

PRODUCT INFORMATION

NAME OF THE MEDICINE

Medical Nitrous Oxide

Chemical structure

A linear but unsymmetrical molecule of the form N-N-O.

CAS No. 10024-97-2

MW: 44.01

Molecular Formula: N₂O

DESCRIPTION

Nitrous oxide is a sweet smelling colourless gas. Nitrous oxide is not very soluble in water but is fifteen times more soluble than oxygen. Water dissolves nitrous oxide, taking 100 volume % and blood plasma 45 volume %. Boiling point: - 88.60C (at 1 bar). Specific gravity at 15⁰ C and 101.3 kPa is 1.53. Density at 115⁰ C and 101.3 kPa is 1.875 kg/m³. Nitrous oxide is an oxidising substance which will support combustion of materials which may not normally burn in air. The molecule is stable and comparatively un-reactive at ordinary temperatures. At elevated temperatures it decomposes to nitrogen and oxygen.

PHARMACOLOGY

Nitrous oxide is not very soluble in water but is fifteen times more soluble than oxygen. Water dissolves nitrous oxide, taking 100 volume % and blood plasma 45 volume %.

Nitrous oxide is eliminated unchanged from the body mostly by the lungs.

Nitrous oxide is an analgesic and a weak anaesthetic. Pain reduction is achieved at a concentration of around 25%. Induction with nitrous oxide is relatively rapid, but a concentration of about 70% is needed to produce unconsciousness. Endorphins are probably involved in the analgesic effect; a concentration of 25% nitrous oxide is usually adequate to provide a marked reduction in pain.

Pharmacokinetic particulars

Nitrous oxide is a low potency inhalation anaesthetic and only slightly soluble. The advantage of this is that concentrations not greater than 70% are used and induction of anaesthesia and recovery occur quickly.

At a constant inspired concentration, the rise time of alveolar concentrations is faster than that of any other anaesthetic agent. The elimination of nitrous oxide is faster than that of any other anaesthetic.

The blood/gas partition coefficient of nitrous oxide at 37°C is 0.46 compared with that of nitrogen of 0.015, causing nitrous oxide to expand into internal gas spaces.

Under normal anaesthesia, the adult body contains 25 litres of gaseous nitrous oxide (this gives some notion of its essential safety and lack of acute toxicity).

The flow of nitrous oxide out from the tissues through the lungs at the end of anaesthesia may lead to a degree of transient hypoxia.

INDICATIONS

Medical Nitrous Oxide is used:

1. General Anaesthesia: when an inhalation anaesthetic is required, the administration is usually accompanied by simultaneous administration of a volatile agent such as halothane, ethrane, etc.

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2. Analgesia with Oxygen:

- relief from severe pain, usually in emergency situations, by inhalation with oxygen.
- useful also in short-term procedures which inevitably involve pain, such as wound and burn dressing, wound debridement and suturing. Administration with oxygen.
- in dental work to provide short-term analgesia for tooth extraction and other brief procedures. Administration with oxygen.

3. Others:

- occasionally as an insufflating agent in laparoscopy.
- in cryosurgery as a refrigerant.

CONTRAINDICATIONS

All these effects are well documented, extremely rare and may follow prolonged exposure to levels of nitrous oxide over 5,000 ppm or to frequent (more than once every two days) exposure to analgesic concentrations. Vitamin B12 in-activations have been reviewed by Nunn.

Nitrous oxide should not be used with any condition where air is entrapped within a body and where its expansion might be dangerous, such as:

head injuries with impairment of consciousness;
artificial, traumatic or spontaneous pneumothorax;
air embolism;
decompression sickness;
following a recent dive;
following air encephalography;
severe bullous emphysema;

during myringoplasty;
gross abdominal distension;
intoxication;
maxillofacial injuries.

Nitrous oxide should not be used as an analgesic or anaesthetic agent for more than 24 hours without monitoring of peripheral blood for features of megaloblastic anaemia and leukopenia.

PRECAUTIONS

General

A simple asphyxiant in the absence of oxygen. Classified as hazardous according to criteria of WorkSafe Australia.

Liquid contact with eyes and skin may cause cold burns.

Addiction to nitrous oxide has been reported.

Scavenging of waste nitrous oxide gas should be used to reduce operating theatre and equivalent treatment room levels to a level below 25 ppm exposure limit of nitrous oxide. Rescue personnel are advised to monitor nitrous oxide concentration before entering confined spaces and poorly ventilated areas which have been contaminated by a nitrous oxide leak.

