

Nitrous oxide 100%v/v medicinal gas, liquefied

Nitrous oxide

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Nitrous oxide is and what it is used for
2. What you need to know before you use Nitrous oxide
3. How to use Nitrous oxide
4. Possible side effects
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1. WHAT NITROUS OXIDE IS AND WHAT IT IS USED FOR

Nitrous oxide is an inhalation gas (intended for breathing in). The active substance is nitrous oxide, otherwise known as "laughing gas". It belongs to the group of general anaesthetics (narcotic agents) and is administered by a doctor.

Nitrous oxide is used for short-term pain relief but also as a component in anaesthesia for use in adults and children from the age of 1 month:

- Nitrous oxide is used in combination with oxygen when painkilling effects that start quickly and stop quickly are wanted and when the treated pain state is of mild to moderate intensity and of limited duration. In these cases, the composition of the combination is always 50% nitrous oxide and 50% oxygen.
- Nitrous oxide mixed with oxygen is also used as a basic anaesthetic in combination with other anaesthetics. In this case, the composition is variable but the mixture always contains a minimum of 21% oxygen.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE NITROUS OXIDE

Do not use Nitrous oxide

- If you inhale medical oxygen regularly or constantly.

- If there is a possibility of accumulation of air or gas in the body. This may apply in cases of untreated pneumothorax ("collapsed lung"), vesicular pulmonary emphysema or decompression sickness ("the bends").
- Following cardiopulmonary bypass with heart lung machine or coronary bypass without heart lung machine.
- In patients with heart failure or cardiac dysfunction (e.g. after cardiac surgery) in order to avoid the risk of further deterioration in heart function.
- For painkilling in patients with a decreased level of consciousness or impaired ability to cooperate and follow instructions due to the risk that further sedation from the nitrous oxide may affect natural protective reflexes
- If there is a sudden obstruction in the gastrointestinal system.
- If there is a possibility of increased pressure in the brain, characterised by severe headache, blurred vision, increased cerebrospinal fluid pressure, signs of neurological losses and impaired consciousness.
- If there are facial injuries at the site where the anaesthesia mask is placed on the face.
- After an injection of gas (e.g. SF₆, C₃F₈) into the eye this may lead to an increased volume in the eye and possibly cause blindness. (The doctor should not use Nitrous oxide until sufficient time has passed.)
- If you have been diagnosed with vitamin B₁₂ deficiency or folic acid deficiency (including in early pregnancy) but have not been treated for this, since use of nitrous oxide can worsen the symptoms caused by vitamin B₁₂ and folic acid deficiency.
- Narcotic drugs enhance the action of Nitrous oxide.
- Medicines containing morphine enhance the analgesic and sedative effects of Nitrous oxide.
- Benzodiazepines and barbiturates (a specific group of drugs with tranquillising, soporific and/or muscle-relaxing properties) enhance the effect of Nitrous oxide and the combination of these drugs with Nitrous oxide may result in loss of consciousness.
- The action of certain muscle relaxants (such as pancuronium, vecuronium) is enhanced by Nitrous oxide.
- The damage caused by sodium nitroprusside (a drug to treat high blood pressure) and methotrexate (a drug used in the treatment of cancer) is increased because the action of vitamin B₁₂ is overridden by Nitrous oxide.
- The damage caused by bleomycin (a drug used in the treatment of cancer) to the lungs may be increased with increased administration of oxygen (such as occurs with treatment with Nitrous oxide).

Warnings and precautions

- If you have a vitamin B₁₂ deficiency, such as may occur in people with pernicious anaemia (malignant form of anaemia) or Crohn's disease (chronic enteric disease), or in vegetarians.
- If you have impaired heart function (if your heart does not perform adequately).
- If you have seriously low blood pressure as a result of shock or heart failure.
- If you have sickle cell anaemia (a specific blood disease in which the red blood cells have an abnormal shape).
- If analgesia involving opium is given in childbirth (the combination of this type of drug with Nitrous oxide may cause loss of consciousness).
- After an injection into the eye (with another agent), sufficient time must have passed before Nitrous oxide is given because otherwise there is a risk of eye problems (including blindness).
- Due to its nitrous oxide content, Nitrous oxide can increase pressure in the middle ear and other air-filled cavities.
- When benzodiazepines are used at the same time (a specific group of drugs with tranquillising, soporific and/or muscle-relaxing properties) because loss of consciousness may occur.
- If you are being treated with bleomycin (a medicine used in the treatment of cancer).

