

BEST PRACTICE AND SAFE USE OF MEDICINAL NITROUS OXIDE

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Prepared by AHG-M.05 Medicinal Nitrous Oxide

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Amendments to Doc 153/08

Section	Change
All	The entire document has been re-written and updated with latest scientific bibliographic publications.

1 Introduction

Nitrous oxide (N₂O) has been used as analgesic agent for more than 150 years; however, inappropriate use has jeopardized its use in clinical practice.

This document reviews the pharmacological properties of N₂O and its intended use in today's clinical practice.

The document provides recommendations for safe use of N₂O and risk minimization strategies that should be respected by all healthcare professionals that are in contact with N₂O.

The document is laid out as follows:

- Describes basic pharmacokinetic and pharmacodynamic characteristics of N₂O, i.e., uptake and elimination by the body and interaction with its biological targets; and
- Shows how these properties are linked to known safety issues of N₂O.

This knowledge provides the rationale for best practice recommendations of safe handling and use of N₂O.

In this document we take a novel approach in presenting safety rules by anchoring each recommendation to a scientific rationale. The goal is to increase knowledge and confidence in N₂O use by providing the logic behind the rules so that healthcare professionals can draw maximum benefit from N₂O use while mitigating risks for patients and healthcare professionals.

2 Scope and purpose

2.1 Scope

This document is intended for use by

- Healthcare professionals (hospitals and outside hospitals),
- Safety workers regulators,
- bioengineering personnel,
- scientific societies,
- EIGA members,
- National Gas Associations and
- national regulatory authorities,
- patients' associations,
- media

It focuses only in the understanding and presentation of clinical best practices of use to mitigate the potential safety risks related to the human exposure to N₂O and N₂O mixtures.

2.2 Purpose

This document aims to promote the safe use of medicinal N₂O and N₂O mixtures and to raise awareness on the misuse of these medicinal products.

3 Definitions

For the purpose of this publication, the following definitions apply.

3.1 Publication terminology

3.1.1 Shall

Indicates that the procedure is mandatory. It is used wherever the criterion for conformance to specific recommendations allows no deviation.

3.1.2 Should

Indicates that a procedure is recommended.

3.1.3 May

Indicates that the procedure is optional.

3.1.4 Will

Is used only to indicate the future, not a degree of requirement.

3.1.5 Can

Indicates a possibility or ability.

3.2 List of Abbreviations

CNS	Central nervous system
ED50	Effective dose leading to 50% of inhibition
EIGA	European Industrial Gases Association
EMONO	Equimolar mixture of oxygen nitrous oxide
GABA	Gamma-aminobutyric acid
N ₂ O	Nitrous oxide
NIOSH	National Institute for Occupational Safety and Health
NMDA	N-methyl-D-aspartate
NOAEL	No-observed-adverse-effect level
O ₂	Oxygen
OEL	Occupational exposure limits
ppm	Parts per million
PONV	postoperative nausea and vomiting
SAM	S-adenosyl methionine
SmPC	Summary of product characteristics
TWA-8	Total weight average during 8 hours

4 Executive summary

N₂O has been in use for more than 150 years due to its analgesic and anaesthetic properties. The main advantage of nitrous oxide is its fast on/off effect, which makes it an attractive agent for rapid analgesia and sedation in paediatrics, dentistry, and obstetrics [1][2]. In these situations, equimolar mixtures of nitrous oxide and oxygen (EMONO) are sufficient to provide analgesic effect while patients are conscious and preserve their reflexes. In general anaesthesia, N₂O as single agent is prohibited due to its low potency as anaesthetic agent. Rather, N₂O is administered together with other anaesthetics to increase their partial alveolar pressure, thereby leading to faster induction of anaesthesia [2].

In recent years, the place of nitrous oxide in modern analgesia and anaesthesia has been questioned due to concerns about nitrous oxide-related toxicities [3]. Known risks of N₂O that are supported by the current evidence base include occupational exposure, diffusion hypoxia, increase in size or pressure of air-or gas-filled spaces, for example increase in intracranial pressure and intraocular pressure,

neurological and haematological toxicities, as well as postoperative nausea and vomiting (PONV) [2]. Given its long history of clinical use and active surveillance of N₂O -related reactions, the safety profile of N₂O is well characterized.

