1. NAME OF THE MEDICINAL PRODUCT

Medicinal oxygen Nippon Gases Scandinavia 100 %, medicinal gas, cryogenic

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxygen 100%

3. PHARMACEUTICAL FORM

Medicinal gas, cryogenic
Colourless, odourless and tasteless

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxygen therapy
- For treatment or prevention of acute and chronic hypoxia irrespective of cause.
- As part of the fresh gas flow in anaesthesia or intensive care.
- As the propellant in nebuliser treatment.
- For treatment of an acute attack of cluster headache.

Hyperbaric oxygen therapy
For treatment of decompression sickness, air/gas emboli from other causes and carbon monoxide poisoning. Treatment of patients who have been exposed to carbon monoxide is especially indicated in pregnant patients or patients who are or have been unconscious, or who have displayed neurological symptoms and/or cardiovascular effects or severe acidosis, irrespective of the measured COHb value.

As adjunct treatment in:
severe osteoradionecrosis, clostridium myonecrosis (gas gangrene).

4.2 Posology and method of administration

Oxygen therapy
Oxygen is administered via the inspiratory air.

Oxygen can also be supplied through a so-called ‘oxygenator’ directly to the blood in cases of, among other things, cardiac surgery with a heart-lung machine, and in other conditions that require extracorporeal circulation.

Oxygen is administered by means of equipment intended for this purpose. With this equipment, the oxygen is supplied to the inspiratory air, and, on expiration, the exhaled gas with any excess of oxygen, passes from the patient and is mixed with the surrounding air (non-rebreathing system). For treatment of cluster headache, oxygen is to be delivered by a facemask, in a non re-breathing system.

For anaesthesia, special equipment is often used in which the exhaled gas recirculates and can, in part, be re-inhaled (circular system with rebreathing).
There are a large number of devices intended for oxygen administration.

Low-flow system
The simplest system, which mixes oxygen with the inhaled air, e.g. a system in which the oxygen is dosed via a simple rotameter and a nasal catheter or face mask.

High-flow system
System intended to supply a gas mixture corresponding to the patient's breath. This system is intended to produce a fixed oxygen concentration that is not affected or diluted by the surrounding air, e.g. Venturimask with a constant oxygen flow in order to give a fixed oxygen concentration in the inhaled air.

Hyperbaric oxygen therapy
Hyperbaric oxygen therapy (HBO) is given in specially constructed pressurised chambers intended for hyperbaric oxygen therapy, in which pressures up to the equivalent of 3 atmospheres (atm) can be maintained. HBO can also be given via a very tightly fitting facemask, a hood that fits around the head, or through a tracheal tube.

Dosage
Oxygen therapy
The aim of treatment is to ensure, by adjusting the oxygen fraction in the inhaled air (FiO_2), that the oxygen partial pressure in arterial blood (PaO_2) does not fall below 8.0 kPa (60 mmHg) or that the oxygen saturation of haemoglobin in arterial blood does not fall below 90%.

The dose (FiO_2) must be adjusted according to each patient's individual needs, taking into account the risk of oxygen toxicity. A general recommendation is to use the lowest dose (FiO_2) necessary to achieve the desired result of treatment. In cases of pronounced hypoxia, oxygen fractions that can involve a risk of oxygen toxicity may be indicated. (See section 4.9).

The treatment must be continuously evaluated and the effect measured by means of PaO_2 or arterial oxygen saturation (SpO_2).

In short-term treatment with oxygen, the oxygen concentration - the fraction in the inhaled gas mixture (FiO_2) (avoid >0.6 = 60% O_2 in the inhaled gas mixture) - must be kept so that, with or without positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP), an arterial oxygen pressure (PaO_2) >8 kPa can be achieved.

Short-term treatment with oxygen must be monitored/followed with the aid of repeated measurements of arterial oxygen pressure (PaO_2) or pulse oximetry, which gives a numerical value for haemoglobin oxygen saturation (SpO_2). However, these are only indirect measurements of the oxygen saturation in tissues. The effect of the treatment should also be evaluated clinically.
In the emergency/acute setting the usual dose for adults to treat or prevent *acute oxygen deficiency* is 3-4 litres per minute when using nasal prongs, or 5-15 litres per minute with a mask.

