Package leaflet: Information for the user

Ninoxan 50% / 50%, medicinal gas, compressed

nitrous oxide / oxygen

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 Ninoxan is and what it is used for

Ninoxan contains a ready mixture of nitrous oxide (medicinal "laughing gas", N_2O) and oxygen (medicinal oxygen, O_2), 50% of each, and should be used by breathing in the gas mixture.

The effects of Ninoxan:
Nitrous oxide constitutes 50% of the gas mixture. Nitrous oxide has a painkilling effect, reduces the sensation of pain and raises the pain threshold. Nitrous oxide also has a relaxing and slightly calming effect. These effects are produced by the effects of nitrous oxide on signal substances in your nervous system.
The 50% concentration of oxygen, around double that in the ambient air, guarantees a safe oxygen content in the inspired gas.

What Ninoxan is used for
Ninoxan should be used when painkilling effects, of rapid onset and rapid resolution are desired and when the treated state of pain is of mild to moderate intensity and of limited duration.

Ninoxan produces an analgesic effect after few breaths and the painkilling effects subside within minutes after use is ceased.

Children
Ninoxan can be used in children older than 1 month.

2. What you need to know before you use Ninoxan

Do not use Ninoxan:
Before using Ninoxan you should tell your doctor if you have any of the following symptoms/conditions:
- **Gas cavities or gas bubbles:** if as a result of a disease, or for any other reason, you suspect that there is air in your pleural cavity outside the lungs, or gas bubbles in the blood or in any other organ (e.g., if you have dived with diving equipment and you may have gas bubbles in the blood

(decompression sickness); or if you have been treated with an injection of gas into the eye, e.g., a retinal detachment, or similar). These gas bubbles can expand and cause damage.
- **Heart disease:** if you have heart failure or severely impaired heart function, since the slightly relaxing effect of nitrous oxide on the heart muscle can further impair cardiac function.
- **Following cardiopulmonary bypass** with heart lung machine or **coronary by-pass** without heart lung machine.
- **Central nervous system injury:** if you have increased pressure in the brain, e.g., as a result of a tumour or bleeding in the brain**.** Nitrous oxide can further increase the pressure in the brain with potential risk of harm.
- **Vitamin deficiency:** if you have diagnosed but untreated vitamin B12 or folic acid deficiency, the use of nitrous oxide may worsen the symptoms caused by vitamin B12 and folic acid deficiency.
- **Dilatation of the gut (Ileus**): if you have severe abdominal discomfort or other symptoms that may indicate ileus since Ninoxan can further increase dilatation of the gut.
- **If you have a facial injury** the use of masks may present difficulties or risks.
- **Decreased level of consciousness** or impaired ability to cooperate and follow instructions because of the risk that further sedation from the nitrous oxide may affect natural protective reflexes.

Warnings and precautions

Talk to your doctor or nurse before you are given Ninoxan 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 Ninoxan is possible in your case.

Tell your doctor if you have any of the following symptoms:
- **Ear discomfort:** e.g. ear inflammation, since Ninoxan can increase the pressure in the middle ear.
- **Vitamin deficiency:** if you are at risk of having vitamin B12 deficiency or folic acid deficiency, e.g. if you have reduced intake or uptake of vitamin B12 or folic acid, or a genetic disorder affecting the metabolism of these vitamins or if you are immunosuppressed. The use of nitrous oxide can worsen the symptoms caused by vitamin B12 and folic acid deficiency.

Your doctor will decide whether Ninoxan is suitable for use.

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.

Children
Ninoxan shall not be used in children younger than 1 month.

Your doctor will decide whether it is appropriate to use Ninoxan.

Other medicines and Ninoxan
Tell your doctor or healthcare professional if you are using, have recently used or might use any other medicines.

If you are taking other medicines that affect the brain or brain function, e.g. benzodiazepines (tranquilizers) or morphine-like medicines, you should tell your doctor. Ninoxan may increase the effects of these medicines. The use of Ninoxan together with other sedatives or medicines that affect the central nervous system increases the risk of side effects.

You should also tell your doctor if you are taking medicines containing methotrexate (e.g. to treat rheumatoid arthritis), bleomycin (cancer treatment), nitrofurantoin and other antibiotics (treatment of infections) or amiodarone (to treat heart disease). Ninoxan increases the side effects of these medicines.