At the end of nitrous oxide/oxygen anaesthesia, withdrawal of the mask leads to an outpouring of nitrous oxide from the lungs and consequent dilution of oxygen in the incoming air. This results in diffusion hypoxia and is counteracted by giving 100% oxygen for a few minutes when the flow of nitrous oxide is stopped.

Suitable manual handling equipment should be used to transport cylinders.

Long Term usage

Care should be taken with long term usage of nitrous oxide. Chronic exposure to nitrous oxide can inactivate vitamin B12 with resulting neurological and haematological related side effects. (see other undesirable effects under adverse reactions section of PI)

Use with caution in the following circumstances:

Administration of nitrous oxide more frequently than every four days should be accompanied by routine blood cell counts for evidence of megaloblastic change in red blood cells and hypersegmentation of neutrophils.

Nitrous oxide should never be given with less than 21% oxygen but a maximum of 30% oxygen should be used during anaesthesia and more at altitude and in the presence of disorders affecting oxygenation.

Nitrous oxide passes into gas containing spaces in the body faster than nitrogen passes out. Prolonged anaesthesia may result in bowel distension, middle ear damage and rupture of ear drums.

Check the following before use:

Nitrous oxide is non-flammable but strongly supports combustion (including some materials which do not normally burn in air). It is highly dangerous when in contact with oils, greases, tarry substances and many plastics due to the risk of spontaneous combustion with high pressure gases.

Operability of oxygen mixing apparatus and availability of oxygen.

Dispensing equipment connection matches cylinder valve outlet.

Cylinder pressure is not a true indicator of quantity remaining in cylinder until all liquid has evaporated. Measure contents by weight.

Effect on fertility:

There is no published material which shows that nitrous oxide is toxic to the human foetus. However no increased incidence of foetal malformation has been discovered in 8 epidemiological studies and case reports in human beings.

Use in pregnancy:

Pregnancy Category A- Drugs which have been taken by a large number of pregnant women and women of childbearing age without a proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Pregnant females may experience spontaneous abortion and low birth weight babies. Epidemiological studies suggest an increased risk of spontaneous abortion and low birth weight in off-spring in female workers employed in operating theatres and dental surgeries. These findings are controversial.

Use in lactation:

No adverse reports of effects on lactation have been reported/ observed.

Paediatric use:

Not applicable

Use in elderly:

Not applicable

Carcinogenicity/mutagenicity:

Mild skeletal teratogenic changes have been observed on pregnant rat embryos when the dam has been exposed to high concentrations of nitrous oxide during the period of organogenesis.

Interactions with other medicines

Nitrous oxide inactivates vitamin B12. There are no major incompatibilities with nitrous oxide.

Effect on laboratory tests

Not applicable

Effect on ability to drive and operate machinery

Nitrous oxide is rapidly eliminated but it is recommended that driving, use of machinery and other psycho-motor activities should not be undertaken until 12 hours have elapsed after nitrous oxide anaesthesia.

Interactions with other drugs:

There are no major incompatibilities with nitrous oxide. Nitrous oxide inactivates vitamin B12.

Use of gas cylinders:

Cylinder should be kept out of the reach of children.

Care is needed in the handling and use of medical nitrous oxide gas cylinders. Nitrous oxide is stored in high pressure gas cylinders as a liquid under pressure at ambient temperature. Rapid opening of the valve and sustained high flow rates can cause the discharged gas to re-liquefy. This liquid can cause cold burns if in contact with the eyes and skin. Cylinders should be used in the vertical position with the valve uppermost. If not liquid may be discharged when the valve is opened.

Nitrous oxide will decompose at temperatures above 400 C and the speed of decomposition increases with increasing temperature. Explosive decomposition can occur at 650 C at atmospheric pressure.

The normal precautions required in the storage and use of medical gas cylinders are applicable. Cylinders should be stored away from sources of ignition, poisons, flammable or combustible materials. They should be secured upright, in a secure area, below 45 C, on a dry well ventilated area constructed of non-combustible material with a firm, level floor (preferably concrete) away from heavy traffic and emergency exits.

Additional information is contained in the Material Safety Data Sheet for Medical nitrous oxide.

Occupational exposure standard

WorkSafe exposure standard TLV TWA is 25 ppm.

