ANVISA NORMATIVE INSTRUCTION – IN No. 301 OF 17 MAY 2024

Establishes the list of medicinal gases classified as medicines subject to notification.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 7, items III and IV, and Article 15, items III and IV of Law no. 9,782 of 26 January 1999, and item VII, paragraph 1 of Article 187 of the Internal Regulation approved by Collegiate Board Resolution – RDC no. 585 of 10 December 2021, adopts the following Normative Instruction, as decided upon in a meeting held on 15 May 2024, and I, Director-President, determine its publication.

Article 1. The list of medicinal gases classified as medicines subject to notification in accordance with Article 15 of Anvisa Collegiate Board Resolution – RDC No. 870 of 17 May 2024, is hereby established in the Annex to this Normative Instruction.

Article 2. This Normative Instruction shall come into force on 1 July 2024.

ANTONIO BARRA TORRES

Director-President

ANNEX

LIST OF MEDICINAL GASES CLASSIFIED AS MEDICINES SUBJECT TO NOTIFICATION

1) Medicinal Air and 2) Synthetic Medicinal Air

Indications: as a substitute for atmospheric air. As a propellant for nebulizing other medications. As a component in the gas flow in inhalation anesthetic procedures. As a filling gas in multi-patient hyperbaric chambers and in mechanical ventilation.

Contraindications: there are no known contraindications.

Precautions: when using medicinal air or synthetic medicinal air in hyperbaric oxygen therapy, the risks inherent to the procedure must be observed.

Adverse reactions: there are no reports of adverse reactions.

Drug interactions: there are no known drug interactions.

Production line: compressed or liquefied medicinal gases.

3) Medicinal Carbon Dioxide

Indications: as an insufflation gas for body cavities in clinical procedures. Prevention and treatment of hypocapnia caused by hyperventilation.

Contraindications: patients with acidosis or respiratory obstruction.

Precautions: leaks of medicinal carbon dioxide in poorly ventilated environments can cause dizziness, drowsiness, narcosis, asphyxia, and death due to lack of oxygen.

Adverse reactions: medicinal carbon dioxide can cause respiratory acidosis, headache, dizziness, confusion, palpitations, hypertension, dyspnea, increased respiration, and depression of the central nervous system. High concentrations can also cause convulsions and loss of consciousness.

Drug interactions: medicinal carbon dioxide interacts with inhaled anesthetic agents in high concentrations and causes arrhythmia.

Production line: compressed or liquefied medicinal gases.

4) Medicinal Nitrogen

Indications: as a component in gas mixtures for respiratory therapy.

Contraindications: there are no known contraindications.

Precautions: nitrogen gas leaks in poorly ventilated environments can cause dizziness, drowsiness, narcosis, asphyxia, and death due to lack of oxygen. Contact of cryogenic nitrogen with the skin can cause severe frostbite.

Adverse reactions: no adverse reactions have been reported.

Drug interactions: no known drug interactions.

Production line: compressed or liquefied medicinal gases and cryogenic medicinal liquids.

5) Medicinal Oxygen

Indications: prevention and treatment of acute and chronic oxygen deficiencies. As an adjuvant in the treatment of respiratory difficulties and increased cardiac effort. As a component in the gas flow for the inhalation of other medications. As ventilatory support in mechanical ventilation procedures. As inhalation gas or as a single-patient chamber filler in hyperbaric oxygen therapy.

Contraindications: patients with an unfavorable ventilatory response to oxygen therapy.

Precautions: when using medicinal oxygen in hyperbaric oxygen therapy, the risks inherent to the procedure must be observed. Oxygen strongly accelerates combustion when in contact with combustible materials or sources of ignition.

Adverse reactions: medicinal oxygen, when administered in high concentrations or for a prolonged period of time, can cause dryness of mucous membranes (nose, mouth, and airways), pain, dry cough, and difficulty breathing, in addition to lung and systemic injuries. In newborns, high concentrations of medicinal oxygen can also cause eye damage, hematologic, cardiac, and cerebral alterations. In patients with chronic obstructive pulmonary disease (COPD), excessive administration of medicinal oxygen can lead to respiratory failure due to hypercapnia.

Drug interactions: administration of medicinal oxygen in high concentrations can increase the risk of pulmonary toxicity in patients using amiodarone, bleomycin, nitrofurantoin, or other antibiotics of this class.

Production line: compressed or liquefied medicinal gases and medicinal cryogenic liquids.

6) Medicinal Nitrous Oxide

Indications: as an adjunct to general inhalation anesthesia in association with oxygen and other anesthetic agents. As a sedative or analgesic agent in minor surgical or diagnostic procedures and in dental treatment.

Contraindications: patients with hypersensitivity to nitrous oxide. Patients who may have gas or air bubbles trapped in the blood, organs, or body cavities. Patients with paralytic ileus or undergoing major intestinal surgeries. Patients with vitamin B12 deficiency (pernicious anemia), folic acid deficiency, or dihydropteridine reductase deficiency, as well as those with other nutritional deficiencies (such as alcoholics). Patients undergoing bleomycin therapy. Patients with increased intracranial pressure, such as in the presence of tumors or hemorrhage. Patients with heart failure or severe hypotension. Patients who have a reduced level of consciousness and/or cooperation, due to the risk of loss of protective reflexes. Pregnant women in the first 6 (six) months of pregnancy.

