.1%) of HMV users resided in the south. A majority of patients prescribed CPAP or BPAP had co-morbid sleep-disordered breathing (57.4% and 59.1%, respectively), while HMV was prescribed most frequently in patients with acute respiratory failure (56.5%), hypoxemia (30.2%), and chronic respiratory failure (28.3%). Sleep disordered breathing was present in 20.3% of patients using HMV. Hospitalization rates were highest in the HMV group. While all forms of NPPV reduced hospitalization rates, HMV was associated most strongly with a reduction in hospitalizations ($p<.001$).

Section Summary: Home Mechanical Ventilation

There is low strength of evidence based on observational studies and claims data that HMV reduces the number of hospital admissions or number of patients with hospitalization compared to either no device or BPAP. Analysis of claims data also suggests that HMV is prescribed most frequently in patients with acute and chronic respiratory failure or hypoxemia. Due to the severity of the condition, high quality prospective controlled trials are unlikely in patients who have failed BPAP. It was also observed that there is high geographic variability in prescribing HMV. This finding suggests a possibility of inappropriate use in some areas of the country. Due to the severity of the condition, high quality prospective controlled trials are unlikely in patients who have failed BPAP. Therefore, HMV may be appropriate in situations where BPAP is not adequate to obtain needed pressures or when daytime use and battery backup is needed.

Summary of Evidence
For individuals who have COPD and OSA who receive CPAP, the evidence includes observational studies. Relevant outcomes are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. Studies of patients with both COPD and OSA who do or do not use CPAP show a mortality benefit in patients with overlap syndrome who are treated with positive airway pressure. The greatest benefits occur in patients with COPD and hypercapnia and in older adults, and individuals with more comorbid conditions and higher complexity ratings. It should be noted that the threshold for what was considered hypercapnia was lower than in other studies on BPAP that used a threshold of $PaCO_2$ > 52 mm Hg. Although the literature indicates that patients with COPD should be screened for OSA due to increased mortality in overlap syndrome, no studies were identified to indicate that CPAP would be prescribed in any manner other than would typically be recommended for patients with clinically significant OSA (see Blue Shield of California Medical Policy: Diagnosis and Medical Management of Obstructive Sleep Apnea). Patients with overlap syndrome can be treated with CPAP and, when CPAP is not tolerated, with BPAP. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have COPD and chronic respiratory failure who receive BPAP, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. The primary limitation of the evidence base is the heterogeneity of patient selection criteria and treatment parameters. The most recent trials indicate that bilevel NPPV improves hypercapnia in both patients with stable hypercapnia and in patients who have stabilized following an acute exacerbation. There is evidence that some health outcomes including function, readmissions, and death are improved; however, the strength of evidence is low. Several factors have been reported to be important to achieve benefit of NPPV. These are severe hypercapnia with $PaCO_2$ > 52 mmHg, use for at least 5 hours per night, and treatment with high intensity pressure. In addition, for patients with hypercapnia following an acute exacerbation, titration should occur at least 2 weeks after hospitalization when hypercapnia has stabilized. Under these conditions, the evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have COPD and chronic respiratory failure when BPAP is inadequate who receive HMV, the evidence includes observational studies and an analysis of administrative claims data. Relevant outcomes are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. There is low strength of evidence based on observational studies and claims data that NPPV reduces the number of hospital admissions or number of patients with hospitalization compared to either no device or BPAP. Due to the severity of the condition, high quality prospective controlled trials are unlikely in patients who have failed BPAP. HMV may be appropriate in situations where BPAP is not adequate to obtain needed pressures or when daytime use and battery backup is needed. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Thoracic Society

Chronic Obstructive Pulmonary Disease

In 2020, the American Thoracic Society published an evidence-based clinical practice guideline on long-term non-invasive ventilation in chronic stable hypercapnic chronic obstructive pulmonary disease (COPD).[2,] The society included the recommendations in Table 6, all of which were conditional due to moderate to very low certainty in the evidence base.

