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Operating Instructions for Inhaled Nitric Oxide Therapy

Purpose	To provide guidelines for the initiation of inhaled nitric oxide therapy via the iNOMax delivery system by completing the pre-use system purge and performance test.
Audience	Physicians, Nursing staff, and Licensed Respiratory Care Practitioners.
Scope	Inhaled Nitric Oxide is a selective pulmonary vasodilator. Nitric Oxide, the active substance in iNOMax is a gaseous blend of 0.08% NO and 99.2% Nitrogen respectively for 800 ppm concentration.
Physician's	Physician orders must include the following:
Order	<ul style="list-style-type: none"> ▪ Mechanical ventilation parameters • Nitric Oxide concentration in ppm • Methemoglobin levels are recommended at 1 hour and 8 hours after initiation of therapy and at physician discretion.
Indications	Inhaled nitric oxide therapy is indicated in term and near-term (>34 weeks) neonates with hypoxic respiratory failure that is associated with: (INO package insert 2014) <ul style="list-style-type: none"> • Meconium aspiration syndrome (MAS) • Pneumonia/ Sepsis • Persistent Pulmonary Hypertension of the Newborn (PPHN) • Congenital Diaphragmatic Hernia (CDH) • Respiratory Distress Syndrome (RDS) • Off label use for post-op Cardiac Patients such as LVAD • Respiratory Failure (ARDS)
Goals	The goals of delivering inhaled nitric oxide are to: <ul style="list-style-type: none"> • Improve and maintain oxygenation • Reduce the need for extracorporeal membrane oxygenation (ECMO) • Relieve primary pulmonary artery hypertension

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Adverse Effects

The adverse effects associated with inhaled nitric oxide therapy include:

- Rebound (abrupt discontinuation of INO may lead to worsening oxygenation and increasing pulmonary artery pressure)
- Methemoglobinemia (increases with dose of INO)
- Increased levels of NO₂
- Inhaled nitric oxide therapy should not be used in patients that are dependent on right-to-left shunting of blood

Equipment

- iNOMax delivery system
- Full NO cylinders

Procedure

Pre-Use System Purge and Performance Test

Step	Action
1	Turn ON iNOMax DSIR. Low calibration automatically starts following the iNOMax DSIR self-test. Check the iNOMax DSIR gas cylinders for the correct product identity labels, cylinder concentration, and expiration date. Ensure that at least one iNOMax DSIR gas cylinder with more than 50 psig is available
2	Connect one of the high pressure regulators to an iNOMax DSIR cylinder and tighten the fitting to the iNOMax cylinder
3	Connect the iNOMax DSIR regulator hose to one of the iNOMax inlets
4	If using the iNOblender with the iNOMax DSIR, connect the iNOblender hose to the iNOMax DS outlet and slide the Quick-Connect cover into place
5	Ensure water trap bottle and water separator cartridge are in place.

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6	Connect the Infrared cable from the iNOMax DSIR cart to the back of the iNOMax DSIR system	
7	Open and then close the cylinder valve.	
8	Check for adequate cylinder pressure, if no pressure decrease is observed in 30 sec., high pressure leak test is complete.	
9	Confirm injector module is out of patient breathing circuit or pre use circuit. Press NEXT button to start the purge process. Low cylinder pressure alarm may activate. Open cylinder valve when purge is complete.	
10	Backup iNOMax Delivery test: <ul style="list-style-type: none"> • Turn the back iNOMax delivery ON (250mL/min) • “Backup ON” alarm will occur • Allow 2-3 minutes for the monitored values to stabilize and make sure the NO and NO2 readings are within the following ranges: <p>NO = 14-26 ppm NO2 = <1.0 ppm</p> <ul style="list-style-type: none"> • Turn the backup iNOMax delivery OFF 	
11	Performance Test Assemble the pre-use set up connectors and tubing (press show diagram button if needed). Set the Oxygen flowmeter to 10 L/min. Press NEXT button to automatically set the INOMAX dose to 40ppm. Allow values to stabilize Compare the iNOMax DSIR monitor values to the values below: <p>NO = 35-45 ppm NO2= <1.5 ppm FiO2 = ≥92 Performance Test is complete. The iNOMax is automatically set to zero.</p>	