This document reviews the different mechanisms of action of N₂O and their relationship to toxic effects. These effects are then discussed within the context of relevant clinical situations. Finally, recommendations are presented for the safe use of nitrous oxide and procedures to mitigate safety risks (Figure 1).

The goal is to raise awareness of the mode of action of nitrous oxide among health care professionals to increase their confidence in the safe use of nitrous oxide with the aim to draw maximum benefit while minimizing toxicities for their patients and personnel.

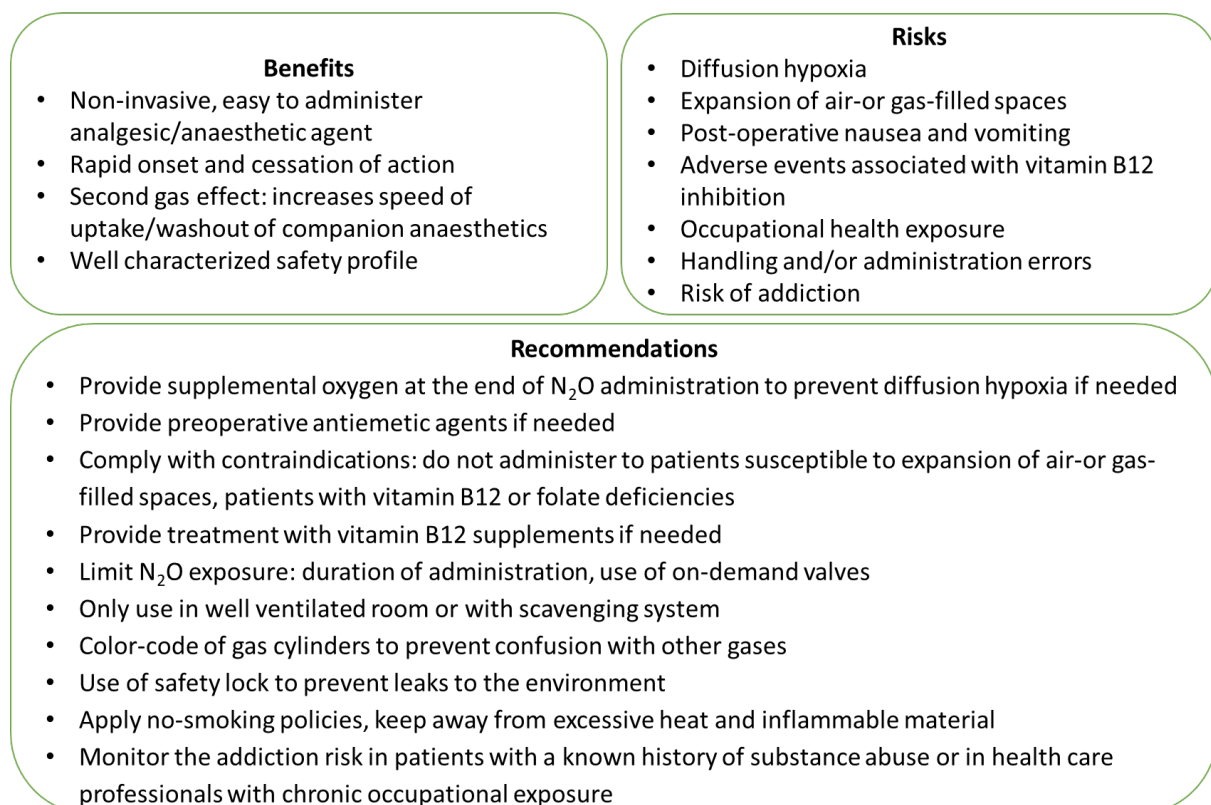


Figure 1 Overview of benefits, risks and recommendations for safe use of N₂O