SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Conoxia 100%, Medicinal gas, cryogenic

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxygen 100%

3. PHARMACEUTICAL FORM

Medicinal gas, cryogenic
Cryogenic oxygen is pale blue. When converted to gas, cryogenic oxygen is colourless, odourless, without taste.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Normobaric oxygen

- For treatment or prevention of acute or chronic hypoxia irrespective of genesis.
- As part of the fresh gas supply in anaesthesia or intensive care.
- As the driving gas in nebulisation therapy.
- As first aid treatment with 100% oxygen in decompression accidents

The treatment is indicated in all age groups

- For treatment of an acute attack of cluster headache

This treatment is indicated in adults only

Hyperbaric oxygen (HBO)Medicinal oxygen under hyperbaric pressure is used for treatment of conditions where it is beneficial to increase the oxygen content of blood and other tissues above which is attainable under normobaric pressure.

- For treatment of decompression sickness, air/gas emboli of other genesis.
- In carbon monoxide poisoning. HBO therapy is indicated essentially in patients who are or have been unconscious, that have shown neurological signs, cardiovascular dysfunction or severe acidosis and in pregnant females all irrespective of carbon monoxide haemoglobin (COHb) levels.

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

The treatment can be used in all age groups (see also section 4.2 and 4.4)

4.2 Posology and method of administration

Posology

Normobaric oxygen

General recommendations
The primary purpose of oxygen therapy, i.e. correction of hypoxia, is to ensure that the partial arterial oxygen pressure (PaO_2) is not less than 8.0 kPa (60 mmHg) or that the oxygen saturation of haemoglobin in arterial blood (SaO_2) is not less than 90%. This is achieved by adjusting the fraction of oxygen in inspired gas. The lowest oxygen fraction of inspired gas needed to achieve the desired result of therapy i.e. a safe PaO_2 should be used. The therapy should be evaluated continuously and the effect of treatment measured with PaO_2/SaO_2 or an estimate of SaO_2 i.e. SpO_2.The oxygen fraction of inspired gas should be adjusted according to each individual patient's unique requirement, taking the risk of oxygen toxicity into account (See overdose, section 4.9). In severe hypoxia, oxygen fractions that may involve a risk of oxygen toxicity can still be indicated.

Acute or chronic hypoxia - Spontaneous breathing - Short term therapy
In emergency medicine, oxygen is commonly administered by nasal prongs with at flow-rate of 2-6 l/min or by face mask with a flow rate of 5-10 l/min. Patients, not at risk of respiratory failure and with an initial SpO_2 <85%, can be treated with 10-15 l/min by mask with a reservoir. Patients with known suspected chronic respiratory disease (e.g. COPD) that may have reduced chemoreceptor sensitivity should be treated with caution as a too liberal use of oxygen may cause respiratory depression. When 100% oxygen is indicated, a face mask with reservoir (oxygen flow should be sufficient to keep the reservoir partially or completely filled – i.e. not collapsed during breathing) or a demand valve system should be used.

The fraction of oxygen in inspired gas should be kept so that with or without positive end-expiratory airway pressure (PEEP) or continuous positive airway pressure (CPAP) a PaO_2>8 kPa is maintained.
The effect of short term oxygen therapy should be monitored by repeated measurements of PaO_2 or by pulse-oximetry, which provides a numerical value for the SpO_2. However, these indices are only indirect measures of tissue oxygenation. Clinical assessment of the treatment is of outmost importance.

Acute or chronic hypoxia - Spontaneous breathing - Long-term therapy
In long-term therapy, oxygen can be administered by specially designed masks, e.g. Venturi-masks where the delivered oxygen concentration can be adjusted and is dependent on the gas flow and the valve on the mask. Concentrations of 24 to 35% are commonly used.

The need for medicinal oxygen should be determined by obtaining arterial blood gas values and/or by monitoring SpO_2. The inspired oxygen should be titrated when used for long term oxygen therapy in patients with chronic hypoxic respiratory failure. A SaO_2/SpO_2 between 88 and 92% is commonly assessed as adequate in patients with chronic obstructive pulmonary disease (COPD). A too liberal administration can increase the oxygen SaO_2/SpO_2 clearly above the patient's normal range, which may cause respiratory depression because of chemoreceptor insensitivity for CO_2 .Blood gases should be monitored to avoid excessive retention of CO_2 in patients with hypercapnia or reduced CO_2-sensitivity, in order to adjust the oxygen therapy.

