

Package leaflet: Information for the user

Nitrous oxide Medicinal SOL 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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Nitrous oxide Medicinal SOL is and what it is used for
2. What you need to know before you use Nitrous oxide Medicinal SOL
3. How to use Nitrous oxide Medicinal SOL
4. Possible side effects
5. How to store Nitrous oxide Medicinal SOL
6. Contents of the pack and other information

1. What Nitrous oxide Medicinal SOL is and what it is used for

Nitrous oxide Medicinal SOL is a colourless, sweet smelling 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).

Nitrous oxide Medicinal SOL is used in adults and children from the age of 1 month:

- In combination with oxygen (50% nitrous oxide and 50% oxygen) for relief of short-term, intermittent, mild to moderate pain.
- In mixture with a minimum of 21% oxygen as a basic anaesthetic in combination with other anaesthetics.

2. What you need to know before you use Nitrous oxide Medicinal SOL

Do not use Nitrous oxide Medicinal SOL if you have:

- To inhale 100% medical oxygen regularly or constantly
- Air trapped in a part of the body where it's expansion may be dangerous, such as in collapsed lung (pneumothorax), in breathing difficulties such as emphysema or in decompression sickness (the bends)
- Undergone a bypass surgery with or without heart lung machine
- In patients with cardiac disease (i.e heart failure or cardiac dysfunction)
- Injuries to the face or jaw disorder
- Head injuries with consciousness disorder

- Severely bloated stomach
- Suspected or known increased pressure in the brain
- 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 Medicinal SOL 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.

Warnings and precautions

Talk to your doctor or pharmacist before using Nitrous oxide Medicinal SOL:

- if you have or have had drug/medication abuse because there is a higher risk of developing dependence to nitrous oxide if you take it repeatedly. Your doctor will decide whether treatment with Nitrous oxide Medicinal SOL is possible in your case.
- Repeated or long-term use of nitrous oxide may increase the risk of vitamin B₁₂ deficiency which may lead to damage of the bone marrow or the nervous system. Your doctor may initiate blood tests before and after the treatment in order to assess the consequences of the possible vitamin B₁₂ deficiency.
- 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 Medicinal SOL may cause loss of consciousness).
- after an injection into the eye (with another agent), sufficient time must have passed before Nitrous oxide Medicinal SOL is given because otherwise there is a risk of eye problems (including blindness).
- due to its nitrous oxide content, Nitrous oxide Medicinal SOL 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).

Children and adolescents

Do not give this medicine to neonates (pre-term or term).

Other medicines and Nitrous oxide Medicinal SOL

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 Medicinal SOL.

- Narcotic drugs enhance the action of Nitrous oxide Medicinal SOL.
- Medicines containing morphine enhance the analgesic and sedative effects of Nitrous oxide Medicinal SOL.
- Benzodiazepines and barbiturates (a specific group of drugs with tranquillising, soporific and/or muscle-relaxing properties) enhance the effect of Nitrous oxide Medicinal SOL and the combination of these drugs with Nitrous oxide Medicinal SOL may result in loss of consciousness.
- The action of certain muscle relaxants (such as pancuronium, vecuronium) is enhanced by Nitrous oxide Medicinal SOL.
- 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 Medicinal SOL.
- 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 Medicinal SOL).

Nitrous oxide Medicinal SOL with food and drink

If Nitrous oxide Medicinal SOL is used as a component of an anaesthetic, nothing may be eaten or drunk 6 hours prior to general anaesthesia because Nitrous oxide Medicinal SOL 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 Medicinal SOL indicate no increased risk of congenital malformations. In rare cases, Nitrous oxide Medicinal SOL may cause breathing problems in newborns. Nitrous oxide Medicinal SOL may be used during pregnancy only if strictly necessary. Long-term or frequent use must be avoided.

Breast-feeding

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

Fertility

There are no relevant human data pertaining to effects of nitrous oxide on fertility. Animal studies suggest that male and female fertility may be affected when exposed to low ($\leq 1\%$) concentrations.