Please ask your doctor if one of the warnings above applies to you or if it has done so in the past.

Other medicines and Nitrous oxide

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

NOTE: the following statements may also apply to the use of medicines prior to or for some time after using Nitrous oxide.

- Protect gas cylinders from falling and other shocks by fixing them in position or storing them in a crate.
- Gas cylinders containing a different type of gas or containing a different composition must be stored separately.
- Store full and empty gas cylinders separately.
- Do not store gas cylinders in the vicinity of a heat source.
- Store gas cylinders covered and protected from atmospheric influences.
- The valves of gas cylinders for nitrous oxide are fitted with a rupture disc to prevent the cylinder bursting if pressure inside the cylinder becomes too high. The rupture disc may fail if the temperature is too high.

Nitrous oxide with food and drink

If Nitrous oxide is used as a component of an anaesthetic, nothing may be eaten or drunk after midnight on the night before the treatment because Nitrous oxide may cause nausea or vomiting (see section 4 "Possible side effects").

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

Limited data on the short-term use of Nitrous oxide during pregnancy indicate no increased risk of congenital malformations. In rare cases, Nitrous oxide may cause breathing problems in newborns. Nitrous oxide may be used during pregnancy only if it is strictly necessary.

Long-term or frequent use must be avoided.

Breast-feeding

It is unknown whether Nitrous oxide is excreted in human milk. It is not necessary to discontinue breast-feeding after short-term administration.

Fertility

Animal studies at low concentration of nitrous oxide ($\leq 1\%$) suggest that there is a slight alteration in male or female fertility.

Driving and using machines

- Do not drive or use any tools or machines for 24 hours after using Nitrous oxide in combination with anaesthetic drugs because Nitrous oxide has a major effect on the ability to drive and operate machines.
- Be careful after short-term administration of Nitrous oxide for pain relief. You may not drive or use machines until any side effects have disappeared and you are once more as alert as before being given the treatment.

3. HOW TO USE NITROUS OXIDE

For inhalation use.

Nitrous oxide is administered by a doctor who will also establish the correct dose.

For short-term use for pain relief

Administration of Nitrous oxide in combination with the same proportion of oxygen has already an analgesic effect after 4 to 5 inhalations, with a maximum pain relief after 2-3 minutes.

The following information is intended for healthcare professionals only:

Special precautions and conditions for storage

- Store gas cylinders between -20°C and $+65^{\circ}\text{C}$.
- Store gas cylinders in a well-ventilated area that is suitable for the storage of medicinal gases.
- Keep gas cylinders away from flammable products.
- Avoid all contact with oil, grease or similar substances.
- Keep gas cylinders upright, except for those gas cylinders with convex bases, which should be stored lying down or in a crate.

This will release the entire contents of the cylinder.

In this event, do not enter the storage area and ventilate the area well until it is cleared for use by an expert.

Instructions for use, processing and disposal

Follow the instructions of your supplier, particularly:

- Nitrous oxide may be administered only once suitable pressure and output regulation has been created between the cylinder and the patient.
- Before the valve on the cylinder is opened, the cylinder must be placed in a vertical position and kept in a vertical position during administration.

Administration of Nitrous oxide should continue throughout the painful procedure, or for as long as the analgesic effect is desired. Following discontinuation of the administration/inhalation, the effects wear off quickly within a few minutes. According to the individual pain relieving reaction in the patient, additional analgesics may be required. When used for pain relief, Nitrous oxide is only given in combination with the same proportion of oxygen (50% nitrous oxide and 50% oxygen). The maximum period of administration does not exceed 1 hour continuously per day. This treatment may not be repeated for more than 15 consecutive days.

