MEDICAL POLICY STATEMENT
Georgia Medicaid

Policy Name & Number	Date Effective
Inhaled Nitric Oxide-GA MCD-MM-1187	

Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Medical Policy Statements prepared by CareSource and its affiliates do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination. According to the rules of Mental Health Parity Addiction Equity Act (MHPAEA), coverage for the diagnosis and treatment of a behavioral health disorder will not be subject to any limitations that are less favorable than the limitations that apply to medical conditions as covered under this policy.

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A. Subject

Inhaled Nitric Oxide (iNO)

B. Background

Inhaled nitric oxide (iNO) is a lipophilic gas that is naturally produced in numerous cells in the body and readily absorbed across pulmonary membranes in the ventilated lung after inhalation. In the body, nitric oxide is involved in oxygen transport to the tissues, the transmission of nerve impulses, and other physiological activities. When administered via inhalation, it is a potent endogenous vasodilator that induces relaxation of vascular and bronchial smooth muscle, vasodilation of blood vessels, and can increase the partial pressure of arterial oxygen. iNO was initially approved by the U.S. Food and Drug

concluded iNO does not lead to reduced ECMO use and Putnam, et al (2016) concluded iNO use in CDH may be associated with increased mortality.

In preterm infants, the most common cause of acute respiratory failure is respiratory distress syndrome as a result of surfactant deficiency. According to the available literature, treatment of preterm infants usually entails exogenous surfactant administration. A systematic review of the evidence (Barrington and Finer, 2003) concluded: "The currently published evidence from randomized trials does not support the use of inhaled nitric oxide in preterm infants with hypoxic respiratory failure." Carey, et al (2018) also concluded that iNO is not associated with reduced in-hospital mortality among premature infants wi

In an Agency for Healthcare Research and Quali Inhaled Nitric Oxide in Preterm Infants, Allen, et al (2010) systematically reviewed the evidence on the use of iNO in preterm infants born at or before 34 weeks gestation age who receive respiratory support. They searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Studies (CENTRAL) and PsycInfo in June 2010. They also searched the proceedings of the 2009 and 2010 Pediatric Academic Societies Meeting and ClinicalTrials.gov. They identified additional studies from reference lists of eligible articles and relevant reviews, as well as from technical experts. Questions were developed in collaboration with technical experts, including the chair of the upcoming National Institutes of Health Office of Medical Applications of Research Consensus Development Conference. These researchers limited their review to randomized controlled trials (RCTs) for the question of survival or occurrence of bronchopulmonary dysplasia (BPD), and for the question on short-term risks. All study designs were considered for long-term pulmonary or neurodevelopmental outcomes, and for questions about whether outcomes varied by subpopulation or by intervention characteristics. Two investigators independently screened search results and abstracted data from eligible articles. These investigators identified a total of 14 RCTs, reported in 23 articles, and 8 observational studies. Chronic Lung Disease (CLD) or BPD studies have shown that there is insufficient evidence to support iNO for the treatment of CLD or BPD.

Mortality rates in the neonatal intensive care unit (NICU) did not differ for infants treated with iNO versus those not 9.54 Tm0 g0 Gre04(i)5(1-yr00009r)-3(tin)13(D)5(42*nBT/F1 11.04 Tf1 0)-42

An American Academy of Pediatrics clinical report on the use of iNO in preterm infants (Kumar, et al, 2014) concluded the following:

1. The results of randomized controlled trials, traditional meta-analyses, and an individualized patient data meta-analysis study indicate that neither rescue nor routine use of iNO improves survival in preterm infants with respiratory failure (Evidence quality, A; Grade of recommendation, strong).
2. The preponderance of evidence does not support treating preterm infants who have respiratory failure with iNO for the purpose of preventing/ameliorating BPD, severe intraventricular hemorrhage, or other neonatal morbidities (Evidence quality, A; Grade of recommendation, strong).
3. The incidence of cerebral palsy, neurodevelopmental impairment, or cognitive impairment in preterm infants treated with iNO is similar to that of control infants (Evidence quality, A).
4. The results of 1 multicenter, randomized controlled trial suggest that treatment with a

insufficient evidence to support iNO in any category of critically ill patients with ARDS. Inhaled nitric oxide resulted in a transient improvement in oxygenation but did not reduce mortality and may be harmful, as it seemed to increase renal impairment.

Studies have shown that treating Malaria with iNO was associated with reduced risk of fine motor impairment. However, these results need to be validated in a larger study.

iNO has been proposed to be of benefit in the intraoperative management of patients in the setting of right ventricular dysfunction after LVAD insertion. However, data supporting favorable clinical outcomes are lacking. Acute pulmonary embolism is typically a complication secondary to migration of a deep venous clot or thrombi to the lungs and is associated with considerable morbidity and mortality. There is insufficient evidence to support iNO for the treatment of PE.

C. Definitions

- **Corrected Gestational Age** – Gestational age at birth plus the number of weeks old equals corrected gestational age. Example: 24 weeks gestational age at birth + 10 weeks old = 34 weeks corrected gestational age.
- **Extracorporeal Membrane Oxygenation (ECMO)** – Temporary support of heart and lung function by partial cardiopulmonary bypass (up to 75% of cardiac output) used for patients who have reversible cardiopulmonary failure from pulmonary, cardiac, or other disease.
- **Hypoxic Respiratory Failure** – A serious condition that develops when the lungs cannot provide oxygen into the blood to reach the tissues of the body.
- **Nitric Oxide (NO)** – Also called nitrogen monoxide, a colorless lipophilic gas that is formed by the oxidation of nitrogen that performs important chemical signaling functions in humans and other animals and has various applications in medicine.
- **Oxygen Index (OI)** – Used to assess severity of hypoxic respiratory failure (HRF) and persistent pulmonary hypertension of the newborn (PPHN). OI = Mean Airway Pressure x Fio2 x 100 / partial pressure of arterial oxygen
- **Persistent Pulmonary Hypertension of the Newborn (PPHN)** – Reflects failure of the pulmonary vasculature to relax at birth which results in increased pulmonary arterial pressure and pulmonary vasculature resistance that leads to shunting of deoxygenated blood into the systemic circulation.

D. Policy

I. CareSource considers the initiation of i

B. Absence of ductal dependent congenital heart disease.
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The MEDICAL Policy Statement detailed above has received due consideration as defined in the MEDICAL Policy Statement Policy and is approved.

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