Pregnancy and breast-feeding

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

Pregnancy
Ninoxan can be used during pregnancy if the doctor considers it clinically needed. It can also be used during delivery. When Ninoxan is used close to delivery, your baby should be supervised for possible adverse effects.

Breast-feeding
Ninoxan can be used during breast-feeding period, however should not be used during breast-feeding itself.

Driving and using machines
Ninoxan has a sedative effect, and it can affect how your mind and body works. For safety reasons, you should therefore avoid driving, operating machinery or performing complicated tasks until you have fully recovered. Check with your healthcare professional when he/she thinks that you are fully recovered.

3. How to use Ninoxan

Ninoxan is always given under the supervision and presence of healthcare professionals familiar with this type of medicine and equipment. Throughout the period during which you use Ninoxan you, and the administration of the medicine, will be monitored to ensure that it is administered safely. After finishing treatment, you should be monitored by competent personnel until you have recovered.

Always use Ninoxan exactly as your doctor has instructed you. He/She should explain how to use Ninoxan, how it works and what effects result from its use. Check with your doctor if you are not sure.

Ninoxan is usually inhaled through a face mask attached to a special valve, which means you have full control of the flow of gas by virtue of your own breathing. The valve is only open during inspiration. Ninoxan can also be administered via a so-called nasal mask.

Regardless of which mask you use, you should breathe normally, with normal breaths in the mask. Ideally you should hold the mask yourself.

You should start using Ninoxan shortly before the painkilling effect is required and continue through the painful process. The effect of Ninoxan wears of within a few minutes after discontinuation of the inhalation.

After you stop using Ninoxan you must rest and recover until you feel you have recovered mentally.

Safety precautions:
- Smoking and open fire is strictly forbidden in rooms where treatment with Ninoxan is taking place.
- Ninoxan is intended for medicinal use only.

Use in children
Ninoxan shall not be used in children younger than 1 month.

If you use more Ninoxan than you should
It is unlikely that you receive too much gas, since the gas is inhaled and controlled by your own breaths and the gas mixture is fixed (with 50% nitrous oxide and 50% oxygen).

If you breathe faster than normal, thus receiving more nitrous oxide than you would with normal breathing, you may feel noticeably tired and out of touch with your surroundings. In this case, you must immediately inform the healthcare professionals and stop inhaling Ninoxan.

If you have any further questions on the use of this medicine, ask your doctor or healthcare professional.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been reported:

Common (may affect up to 1 in 10 people):
- Dizziness, vertigo (a feeling of dizziness or "spinning"), feeling faint.
- Light headaches**.**
- Euphoria.
- Nausea and vomiting.

Uncommon (may affect up to 1 in 100 people):
- Severe tiredness.
- Feeling of pressure in the middle ear, if Ninoxan is used for prolonged period.
- Abdominal bloating, because Ninoxan slowly increases the volume of gas in the intestines.

Very rare (may affect up to 1 in 10,000 people)
- Effects on nerve function, numbness and weakness, usually in the legs.

Not known (frequency cannot be estimated from the available data):
- Effects on bone marrow, which can cause anaemia. Low levels of white blood cells.
- Psychiatric effects, including psychosis, confusion and anxiety.
- Headache.
- Respiratory depression.
- Generalised seizures
- Addicition
- Effects on nerve function, sensations of numbness and weakness, usually in the legs

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Ninoxan

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

Do not use this medicine after the expiry date which is stated on the gas cylinder after EXP. The expiry date refers to the last day of that month.

Do not store below -5 °C.
The mixture is unstable below -5 ºC. On suspicion that Ninoxan has been stored at temperatures below -5 ºC, the cylinders should be stored in a horizontal position at a temperature above 10 ºC for at least 48 hours before use.

When it is used in emergency service vehicles, the cylinders must be protected from the cold and firmly secured, inside and outside of the vehicles.

Keep the cylinder in a storage area reserved for medical gases.

Different gas types must be separated from each other. Full and empty gas cylinders must be stored separately.
No smoking. Must not be exposed to strong heat.
Vapour may cause drowsiness and dizziness.
Keep away from combustible material.
If at risk of fire, move to a safe place.
Keep the cylinder clean, dry and free of oil and grease.
Keep in upright position.
Make sure the cylinder is not knocked over or dropped.
Store and transport with valves closed.