Driving and using machines

- Do not drive or use any tools or machines for 24 hours after using Nitrous oxide Medicinal SOL in combination with anaesthetic drugs because Nitrous oxide Medicinal SOL has a major effect on the ability to drive and operate machines.
- Be careful after short-term administration of Nitrous oxide Medicinal SOL 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 Medicinal SOL

For inhalation use.

Nitrous oxide Medicinal SOL will be given to you by a doctor who will also establish the correct dose.

For short-term use for pain relief

When used for pain relief, Nitrous oxide Medicinal SOL is only given in combination with the same proportion of oxygen (50% nitrous oxide and 50% oxygen).

Analgesic effect occurs after 4 to 5 inhalations, with a maximum pain relief after 2-3 minutes. Administration of Nitrous oxide Medicinal SOL 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.

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.

According to the individual pain-relieving reaction in the patient, additional analgesics may be required.

For use in combination with anaesthetic drugs

When used in combination with anaesthetic medicines, Nitrous oxide Medicinal SOL is only given after being mixed with a minimum of 21% oxygen. Nitrous oxide Medicinal SOL alone is unable to cause anaesthesia. Combination of anaesthetic medicines with Nitrous oxide Medicinal SOL means that 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 Medicinal SOL

Nitrous oxide (medical) will be administered via inhalation and you will be given a facemask mouthpiece or nasal prongs to use. The facemask or mouthpiece is connected to nitrous oxide (medical) via a suitable medical device. The device must be operated in the manner described by the manufacturer. These systems will only be used to give you nitrous oxide under the direct supervision of attendant and suitably trained medical personnel in well-ventilated areas to prevent exhaled Nitrous oxide Medicinal SOL entering the ambient air.

If you use more Nitrous oxide Medicinal SOL than you should

The consequences of Nitrous oxide Medicinal SOL overdose result in acute oxygen shortage. In the event of an overdose, administration of Nitrous oxide Medicinal SOL 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 Medicinal SOL

After you stop using Nitrous oxide Medicinal SOL 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, pharmacist or nurse.

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

- Megaloblastic anaemia (a type of anaemia due to vitamin B₁₂ deficiency caused by nitrous oxide)
- Granulocytopenia (complete deficiency of one type of blood cells)

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.
- Addiction (with frequency unknown).

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, pins and needles throughout the body, myeloneuropathy, epilepsy, generalised seizures (with a frequency not known), sedation, dizziness, increased pressure in the skull, symptoms of paralysis in both legs with muscle cramps.
- Effects on nerve function, sensations of numbness and weakness, usually in the legs (with frequency unknown).
- 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 Medicinal SOL is used after an injection of a gas-forming drug into the eye.

Ear and labyrinth disorders

- Middle ear damage and ear drum rupture

Cardiac disorders

- Cardiac arrhythmia
- Heart failure
- Raised blood pressure in the lungs
- 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.

Gastrointestinal disorders

- Nausea
- Vomiting
- Temporary increase of pressure and/or volume in the intestines and abdominal cavity

Hepatobiliary and pancreatic disorders

- Jaundice
- Increase in liver enzyme concentration.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

HPRa Pharmacovigilance Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie.

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

5. How to store Nitrous oxide Medicinal SOL

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

Nitrous oxide Medicinal SOL 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 Medicinal SOL contains

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

What Nitrous oxide Medicinal SOL looks like and contents of the pack

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

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 France S.A.S.
ZI des Béthunes
8 Rue du Compas
95310 Saint Ouen L'Aumone
France

Or

TAE - Technika Aeria Ellados
Thesi Stefani, ASPROPYRGOS
ATTIKI, GR-193 00 Greece

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

SOL S.p.A.
Via Borgazzi 27
20900 Monza Italy

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: | Medicinnální oxid dusný SOL 100% medicinnální plyn, zkapalněný |
| Greece: | Φαρμακευτικό Πρωτοξείδιο 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 |
| Luxemburg: | 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: | Medicinnálny oxid dusný SOL 100%, medicinnálny 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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The following information is intended for healthcare professionals only:

Safety directions

Repeated administration or exposure to nitrous oxide may lead to addiction. Caution should be exercised in healthcare professionals with occupational exposure to nitrous oxide.

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.
- 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. 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 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.