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12	<p>iNOblender Test: If using the iNOblender with the iNOmax DS, connect the Pre-Use set-up to the oxygen flowmeter and disconnect the Pre-Use set-up from the iNOblender.</p> <ul style="list-style-type: none"> Remove the Pre-Use set-up from the iNOblender. Remove the Pre-Use set-up from the Pre-Use set-up and reconnect the adapter cover into place. On the iNOblender, set the iNOmax dose to 40 ppm and the O2 flow to 10 L/min. Verify that the monitored value for NO is within the following range: NO= 32-48 ppm Turn the dose and flow to zero and remove the Pre-Use set-up from the iNOblender. <p>Ensure water bottle and water separator cartridge are in place. Connect the Infrared cable from the iNOmax cart to the back of the iNOmax DS system. Turn the iNOmax DS ON. Open and then close the cylinder valve.</p>
13	<p>Purge the Regulator Supply Line</p> <p>Check for adequate cylinder pressure (if there is any decrease, make sure the backup NO cylinder is connected to a patient).</p> <ul style="list-style-type: none"> If not immediately connecting to a patient, turn the iNOmax cylinder OFF. Purge the pressure from the regulator using the purge port on the back of the iNOmax DS unit. Reconnect the regulator line to the iNOmax DS inlet. If the iNOmax DS unit is depressurized and not used within 12 hours, repeat the pre-use procedure.

Initiation of Therapy with Conventional Mechanical Ventilation, Infant Nasal CPAP (NCPAP), and High Flow Nasal Cannula Systems (HFNC)

Step	Action
1	Perform pre-use system purge and performance test as outlined above
2	Insert the Injector Module on the dry side of the breathing circuit prior to the humidifier (following the directional arrow located on the Injector Module) using a 15mm and 22mm adapter.

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3	Neonatal Application Insert 6” extension tubing with sample tee adapter at the patient wye on the inspiratory side of the breathing circuit distal to the temperature probe adapter. This extension tubing minimizes sampling of mixed inspiratory/ expiratory gases (6” extension tubing NOT NEEDED for NCPAP or HFNC) Adult Application: Insert a Sample Tee Adapter on the inspiratory side of the breathing circuit, and connect the sample tee adapter to the gas sample line.	
4	Set the iNOmax dose to be delivered to the patient.	
5	After the monitored values have stabilized, set or change the user-adjustable alarms to the appropriate ranges. NO₂ high alarm should be set at 3.0 ppm NO alarms should be set ± 5 ppm of desired level	
6	Attach an appropriate sized resuscitation bag to the iNOblender for the manual delivery of NO.	

Initiation of Therapy with High Frequency Oscillatory Ventilation (HFOV)

Step	Action
1	Perform pre-use system purge and performance test as outlined above
2	Assemble Injector Module for patient delivery of NO as outlined in the Delivery System pocket guide (page 37-38). Ensure the injector module is on the dry side of the heater. Note: Omission of the one-way valve may result in high NO delivery.
4	Insert patient gas sample line connection as outlined in the Operation Manual using a 90° luer elbow adapter.
5	After connecting the iNOmax delivery system to the patient HFOV Circuit, set the nitric oxide dose to be delivered.

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6	After the monitored values have stabilized, set or change the user-adjustable alarms to the appropriate ranges. <p style="text-align: center;"> NO₂ high alarm should be set at 3.0 ppm NO alarms should be set ± 5 ppm of desired level </p>	
7	Attach an appropriate sized resuscitation bag to the iNOblender for the manual delivery of NO.	

Assessment of Outcome

1. Arterial, venous and capillary blood gas values
2. Pulse oximetry
3. Pulmonary artery pressures

Monitoring during iNO

The risk of methemoglobinemia increases with the dose of nitric oxide. In clinical trials, the maximum methemoglobin levels were typically reached 8 hours after the initiation of therapy, though peak levels were seen as late as 40 hours after the start of therapy (iNO package insert, 2014).