Cold burns

Local pain usually gives warning of freezing, but sometimes no pain is felt or is short lived. Frozen tissues are painless and appear waxy, with a pale yellowish colour. Thawing of the frozen tissue can cause intense pain. Shock may occur if the area is large.

Loosen any clothing that may restrict blood circulation and seek immediate hospital attention for all but the most superficial injuries. Do not apply direct heat to the affected parts, but if possible place the affected part in lukewarm water. Sterile dry dressings should be used to protect damaged tissues from infection or further injury, but they should not be allowed to restrict the blood circulation. Alcohol and cigarettes should not be given.

Other special warnings and precautions

Administration of nitrous oxide, more frequently than every 4 days should be accompanied by routine blood cell counts for evidence of megaloblastic change in red cells and hypersegmentation of neutrophils.

Nitrous oxide should never be given with less than 21% oxygen, but a maximum of 30% oxygen should be used during anaesthesia (except when used in combination with a volatile anaesthetic agent) and more at altitude and in the presence of disorders affecting oxygenation.

Scavenging of waste nitrous oxide gas should be used to reduce operating theatre and equivalent treatment room levels to a level below 25 ppm of ambient nitrous oxide.

At the end of a nitrous oxide/oxygen anaesthesia, withdrawal of the mask leads to an outpouring of nitrous oxide from the lung and consequent dilution of oxygen in incoming air. This results in diffusion hypoxia and should be counteracted by giving 100% oxygen for a few minutes when the flow of nitrous oxide is stopped.

ADVERSE EFFECTS

Nitrous oxide is an asphyxiant in the absence of oxygen.

Effects on ability to drive and to use machines

Other undesirable effects (frequency & seriousness)

The use of nitrous oxide causes inactivation of vitamin B12 which is a co-factor of methionine synthase. Folate metabolism is consequently interfered with and DNA synthesis is impaired following prolonged nitrous oxide administration. These disturbances result in megaloblastic bone marrow changes. Exceptionally heavy occupational exposure and addiction have resulted in myeloneuropathy and subacute combined degeneration.

These effects include rarely - drowsiness, confusion, paraesthesiae in the legs, hyper-reflexia and weakness of the intrinsic hand muscles.

If these effects occur, usage of nitrous oxide should be stopped and daily vitamin B12 replacement administered. Effects should then be expected to be reversed gradually.

All these effects are well documented, extremely rare and may follow prolonged exposure to levels of nitrous oxide over 5,000 ppm or to frequent (more than once every two days) exposure to analgesic concentrations.

It has been suggested that prolonged occupational exposure to high levels of nitrous oxide may affect a woman's ability to become pregnant.

Nitrous oxide passes into all gas containing spaces in the body faster than nitrogen passes out. The main contra-indications which follow from this are listed above, but in addition prolonged anaesthesia may result in bowel distension, middle ear damage and rupture of ear drums.

Addiction to nitrous oxide has been reported.

DOSAGE AND ADMINISTRATION

Where the clinical indication is the production of general anaesthesia it should be noted that:

in the average adult, nitrous oxide is administered by inhalation through a suitable anaesthetic apparatus in concentrations up to 80% with oxygen as the balance.

as people age, there is a steady reduction in the indices of cardiac and respiratory function evidenced by a lowering of cardiac output and in lung ventilation and perfusion. In addition there is an increase in dead space in the lung which increases minute ventilation. Cerebral blood flow is reduced by up to 30%. The result of these changes mean that susceptibility to anaesthesia is increased. Nitrous oxide is, therefore, more useful in the elderly and the depressant effects of added agents are reduced.

There are no essential differences in clinical indications between the adult and child.

Nitrous oxide is strongly recommended in the anaesthesia of neonates.

In obstetrical anaesthesia, the nitrous oxide level is kept below 70% to allow a substantial oxygen level to be provided. Nitrous oxide plays a major role because injected agents depress the breathing of the infant and volatile agents depress uterine contraction.

As a general rule, the more ill the patient, the more susceptible is the patient to other anaesthetic agents and the more nitrous oxide is relied upon.

Routes of administration

Nitrous oxide administered through a face mask or tracheal tube by means of an anaesthetic apparatus. The gas is breathed in by the patient and absorbed through the lungs.

Nitrous oxide should only be administered by medical personnel trained in the appropriate techniques.

Cylinders should only be used in conjunction with medical nitrous oxide gas pressure regulators.