For use in combination with anaesthetic drugs

When used in combination with anaesthetic drugs, Nitrous oxide is only given after being mixed with a minimum of 21% oxygen. Nitrous oxide alone is unable to cause anaesthesia. Combination of anaesthetic drugs with Nitrous oxide means that all the agents are taken up more rapidly and smaller amounts of the other anaesthetic drugs are required. The effect can generally be noticed within 2 to 5 minutes.

Instructions for the use of Nitrous oxide

Nitrous oxide is only given after being mixed with a minimum of 21% oxygen and using equipment designed for this purpose and utilising a well-fitting mask.

Nitrous oxide is always given by a doctor.

It is administered in well-ventilated areas, using gas scavenging with a double mask, for example, to prevent exhaled Nitrous oxide entering the ambient air.

If you use more Nitrous oxide than you should

The consequences of Nitrous oxide overdose result in acute oxygen shortage. In the event of an overdose, administration of Nitrous oxide must be stopped immediately and you will need to be ventilated with air or oxygen until the oxygen concentration in your blood returns to normal.

If you stop using Nitrous oxide

After you stop using Nitrous oxide and medical oxygen an oxygen shortage may develop. To prevent this from occurring, you can be temporarily ventilated with 100% oxygen. If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects below have been classified by organ system. Few accurate data are known regarding the frequency of the side effects but side effects occur more often with a higher dosage and/or longer period of administration. Nausea and vomiting are the most common side effects.

Blood and lymphatic system disorders:

Severe disruptions of the complete blood count (megaloblastic anaemia, granulocytopenia) have been observed after administration for longer than 24 hours. It is assumed that a single exposure for up to 6 hours involves no risk.

Nervous system disorders:

Decreased circulation in the brain and decreased glucose consumption by the brain.

Psychedelic effects may occur even if no other anaesthetic drug is used.

Neurological effects: spinal cord disorders,

neuropathy, epilepsy, increased pressure in the skull, symptoms of paralysis in both legs with muscle cramps.

Psychiatric disorders: psychosis (serious mental illness in which control over one's own behaviour and actions is impaired), confusion and headache, but also effects reducing anxiety and improving mood.

Temperature disorders:

Very severe decrease and/or increase in body temperature.

Eye disorders:

Slowed eye movements.

Temporary increase in pressure and/or volume of the eye if Nitrous oxide is used after an injection of a gasforming drug into the eye.

Ear and labyrinth disorders:

Temporary increase in pressure and/or volume of the enclosed cavities in the middle ear.

Cardiac and vascular disorders

Cardiac arrhythmia, heart failure, raised blood pressure in the lungs and low blood pressure in the body.

Respiratory, thoracic and mediastinal disorders:

Respiratory depression, air in the chest cavity, subcutaneous emphysema and symptoms comparable to a respiratory infection. Oxygen shortage for a few minutes after ending the administration of Nitrous oxide.

Gastrointestinal disorders

Nausea and regularly, vomiting.

Temporary increase of pressure and/or volume in the intestines and abdominal cavity.

Hepatobiliary and pancreatic disorders:

Jaundice and increase in liver enzyme concentration.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE NITROUS OXIDE

Keep this medicine out of the sight and reach of children.

Nitrous oxide is stored and kept by qualified staff in accordance with the instructions provided by the manufacturer and the relevant regulations.

Do not use this medicine after the expiry date which is stated on the label after {Exp.}.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Nitrous oxide contains

- The active substance is nitrous oxide (dinitrogen monoxide).
- Nitrous oxide contains no other ingredients.

What Nitrous oxide looks like and contents of the pack

- Nitrous oxide is an inhalation gas (intended for breathing in) and is packed in liquid form in pressurised gas cylinders. The cylinders are colour-coded : body is pure white (RAL 9010) and the shoulder is gentian blue (RAL 5010).

- The table below gives the content of the various gas cylinders (in litres) and the associated number of kilograms of nitrous oxide gas at a pressure of 45 bar (at 15°C).