In long-term treatment, the need for extra oxygen is guided by the result of arterial blood gas measurements. For adjusting oxygen therapy in patients with hypercapnia, blood gases must be monitored in order to avoid a marked increase in arterial carbon dioxide tension.

If the oxygen is mixed with other gases, the concentration of oxygen in the inhaled gas mixture (FiO_2) must not be lower than 21 % and may be up to 100 %.

Neonates may be given up to 100 % oxygen if required. However, treatment must be strictly monitored, so that the oxygen concentration can be reduced rapidly when the patient´s condition so allows. A general recommendation is to avoid oxygen concentrations that exceed 40 % in order to reduce the risk of damage to the ocular lens and the formation of atelectasis.

For treatment of cluster headache, oxygen is to be delivered by a facemask, in a non rebreathing system. Oxygen therapy should be instituted early after onset of the attack and should last for about 15 minutes or until the pain has disappeared. Usually a flow of 7 to 10 l/min is sufficient but a flow up to 15 l/min might be necessary to some patients to reach efficacy. Oxygen should be discontinued if no effect occurs after 15 to 20 minutes.

Hyperbaric oxygen therapy
Hyperbaric oxygen therapy (HBO) involves administering 100 % oxygen at a pressure exceeding 1.4 times atmospheric pressure at sea level (1 atmosphere = 101.3 kPa = 760 mmHg). For safety reasons the pressure in HBO should not exceed 3 atmospheres. The duration of one treatment session with HBO at a pressure corresponding to 2 to 3 atm is normally between 60 minutes and 4–6 hours, depending on the indication. Treatments may be repeated 2–3 times daily if necessary, depending on the indication and the clinical condition. Repeated treatments are most often necessary for the treatment of soft tissue infections and ischaemic ulcers that do not respond to conventional therapy. HBO must be given by personnel who are competent to do so. Increasing and reducing the pressure must be done slowly in order to avoid the risk of pressure damage (barotrauma).

4.3 Contraindications

None known.

4.4 Special warnings and precautions for use

High oxygen concentrations should be given for the shortest possible time required to achieve the desired result, and must be monitored with repeated checks of arterial gas pressure (PaO_2) or haemoglobin oxygen saturation (SpO_2) and the inhaled oxygen concentration (FiO_2).

There is evidence in the literature that the risk of oxygen toxicity can be considered negligible if the treatment follows these guidelines:

- Oxygen in concentrations up to 100 % (FiO_2 1.0) should not be given for more than 6 hours
- Oxygen in concentrations above 60–70 % (FiO_2 0.6–0.7) should not be given for more than 24 hours
- Oxygen in concentrations above 40–50 % (FiO_2 0.4–0.5) should not be given during the next 24 hours.
- Oxygen concentrations >40 % (FiO_2 >0.4) can potentially cause damage after 2 days.

These general guidelines are not applicable to premature infants on account of the risk of retrolental fibroplasia, which has been described from the use of lower oxygen concentrations.

Special care must be observed when treating neonates and premature infants. To minimise the risk of ocular damage, retrolental fibrosis, and/or other negative effects, the aim must be to keep the concentration to the absolute lowest that gives the desired result and avoid large variations in the arterial oxygen pressure.

With high concentrations of oxygen in the inspiratory air/gas, the concentration/pressure of nitrogen is reduced. As a result, the concentration of nitrogen in tissues and lungs (the alveoli) falls. If oxygen is taken up from the alveoli into the blood more rapidly than it is supplied in the inspiratory gas, alveolar collapse can occur (development of atelectasis). The development of atelectatic sections of the lungs leads to a risk of poorer arterial blood oxygen saturation, despite good perfusion, due to lack of gas exchange in the atelectatic sections of the lungs; the ventilation/perfusion ratio worsens, leading to intrapulmonary shunt.

High concentrations of oxygen in vulnerable patients, with reduced sensitivity to the carbon dioxide tension in arterial blood, can cause carbon dioxide retention, which in extreme cases can lead to carbon dioxide narcosis.

In hyperbaric oxygen therapy, the pressure should be increased and reduced slowly in order to avoid the risk of pressure damage (barotrauma).

