

Inhaled Nitric Oxide Service An alternative of life



[logo:] Medigas

[logo:] NOMIX



INO Therapeutics LLC Exhibit 2026 Praxair Distrib., Inc. v. INO Therapeutics LLC Case IPR2015-00889

## What is Nitric Oxide?

Nitric Oxide (NO) is a diatomic gas which is synthesized in various cells of the body and which has a crucial role as a cellular messenger molecule. The transduction systems of signals in which nitric oxide intervenes are especially relevant in the brain and the cardiovascular system.



Nitric Oxide plays a very important role in maintaining both the vascular as well as systemic and pulmonary tone. It is produced in the endothelial cells along with prostacyclin (PGI2) and is identified with the sedative factor of the endothelium, currently being considered an endogenous vasodilator. NO is synthesized from L-arginine amino acid by the action of the NO Synthases and acts in the smooth vascular muscle activating Guanylate Cyclase which transforms the GTP into GMPC, causing relaxation.

Inhaled Nitric Oxide is a drug approved by the FDA (Federal Drug Administration) on December 23, 1999 and is currently used widely in different countries of the world with proven success.

### **Newborn Pulmonary Hypertension**

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In newborns, the release of Nitric Oxide is produced in part by the increase in the pulmonary blood flow, by the increase in oxygenation and by ventilation. These findings led to the postulation of the hypothesis that a decrease in the capacity to release endogenous Nitric Oxide may contribute to the physiopathology of the "Newborn Pulmonary Hypertension Syndrome." In addition to decreasing the pulmonary vascular resistance, inhaled nitric oxide may improve oxygenation in increasing the ventilation/perfusion relationship.



### Inhaled Nitric Oxide may prevent serious pulmonary disorders.

The inhalation of Nitric Oxide is a therapy that has notably improved the treatment of various mortal illnesses, and it may also prevent the development of pulmonary vascular illness, a disorder which affects around one in every 500 children. In principle, children born prematurely or who have congenital heart defects are the ones who are most benefitting from the application

of this therapy.

Until now, there has been no form of preventing the risk of pulmonary vascular illness in children in risk situations, and the treatments which were applied were not very effective. The therapy with nitric oxide has the potential to notably increase the quality of life and even save the lives of children in risk situations.



Praxair, the leader in the production and marketing of industrial and medicinal gases, through Medigas, provides the medical and hospital sector with the application service of NOMIX Inhaled Nitric Oxide as an alternative in the treatment of newborn pulmonary hypertension.

# Characteristics and advantages of the administration of Inhaled Nitric Oxide:

- Selective dilation of pulmonary blood vessels
- Regulator of vascular tone
- Reduces pulmonary hypertension, improving oxygenation
- Improves the outlook with newborns with respiratory failure associated with primary pulmonary hypertension
- Does not alter systemic arterial pressure
- The therapy of Inhaled Nitric Oxide in high risk surgeries to correct congenital cardiac injuries in pediatric patients reduces the risk of pulmonary hypertension
- The therapy of Inhaled Nitric Oxide increases the systemic oxygenation in pediatric patients with pulmonary hypertension
- Low cost



### Components of the supply system of Inhaled Nitric Oxide:

- Nitric Oxide Monitor
- Mixture of Nitric Oxide and Nitrogen
- Pressure regulator
- Precision flowmeter
- Connections and pipes

The NOMIX service is available 24 hours a day, 365 days a year in the main cities in the Mexican Republic

# [logo:] NOMIX

## The alternative treatment for persistent Pulmonary Hypertension in newborns

The NOMIX service (application of Inhaled Nitric Oxide) includes:

- Supply of Nitric Oxide gaseous mixture
- Control equipment for the dosing of Nitric Oxide to patients
- Nitric oxide concentration monitoring system
- Technical personnel specialized in supporting the application



### **Quality Guarantee**

The gaseous mixture utilized in the NOMIX service is manufactured by Praxair under the highest quality and production standards, certified through the most precise and modern chemical analysis techniques in our plant in Tultitlán, State of Mexico.

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