Methemoglobin Range	Action
>10%	Discontinue iNO, repeat metHb every 2 hours until <5%; if needed, restart therapy at 50% of the iNO at discontinuation
5-10%	Wean iNO by 50% and repeat metHb in 2 hours; repeat sequence until metHb is <5%
<5%	No Action Needed

Infection Control Follow procedures as outlined Healthcare Epidemiology Policies and Control Procedures: #2.24 Respiratory Care Services.

<http://www.utmb.edu/policy/hcepidem/search/02-24.pdf>

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Use of Inhaled Nitric Oxide (iNO) Clinical Practice Guideline

Definitions (Jumar 2007, Carriedo 2003)

Responder: A patient is classified as a responder to iNO therapy if the post-ductal PaO₂ increases 20mmHg within 30 minutes of starting iNO without any change in the inspired oxygen concentration. If there is no increase with the initial dose (5-15 ppm), iNO should be increased to 20 ppm.

Non-Responder: If, after 30 minutes at 20 ppm, the post-ductal PaO₂ does not increase >20mmHg, the patient is classified as a non-responder and therapy should be discontinued, as follows:

Recommended Weaning Strategy for Discontinuation of iNO – Non-Responders	
Time (min)	iNO Concentration (ppm)
0	20
30	10
60	5
90	2
120	0

- The patient should be classified as a responder or a non-responder after <1 hour of iNO. Non-responders should start the weaning process, as above.
- An increase in O₂ saturation >10% will be considered equivalent to an increase in PaO₂ >20 mmHg.

Weaning from iNO (Davidson, 1999)

Responders may be weaned from iNO when any of the following conditions are met:

- PaO₂ >60 on FiO₂ <.60
- Oxygenation Index (OI) <10
- If PaO₂ or SpO₂ falls >10% mmHg after any weaning step, the dose of iNO may be increased back to the previous dose, with appropriate increases in FiO₂