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with high concentrations of oxygen and drugs that cause pulmonary toxicity, such as bleomycin, can exacerbate harmful effects caused by these drugs.

4.6 Fertility, pregnancy and lactation

Oxygen may be used during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Oxygen therapy has only slight effects on pulmonary and cardiovascular functions.

Treatment with high oxygen concentrations results in reduced nitrogen pressure in the inspiratory air/gas, thereby reducing the nitrogen concentration in tissues and lungs. This can lead to resorption atelectasis caused by reduced alveolar volume in combination with oxygen induced effects on surfactant. This can lead to a worsening ventilation/perfusion ratio and thus poorer oxygen saturation (see section 4.4).

Heart rate and cardiac output decrease to some degree when 100 % oxygen is administered for shorter periods and under normobaric conditions.

Early symptoms of oxygen toxicity are pleuritic pain and dry cough.

Vital capacity is reduced to some degree after treatment with 100 % oxygen for prolonged periods (approx. 18 hours). In cases of continuous treatment with 100 % oxygen for more than 24–48 hours a condition of acute respiratory distress syndrome (ARDS) can develop. Prolonged treatment with 100 % oxygen can also have toxic effects on other organs.

Toxic effects of high concentrations of oxygen are due to both the concentration of oxygen and the duration of exposure. Clinical symptoms are not usually seen until after 6–12 hours.

Retrolental fibroplasia with fibroblast infiltration of the retina in neonates, which can cause blindness, has been considered as possibly linked to treatment with high concentrations of oxygen (>40 %).

Other negative effects of long-term oxygen therapy with high oxygen concentrations (FiO_2 1.0) are haemolytic anaemia, pulmonary fibrosis, and effects on the heart, kidneys and liver. These conditions can affect patients of all ages.

To reduce the risk of parenchymal damage, including in the lungs (bronchopulmonary dysplasia), it is of the greatest importance to monitor arterial oxygen pressure (PaO_2) continually and to aim for the lowest oxygen concentration that produces the desired effect (see section 4.4).

Side effects of HBO are usually mild and reversible. HBO treatment can cause rupture of the eardrum, sinus pain, reversible muscle pain, and multifarious effects on the CNS ranging from nausea, dizziness, anxiety, confusion and muscle twitching, to unconsciousness and epileptic seizures. CNS symptoms can occur in HBO therapy when given at more than 2 atm for more than a couple of hours. At higher pressures, symptoms may occur earlier. Competent personnel must monitor the patient.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.*

4.9 Overdose

Overdoses with oxygen do not occur outside treatment in intensive care, and the risks of these are greater with hyperbaric oxygen therapy.

In oxygen intoxication, (symptoms of oxygen toxicity), the oxygen therapy should be reduced or if possible stopped, and symptomatic treatment should be started in order to maintain vital functions (e.g. artificial ventilation/assisted ventilation should be given if the patient shows signs of failing respiration).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Medicinal Gases, Oxygen, ATC code: V03AN01

Oxygen constitutes approx. 21% of air. Oxygen is vital for human life and must be supplied continually to all tissues in order to maintain the cells' energy production. Oxygen is transported in inhaled air via the airways to the lungs. In the pulmonary alveoli, as a result of the difference in partial pressure, gas exchange takes place from the inhaled air/gas mixture to the capillary blood. The oxygen is transported further in the systemic circulation, for the most part bound to haemoglobin, to capillary beds in the various tissues of the body. The oxygen is transported with the aid of the pressure gradient out to the various cells, its goal being the mitochondria in the individual cells, where it takes part in an enzymatic chain reaction, which creates energy. By increasing the oxygen fraction in the inhaled air/gas mixture, the partial pressure gradient that controls the transport of oxygen to the cells increases.

Giving oxygen at a pressure higher than atmospheric pressure (HBO) considerably increases the amount of oxygen that is transported with the blood to the peripheral tissues. Intermittent hyperbaric oxygen therapy causes oxygen transport even within oedematous tissues and tissues with inadequate perfusion, and in this way can maintain cellular energy production and function.
In accordance with Boyle's law, HBO reduces the volume of gas bubbles in tissues in relation to the pressure with which it is given.

HBO counteracts the growth of anaerobic bacteria.