Table 6. American Thoracic Society Recommendations

Recommendation	Strength of Recommendation	Level of Certainty
"We suggest the use of nocturnal noninvasive ventilation (NIV) in addition to usual care for patients with chronic stable hypercapnic COPD."	Conditional	Moderate
"We suggest that patients with chronic stable hypercapnic COPD undergo screening for obstructive sleep apnea before initiation of long-term NIV."	Conditional	Very low
"We suggest not initiating long-term NIV during an admission for acute on-chronic hypercapnic respiratory failure, favoring instead reassessment for NIV at 2–4 weeks after resolution."	Conditional	Low
"We suggest not using an in-laboratory overnight polysomnogram (PSG) to titrate NIV in patients with chronic stable hypercapnic COPD who are initiating NIV."	Conditional	Very low
"We suggest NIV with targeted normalization of $PaCO_2$ in patients with hypercapnic COPD on long-term NIV."	Conditional	Low

COPD: chronic obstructive pulmonary disease; NIV: non-invasive ventilation; PaCO2: pressure of carbon dioxide; PSG: polysomnogram.
Hypercapnic COPD defined as PaC_{O2} > 45 mmHg.

American College of Chest Physicians et al

In 2021, the American College of Chest Physicians, the American Association for Respiratory Care, the American Academy of Sleep Medicine, and the American Thoracic Society published a technical expert panel report on optimal noninvasive ventilation for COPD.[18,] The panel recommends that overnight oxygen saturation should not be part of the criteria for bilevel positive airway pressure (BPAP) and that home mechanical ventilators be considered when patients need any of the following:

- "Higher inspiratory pressures than those deliverable by E0471
- FIO_2 higher than 40% or 5 L/min nasally
- Ventilator support for 10 h per day or greater (i.e., daytime use)
- Both sophisticated alarms and accompanying internal battery (high-dependency patient)
- Mouthpiece ventilation during the day
- Persistence of hypercapnia with $PaCO_2 \geq$ 52 mm Hg despite adequate adherence to BPAP therapy"

The panel strongly recommended the use of respiratory therapists in the home for initiation and ongoing support for positive pressure ventilation with either BPAP or home ventilators.

National Institute for Health and Care Excellence Global

In 2019, the United Kingdom's National Institute for Health and Care Excellence (NICE) published a guideline for the diagnosis and management of COPD.[19,] NICE recommends that patients with COPD who have chronic hypercapnic respiratory failure despite adequate pharmacologic and oxygen therapy should be referred to a specialist center for consideration of long-term, non-invasive ventilation.

Global Initiative for Chronic Obstructive Pulmonary Disease

The Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) published a revised report for 2022.[1,] GOLD recommendations include:

- "Pulmonary rehabilitation improves dyspnea, health status and exercise tolerance in stable patients (Evidence A)."
- "Pulmonary rehabilitation reduces hospitalization among patients who have had a recent exacerbation (≤ 4 weeks from prior hospitalization)(Evidence B).
- "In patients with severe resting hypoxemia long-term oxygen therapy is indicated (Evidence A)."
- "In patients with stable COPD and moderate resting or exercise-induced arterial desaturation, prescription of long-term oxygen does not lengthen time to death or first hospitalization or provide sustained benefit in health status, lung function and 6-minute walk distance (Evidence A).
- "In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long term non-invasive ventilation may be considered (Evidence: B)." Pronounced daytime persistent hypercapnia was reported as ($PaCO_2 \geq$ 52 mmHg).

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.
The Centers for Medicare and Medicaid Services has requested topic review by the Agency for Healthcare Research and Quality (AHRQ). The technology assessment was published February 2020.[16,]

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 7.

Table 7. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01037387	Effect of the Noninvasive Mechanical Ventilation on the Daily Physical Activity and the Inflammatory Biomarkers in Stable Patients With COPD	50	Dec 2021
NCT02811588	Registry of Stable Hypercapnic Chronic Obstructive Pulmonary Disease Treated With Non-Invasive Ventilation Amendment: Home Tele-Monitoring of Non-Invasive Ventilation in Chronic Obstructive Pulmonary Disease	550	Jun 2023
NCT03647462	The Impact of Early Diagnosis and Treatment of OSA on Hospital Readmission in Hospitalized Chronic Obstructive Pulmonary Disease Patients: the COPD Readmit Clinical Trial	100	Apr 2025
NCT03221101	Home Non Invasive Ventilation Versus Long Term Oxygen Therapy Alone in COPD Survivors After Acute Hypercapnic Respiratory Failure. A French Multicenter Randomized Controlled Trial	86	Dec 2025
Unpublished			
NCT01513655[a]	Home Non Invasive Ventilation (NIV) Treatment for COPD-patients After a NIV-treated Exacerbation	150	July 2020 (unknown)
NCT03766542	Optimal Positive Airway Pressure in Overlap Syndrome: a Randomized Controlled Trial	70	Sep 2020 (unknown)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - Clinical findings (i.e., pertinent symptoms and duration)
  - Comorbidities
  - Activity and functional limitations
  - Reason for device
  - Pertinent past procedural and surgical history (e.g., for OSA or lungs)
  - Past and present pertinent diagnostic testing and results (including but not limited to daytime arterial blood gas (ABG) with PaCO2, PaO2 or pH)
  - Prior conservative treatments, duration, and response
  - Treatment plan (i.e., surgical intervention, CPAP, BiPAP)
- Consultation report(s), when applicable
- Radiology report(s) and interpretation (i.e., MRI, CT, discogram) when applicable