Recommended Weaning Strategy for Discontinuation from iNO therapy – Responders*

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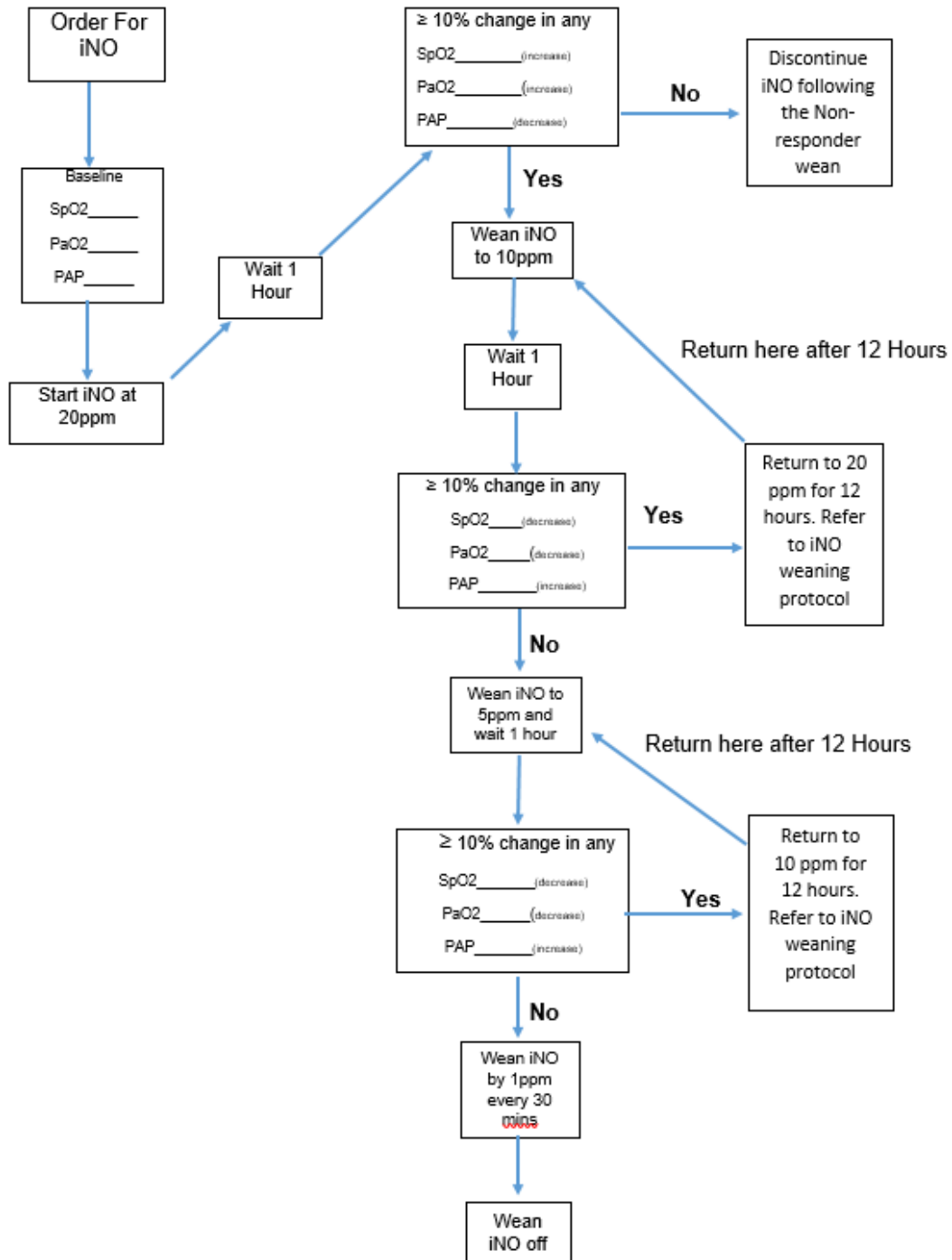
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Time (hours)	iNO Concentration (ppm)			
0 (Start of Wean)	5	10	15	20
1	4	5	10	15
2	3	4	5	10
3	2	3	4	5
4	1	2	3	4
5	0	1	2	3
6	-	0	1	2
7	-	-	0	1
8	-	-	-	0
Total	5	6	7	8

Implementation of iNO



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**Deviations from this strategy may be indicated if the patient is particularly sensitive to changes.*

Safety Oxygen safety techniques as outlined in the iNOmax Manual will be followed.

Precautions

All alarms on ventilators will be activated at all times.
 All alarms on INOvent delivery system will be activated at all times.

References

Sensormedics High Frequency Oscillatory Ventilator Operating Manual.
 Whitaker, K., Comprehensive Perinatal and Pediatric Respiratory Care, Delmar, Albany, New York, 2001.

Cornfield DN, Abman SH. Inhalational nitric oxide in pulmonary parenchymal and vascular disease. Journal of Laboratory Clinical Medicine 1996 Jun; 127(6): 530-539.

Miller CL. Nitric oxide therapy for the persistent pulmonary hypertension of the newborn. Neonatal Network 1995 Dec; 14(8): 9-15.

Angelucci P. A new weapon against ARDS...adult respiratory distress syndrome. RN 1996 Nov; 59(11): 22-25.

References

Respiratory Care. May 2015 Vol.60 No.5

Barrington K, Finer N. Inhaled Nitric Oxide for Preterm Infants: A Systematic Review. Pediatrics. 2007; 120; 1088-1099.
 Carriedo H, Rhine W. Withdrawal of Inhaled Nitric Oxide from Non-Responders After Short Exposure. Journal of Perinatology. 2003; 23:556-558
 Davidson D, Barefield E, Kattwinkel J, et al. Safety of Withdrawing Inhaled Nitric Oxide Therapy in Persistent Pulmonary Hypertension of the Newborn. Pediatrics. 1999; 104; 231-236
 INOmax® [Package Insert]. Clinton, NJ: INO Therapeutics, Inc; 1999. Revised April 2004.
 Kumar VH, Hutchison AA, et al. Characteristics of Pulmonary Hypertension in Preterm Infants. Journal of Perinatology. 2