5.2 Pharmacokinetic properties

Inhaled oxygen is absorbed by a pressure-dependent gas exchange between alveolar gas and the capillary blood that passes the alveoli.

Oxygen is transported by the systemic circulation to all tissues in the body, mainly bound reversibly to haemoglobin. Only a very small proportion is freely dissolved in plasma. On passage through tissue, partial pressure-dependent transport of the oxygen to the individual cells takes place. Oxygen is a vital component in the intermediate metabolism of the cell. It is critical to the cell's metabolism, among other things, in order to create energy through the aerobic ATP production in the mitochondria.

Oxygen accelerates the release of carbon monoxide that is bound to haemoglobin, myoglobin and other iron-containing proteins, and thus counteracts the negative blocking effects caused by carbon monoxide binding to iron.

Hyperbaric oxygen therapy further accelerates the release of carbon monoxide, compared with 100 % oxygen under normal pressure.

Oxygen that is absorbed in the body is eliminated almost completely as carbon dioxide formed in the intermediate metabolism.

5.3 Preclinical safety data

There are no preclinical data of relevance for safety assessment other than what have already been considered in the summary of product characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

Not relevant

6.3 Shelf life

Cryogenic vessels <30 litres: 1 month.
Cryogenic vessels ≥30 litres: 45 days.

6.4 Special precautions for storage

Storage instructions relating to the medicinal product
Do not store above 45°C. Store in a well-ventilated space.

Storage instructions relating to gas containers and gases under pressure
Contact with combustible material may cause fire.
Keep away from combustible material.
No smoking.
Risk of explosion in cases of contact with oil and grease.
Must not be exposed to strong heat. If at risk of fire – move to a safe place.
Handle carefully. Ensure that the vessel is not dropped or exposed to knocks.
Keep the vessel clean and dry. Store in a ventilated place reserved for medicinal gases.
Store and transport upright with valves closed.

The temperature of cryogenic oxygen is approx. -180 °C. Touching cold surfaces on cryogenic oxygen systems, such as the valves, pipes or couplings, can cause sever cryogenic burns or frostbite. When handling cryogenic oxygen systems do not allow cryogenic oxygen or frosted systems to come in contact with the skin or non-protective clothing.

6.5 Nature and contents of container

All packs are vacuum-isolated containers made of stainless steel and aluminium intended for storing low temperature condensed gases at approx. –180 °C. The tanks are equipped with pressure regulation and a safety valve, which opens at a predefined pressure to release pressure that builds up due to evaporation of the liquid oxygen. The following sizes are used:

Not all pack sizes may be marketed.

Packs:

- Cryogenic vessels for homecare use by patients, sizes:
  - (Filled by the patient or health care professionals): 0.3, 0.33, 0.38, 0.5, 0.6, 0.85, 1.2, 1,23
  - (Filled by MAH): 10.7, 12, 15, 21, 21.6, 30, 31, 31.2, 36, 38.3, 40, 41, 46, 46.6, 60 and 196 litres.
  - Stainless steel Mobile Cryogenic vessel with the following capacity: [11.780 kg to 31.690 kg].

6.6 Special precautions for disposal

General
Medicinal gases must only be used for medicinal purposes.
Different gas types and gas qualities must be separated from each other. Full and empty containers must be stored separately.

Never use grease, oil or similar substances for lubricating screw threads that jam.
Handle valves and devices to match with clean and grease-free (hand cream, etc.) hands.
Check that the containers are sealed before they are taken into use.
Remaining pressure at return should be >2 bar (200 kPa).

Preparation for use
Remove the seal from the outlet before use.
Use only equipment intended for connection to medicinal liquefied oxygen.

Use
Smoking and open flames are forbidden in rooms where oxygen therapy is being carried out.
Close down the apparatus in the event of fire or if it is not being used.
Carry to safety in the event of fire.

During transport in vehicles the cryogenic vessels must be fastened down.

7. MARKETING AUTHORISATION HOLDER

Nippon Sanso Norge AS
P.O. Box 23, Haugenstua
N-0915 Oslo, Norway

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 October 2007
Date of latest renewal: 10 February 2012

10. DATE OF REVISION OF THE TEXT

04/2026