6. Contents of the pack and other information

What Ninoxan contains:

- The active substances are: Nitrous oxide 50% = medicinal laughing gas (chemical formula: N_2O) and Oxygen 50% = medicinal oxygen (chemical formula: O_2)
- Ninoxan does not contain any other ingredient

What Ninoxan looks like and contents of the pack
Ninoxan is a colourless, odourless gas, provided in a gas cylinder of steel or aluminium with a valve to control the flow of gas.

The cylinders are identified through specific colors (white body with blue and white shoulder, with two horizontal bands and the blue is the lower).

Pack sizes:
Aluminium cylinder with integrated valve or normal PRV valve:
2-litres filled at 170 bar gives 0.56 m3 gas at atmospheric pressure and 15 °C.
5-litres filled at 170 bar gives 1.4 m^3 gas at atmospheric pressure and 15 °C.
10-litres filled at 170 bar gives 2.8 m^3 gas at atmospheric pressure and 15 °C.

Seamless steel gas cylinder with integrated valve or normal PRV valve:
5-litres filled at 170 bar gives 1.4 m^3 gas at atmospheric pressure and 15 °C.
10-litres filled at 170 bar gives 2.8 m^3 gas at atmospheric pressure and 15 °C.

Seamless steel gas cylinder with normal PRV valve:
50-litres filled at 170 bar gives 14 m^3 gas at atmospheric pressure and 15°C.

Not all pack sizes may be marketed.

Marketing Authorisation Holder:

To be completed nationally.

Manufacturer:

To be completed nationally.

This leaflet was last revised in
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The following information is intended for healthcare professionals only:

Safety Instructions

Special precautions must be taken when working with nitrous oxide. Nitrous oxide should be administered according to local guidelines.
Repeated administration or exposure to nitrous oxide may lead to addiction. Caution should be exercised in healthcare professionals with occupational exposure to nitrous oxide.
Ninoxan should only be used in areas that are well ventilated and where there is special equipment to remove the excess of gas. Using an extractor system and ensuring good ventilation, high atmospheric concentrations of nitrous oxide in ambient air are avoided.
High concentrations of nitrous oxide in the ambient air can cause negative health effects in personnel or other people close to the place of administration. There are nationally set hygienic limit values for the concentration of nitrous oxide in the ambient air. These should not be exceeded, in order to ensure that the personnel are not exposed to risks. The so-called "Threshold Limit Values TLV" of occupational exposure to chemicals are often expressed as TWA (*time weight average*), which is the average value over a working day, and STEL (*short-term exposure Limit*), which is the average value over a shorter exposure.

Ninoxan is an unstable mixture below -5 °C. Lower temperatures can cause a temporary liquefaction of the nitrous oxide, which would lead to a uneven mix, with too much oxygen at the beginning of the administration (mixture with less analgesic effect) and too much nitrous oxide at the end (hypoxic mixture) of the inhalation.

On suspicion that Ninoxan has been stored at temperatures below -5 ºC, the cylinders should be stored in a horizontal position at a temperature above 10 ºC for at least 48 hours before use. It is recommended that the cylinder is shaken by inverting it completely at least three times to ensure homogenization before use.

Keep the cylinder in a storage area reserved for medical gases. Different gas types must be separated from each other. Full and empty gas cylinders must be stored separately.

When it is used in emergency service vehicles, the cylinders must be protected from the cold and firmly secured, inside and outside of the vehicles.

Other instructions:

- Keep away from combustible materials. No smoking.
- Open the valve slowly and carefully. Never use oil or grease, even if the cylinder valve difficult to open or if the regulator is difficult to connect. Never force the valve, use only connection devices and seals compatible with the specific mixture of gas and for oxidizing gases. Never use a tool to connect a pressure/flow regulator that is intended to be connected manually, as this can damage the coupling.
- Close the cylinder valve in case of fire, or when not in use. Store and transport the cylinders always with the valves closed, even when they are empty.
- When the cylinder is in use it must be fixed in a suitable support. Keep containers upright, however the cylinders should be stored in horizontal position when there is a suspicion that the cylinder has been stored at temperatures below -5 ºC.
- The gas cylinder should be replaced when the pressure in the cylinder has dropped to a point where the indicator on the valve is within the yellow field.
- When a small quantity of gas is left in the gas cylinder, the cylinder valve must be closed. It is important that a small amount of pressure be left in the cylinder to avoid the entrance of contaminants. Keep full and empty cylinders separated.
- After use, the cylinder valve must be closed hand-tight. Depressurize the regulator or connection.
- For more details read the Summary of Product Characteristics (SmPC) or contact the provider.