Precautions: after administration of medicinal nitrous oxide, the patient must wait sufficient time for recovery of psychomotor functions before driving vehicles or operating machinery. Chronic exposure to medicinal nitrous oxide can cause brain damage, peripheral nerve damage, hematological changes, and death; therefore, hematological monitoring should be performed

on chronically exposed patients and professionals. Leakage of medicinal nitrous oxide in poorly ventilated environments can cause dizziness, drowsiness, narcosis, asphyxia, and death due to lack of oxygen.

Adverse reactions: nausea and vomiting. Headaches and dizziness. Cardiac dysrhythmia. It may lead to increased pneumothorax, air embolism, pressure in the middle ear and sinuses, distension of intestinal loops and gas bubbles in the epidural space. Diffusional hypoxia (Fink's hypoxia).

Drug interactions: medicinal nitrous oxide potentiates the effects of methotrexate. Administration of medicinal nitrous oxide concomitantly with other central nervous system depressant medicines, such as morphine derivatives or benzodiazepines, may result in increased sedation and, consequently, affect breathing, blood circulation, and protective reflexes.

Production line: compressed or liquefied medicinal gases.

7) Medicinal Oxygen 50% + Medicinal Nitrous Oxide 50%

Indications: as a sedative or analgesic agent in minor surgical or diagnostic procedures and in dental treatment.

Contraindications: patients with hypersensitivity to nitrous oxide. Patients who may have gas or air bubbles trapped in their blood, organs, or body cavities. Patients with paralytic ileus or undergoing major intestinal surgery. Patients with vitamin B12 deficiency (pernicious anemia), folic acid deficiency, or dihydropteridine reductase deficiency, and those with other nutritional deficiencies (such as alcoholics). Patients undergoing bleomycin therapy. Patients with increased intracranial pressure, such as in the presence of tumors or hemorrhage. Patients with heart failure or severe hypotension. Patients who have a reduced level of consciousness and/or cooperation, due to the risk of loss of protective reflexes. Pregnant women in the first six months of pregnancy.

Precautions: after administration of medicinal oxygen 50% + medicinal nitrous oxide 50%, the patient must wait sufficient time for recovery of psychomotor functions before driving vehicles or operating machinery. Chronic exposure to 50% medicinal oxygen + 50% medicinal nitrous oxide can cause brain damage, peripheral nerve damage, hematologic changes, and death; therefore, hematologic monitoring should be performed on chronically exposed patients and professionals.

Adverse reactions: nausea and vomiting. Headaches and dizziness. Cardiac dysrhythmia. It may lead to increased pneumothorax, air embolism, pressure in the middle ear and sinuses, distension of intestinal loops, and gas bubbles in the epidural space. Diffusional hypoxia (Fink's hypoxia).

Drug interactions: 50% medicinal oxygen + 50% medicinal nitrous oxide potentiates the effects of methotrexate. The administration of medicinal oxygen 50% + medicinal nitrous oxide 50% concomitantly with other central nervous system depressant medicines, such as morphine derivatives or benzodiazepines, may result in high sedation and, consequently, affect respiration, blood circulation, and protective reflexes. The administration of a gas mixture containing oxygen in high concentrations may increase the risk of pulmonary toxicity in patients taking amiodarone, bleomycin, nitrofurantoin, or other antibiotics of this class.

Production line: compressed or liquefied medicinal gases.

8) Medicinal Helium

Indications: as a component in gas mixtures for respiratory therapy.

Contraindications: there are no known contraindications.

Precautions: due to the higher thermal conductivity of medicinal helium, it may be necessary to humidify and heat the mixture before administration to prevent hypothermia in vulnerable patients, such as pediatric patients. Leakage of medicinal helium in poorly ventilated environments can cause dizziness, drowsiness, asphyxia, and death due to lack of oxygen.

Adverse reactions: temporary change in tone of voice due to the lower density of medicinal helium in relation to room air. Hypothermia, especially in vulnerable patients, such as pediatric patients, due to the high thermal conductivity of medicinal helium.

Drug interactions: there are no known drug interactions.

Production line: compressed or liquefied medicinal gases.

9) Medicinal Helium 79% + Medicinal Oxygen 21%

Indications: as an adjuvant in clearing the upper and lower airways to reduce respiratory effort. As a vehicle for the inhalation of other medications.

Contraindications: there are no known contraindications.

Precautions: due to the greater thermal conductivity of medicinal helium, it may be necessary to humidify and heat the mixture before administration to avoid hypothermia in vulnerable patients, such as pediatric patients.

Adverse reactions: temporary change in tone of voice due to the lower density of medicinal helium in relation to room air. Hypothermia, especially in vulnerable patients, such as pediatric patients, due to the high thermal conductivity of medicinal helium.

Drug interactions: there are no known drug interactions.

Production line: compressed or liquefied medicinal gases.