Post Service (in addition to the above, please include the following):

- Results/reports of tests performed including after interventions
- Procedure report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	None	
HCPCS	E0466	Home ventilator, any type, used with noninvasive interface, (e.g., mask, chest shell)
	E0470	Respiratory assist device, bi-level pressure capability, without backup rate feature, used with noninvasive interface, e.g., nasal or facial

Type	Code	Description
		mask (intermittent assist device with continuous positive airway pressure device)
	E0471	Respiratory assist device, bi-level pressure capability, with back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
	E0601	Continuous positive airway pressure (CPAP) device

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
04/01/2022	New policy.
06/01/2022	Policy statement and guidelines updated

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE **Red font: Verbiage removed**	**AFTER** **Blue font: Verbiage Changes/Additions**
Non-Invasive Positive Airway Pressure for Chronic Obstructive Pulmonary Disease 8.01.64 **Policy Statement:** For patients with chronic obstructive pulmonary disease (COPD) without hypercapnia ($PaCO_2$ less than 52 mmHg) and with obstructive sleep apnea, see Blue Shield of California Medical Policy: Diagnosis and Medical Management of Obstructive Sleep Apnea. Nocturnal bilevel positive airway pressure with backup rate may be considered **medically necessary** for patients with COPD and chronic respiratory failure who meet **either** of the following: I. Chronic stable daytime (awake) hypercapnia ($PaCO_2$ greater than or equal to 52 mmHg) II. Daytime (awake) hypercapnia ($PaCO_2$ greater than or equal to 52 mmHg) at least 2 weeks after resolution of an acute exacerbation with decompensated acidosis Individuals with COPD who are started on bilevel positive airway pressure at discharge from hospitalization may continue for up to 3 months to provide time to stabilize and complete reevaluation. Non-invasive home mechanical ventilation may be considered **medically necessary** for patients with COPD who meet the following criteria: I. Qualify for a bilevel positive airway pressure device **AND** meet at least **one** of the following: A. Higher pressure (e.g., greater than 25 cm H_2O) is needed to reduce hypercapnia than can be achieved with a bilevel device during titration B. Severe hypoxemia requiring FIO_2 greater than 40% or greater than 5 L/min C. Daytime use (battery operated unit) is required to reduce hypercapnia	**Non-Invasive Positive Airway Pressure for Chronic Obstructive Pulmonary Disease 8.01.64** **Policy Statement:** For patients with chronic obstructive pulmonary disease (COPD) without hypercapnia ($PaCO_2$ less than 52 mmHg) and with obstructive sleep apnea, see Blue Shield of California Medical Policy: Diagnosis and Medical Management of Obstructive Sleep Apnea. Nocturnal bilevel positive airway pressure with backup rate may be considered **medically necessary** for patients with COPD and chronic respiratory failure who meet **either** of the following: I. Chronic stable daytime (awake) hypercapnia ($PaCO_2$ greater than or equal to 52 mmHg) II. Daytime (awake) hypercapnia ($PaCO_2$ greater than or equal to 52 mmHg) at least 2 weeks after discharge from the hospital for an acute exacerbation with decompensated acidosis Individuals with COPD who are started on bilevel positive airway pressure at discharge from hospitalization may continue for up to 3 months to provide time to stabilize and complete reevaluation. Non-invasive home mechanical ventilation may be considered **medically necessary** for patients with COPD who meet the following criteria: I. Qualify for a bilevel positive airway pressure device **AND** meet at least **one** of the following: A. Higher pressure (e.g., greater than 25 cm H_2O) is needed to reduce hypercapnia than can be achieved with a bilevel device during titration B. Severe hypoxemia requiring FIO_2 greater than 40% or greater than 5 L/min C. Daytime use (battery operated unit) is required to reduce hypercapnia

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Non-invasive positive airway pressure for COPD is considered **investigational** under all other conditions.	Non-invasive positive airway pressure for COPD is considered **investigational** under all other conditions.