Content in litres (x)	Amount of kg nitrous oxide gas (y)	Content in litres (x)	Amount of kg nitrous oxide gas (y)
1	0.75	40	30
2	1.5	50	37.5
3	2.25	12*40	360
5	3.75	12*50	450
10	7.5	16*40	480
20	15	16*50	600
30	22.5		

Not all pack sizes may be marketed.

Marketing authorisation holder and manufacturer

Marketing Authorisation holder

SOL S.p.A.

via Borgazzi 27, 20900 Monza, Italy

Manufacturer

SOL Nederland B.V. - Swaardvenstraat 11
5048 AV Tilburg, The Netherlands

Or

BTG Sprl

Zoning Ouest 15, 7860 Lessines, Belgium

Or

SOL S.p.A.

via Acquaviva 4, 26100 Cremona, Italy

Or

SOL Hellas S.A. - Thesi Paxi Patima Stefanis

19200 Kamari Boiotias, Greece

Or

SOL France S.A.S.

ZI des Béthunes, 8 Rue du Compas

95310 Saint Ouen L'Aumone, France

This medicinal product is authorised in the Member States of the EEA under the following names:

- Belgium: Protoxyde d'azote Médicinal SOL 100 % v/v, gaz médicinal liquéfié
- Bulgaria: Медицински диазотен оксид SOL 100 % v/v, втечен медицински газ
- Czech Republic: Medicinální oxid dusný SOL 100% medicínální plyn, zkapalněný
- Greece: Φαρμακευτικό Πρωτοξειδίο του Αζώτου SOL, 100% v/v, ιατρικό αέριο, υγροποιημένο
- Hungary: SOL Orvosi Dinitrogén-oxid, 100% v/v, Cseppfolyósított orvosi gáz
- Ireland: Nitrous oxide Medicinal SOL, 100 % v/v, medicinal gas, liquefied
- Luxembourg: Protoxyde d'azote Médicinal SOL 100 % v/v, gaz médicinal liquéfié
- Romania: Protoxid de azot SOL 100 % gaz medicinal lichefiat
- Slovenia: Medicinski didušikov oksid SOL 100 % medicinski plin, utekočinjen
- Slovakia: Medicinálny oxid dusný SOL 100%, medicínálny plyn skvapalnený
- Spain: Óxido nitroso medicinal SOLGROUP, 100 % v/v, gas licuado medicinal
- The Netherlands: Distikstofoxide Medicinaal SOL, medicinaal gas, vloeibaar gemaakt 100% v/v
- UK: Nitrous oxide 100%v/v medicinal gas, liquefied

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- Administration of nitrous oxide must take place at the same time as administration of oxygen by means of a secure mixer; the pressure of nitrous oxide in the lines must always be lower than the oxygen pressure.
- If a variable mixer is used, monitoring with an oxygen analyser is recommended.
- The gas cylinder may not be used if it has sustained visible damage or if it is suspected of being damaged or of having been exposed to extreme temperatures.
- All contact with oil, grease or similar substances must be avoided.
- Only apparatus that is suitable for the specific type of gas cylinder and gas may be used.

- No tongs, forceps or other instruments may be used to open or close the cylinder valve so as to avoid damaging it.
- The packaging type may not be changed.
- In the event of a leak, the gas cylinder valve must be closed immediately if this can be achieved safely. If it is not possible to close the valve, the gas cylinder must be taken to a safe place out of doors and allowed to run empty.
- Close the valves of empty gas cylinders.
- Siphoning off compressed gas is not allowed.
- Installations to be used, with central storage, distribution networks, pipeline system, terminal units and connections must comply with the relevant applicable legislation.

- Nitrous oxide may cause glowing or smouldering materials to ignite suddenly; it is therefore prohibited to smoke or have an open flame in the vicinity of a gas cylinder.
- Nitrous oxide is a nontoxic, non-flammable gas, heavier than air and will feed a fire. It may form explosive mixtures in combination with flammable anaesthetic gases or vapours, even in the absence of oxygen.
- Return the cylinders to the supplier once they are empty.