OVERDOSE

Inappropriate, unwitting or deliberate inhalation of nitrous oxide will ultimately result in unconsciousness, passing through stages of increasing light-headedness and intoxication, and, if the victim were to be within a confined space, death from anoxia could result.

The treatment is fresh air, mouth-to-mouth resuscitation and, if necessary, the use of an oxygen resuscitator.

PRESENTATION AND STORAGE

Pharmaceutical form

Compressed medical gas (for medicinal use only) – nitrous oxide 100% v/v supplied in cylinders in accordance with AS2030 and fitted with AS2472, pin index, valve outlet.

The cylinder colour code is –white body with ultramarine shoulder as per AS4484.

Cyl Size	nominal water capacity (L)
C	2.8
D	9.5
E	23
G	50
6 pack	300
12 pack	600

Instructions for Use / Handling

Care is needed in the handling and use of **Medical Nitrous Oxide** gas cylinders. Refer to the respective safety data sheet (SDS) and the “caution” section on the product label.

Preparation for use

1. Cylinder valves should be opened momentarily prior to use to blow any foreign matter out of the outlet.
2. Ensure that the connecting face on the yoke, manifold or regulator is clean and the sealing washer or ‘O’ ring where fitted is in good condition.
3. Cylinder valves must be opened slowly.
4. Only the appropriate regulator should be used for the particular gas concerned.
5. Cylinder valves and any associated equipment must never be lubricated and must be kept free from oil and grease.

Leaks

1. Should leaks occur this will usually be evident by a hissing noise.
2. Leaks can be found by brushing the suspected area with an approved leak test solution.
3. There are no user serviceable parts associated with these valves, do not attempt to correct any problems with leakage from any part of the valve itself. Label any faulty containers appropriately and return them to Coregas for repair.
4. Sealing or jointing compounds must never be used to cure a leak.
5. Never use excessive force when connecting equipment to cylinders.

Handling of Cylinders

1. Cylinders should be handled with care and not knocked violently or allowed to fall.
2. Cylinders should only be moved with the appropriate size and type of trolley.
3. When in use cylinders should be firmly secured to a suitable cylinder support.
4. Cylinders containing liquefiable gas must always be used vertically with the valve uppermost.

5. Medical gases must only be used for medicinal purposes.
6. Smoking and naked lights must not be allowed within the vicinity of cylinders or pipeline outlets.
7. After use, cylinder valves should be closed using moderate force only and the pressure in the regulator or tailpipe released.
8. When empty the cylinder valve must be closed.
9. Immediately return used cylinders to the used cylinder store for return to Coregas.

STORAGE:

Cylinders should be kept out of the reach of children.

Nitrous oxide is non-flammable but strongly supports combustion (including some materials which do not normally burn in air). It is highly dangerous when in contact with oils, greases, tarry substances and many plastics due to the risk of spontaneous combustion with high pressure gases.

Cylinders should be stored away from sources of ignition, poisons, flammable or combustible materials. They should be secured upright, in a secure area, below 45 C, on a dry well ventilated area constructed of non-combustible material with a firm, level floor (preferably concrete) away from heavy traffic and emergency exits.

The normal precautions required in the storage of medical gas cylinders as described below are applicable.

- Cylinders should be stored under cover, preferably inside, kept dry and clean and not subjected to extremes of heat or cold.
- Cylinders should not be stored near stocks of combustible materials or near sources of heat.
- Warning notices prohibiting smoking and naked lights must be posted clearly.
- Emergency services should be advised of the location of the cylinder store.
- Medical cylinders containing different gases should be segregated and identified within the store.
- Full and empty cylinders should be stored separately. Full cylinders should be used in strict rotation.
- Cylinders must not be repainted, have any markings obscured or labels removed.
- D size cylinders and larger should be stored vertically; C size cylinders can be stored horizontally.
- Precautions should be taken to protect cylinders from theft.

NAME AND ADDRESS OF SPONSOR

COREGAS PTY LTD.
A.C.N. 001 255 312.
66 Loftus Road.
Yennora 2161.

POISON SCHEDULE OF THE MEDICINE

Unscheduled.

DATE OF APPROVAL

TGA approval: 21/10/1991

Date of first inclusion in the Australian Register of Therapeutic Goods: 21/10/1991

Date of most recent amendment: 30/05/2013

AUST R: 27183