Fresh gas supply in anaesthesia or intensive care - Assisted or controlled ventilation
Oxygen is commonly used in the intensive care setting. The inhaled oxygen should be titrated to the individual patient’s need. The oxygen is commonly administered by assisted or controlled ventilation. A PEEP is commonly applied to facilitate the ventilation/perfusion matching, recruiting airways and lung volumes, and thereby subsequently decreasing shunt.

During general anaesthesia a fraction of inspired oxygen about 0.3 is usually adequate. Higher fractions can be used in patients when found necessary.
If the oxygen is mixed with other gases, the oxygen fraction should be maintained at least at 0.21 in the inhaled gas mixture. The fraction of inspired oxygen can be increased up to 1.0.

Nebulisation
When oxygen is used for nebulisation, it can be used as a sole driving gas (100% in sufficient flow rate in order to nebulise the fluid in the nebulisation chamber) or mixed with air. In nebulisation therapy, the flow of oxygen and/or oxygen mixed with air is usually a continuous flow of 6-8 l/min.

First aid treatment
For emergencies where 100% oxygen is indicated, a face mask with reservoir (oxygen flow sufficient to keep the reservoir un-collapsed during breathing) or a demand valve system should be used.
Administration of pure oxygen (FiO_2 1.0) in the early management of divers exhibiting signs and/or symptoms of diving disease facilitates the diffusion/elimination of nitrogen from the blood and tissues subsequently resulting in reduction of nitrogen bubbles and gas emboli.

Cluster Headache
For treatment of cluster headache, oxygen is to be delivered by a facemask, in a non re-breathing 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.

Paediatric population
The safety and efficacy of oxygen in children of all ages is well established. The dosing instructions for the paediatric population are the same as for adults, except for new-borns (term, near term, and preterm). In new-borns careful monitoring should be performed during the treatment. Oxygen in concentrations up to 100% can be administered in order to ascertain adequate oxygenation but for shortest time possible. Oxygen may be used during resuscitation in new-borns but guidelines recommend that air is used initially. The lowest effective concentration should be sought in order to achieve an adequate oxygenation. Oxygen in low concentrations up to 40% (FiO_2 0.4) in combination with CPAP is recommended as an initial therapy.

Hyperbaric oxygen
General recommendations
Only well qualified healthcare professionals should administer HBO. HBO means that 100% oxygen is delivered at a pressure above the atmospheric pressure at sea level (1 atmosphere=101.3 kPa= 760 mmHg). For safety reasons the pressure of HBO should not exceed 3 atmospheres.

The duration of a single treatment with HBO at a pressure of 2-3 atmospheres is normally between 60 min and 4-6 h depending on the indication. Sessions may, if necessary, be repeated 2-3 times a day, depending on the indication and the patient's clinical condition. Compression and decompression should be slow in accordance with common routines in order to avoid the risk of pressure damage i.e. baro-trauma. The length and frequency of treatment should be decided by the attending physician taking the patient's physical and medicinal status into account.

Paediatric population
HBO can be used in children of any age. The length and frequency of treatment should be decided by the attending physician taking the patient's physical and disease status into account.

<u>Method of administration</u>

Precautions to be taken before handling or administering the medicinal product, see special precautions for disposal and other handling (section 6.6).

Oxygen is administered with the inspiratory air. On exhalation the exhaled gas, with any oxygen excess, leaves the patient and is mixed with the surrounding air.
Oxygen should be administered via special equipment.

Normobaric oxygen
Spontaneous breathing
There are a large number of devices intended for the administration of oxygen in spontaneous breathing patients for example:

- Low-flow systems

The simplest systems, which deliver a mixture of oxygen to the inspiratory air, e.g. a system in which the oxygen is administered via a simple rotameter connected to a nasal catheter or facemask.

- High-flow systems

Systems designed to provide a gas mixture corresponding to the patient's entire inspiratory atmosphere. These systems are designed to deliver a fixed concentration of oxygen that is not influenced (diluted) by the surrounding air, e.g. Venturi masks with a fixed flow of oxygen in order to give a fixed concentration of oxygen in the inspired air.

- Demand valve

A demand valve system (i.e. a valve triggered by spontaneous ventilation) is system designed to deliver 100% oxygen without entrainment of ambient air, intended for short duration of administration by mask.

Assisted and controlled ventilation
When oxygen is administered by assisted or controlled ventilation, an oxygen air mixture is commonly used in order to achieve a desired oxygen fraction. The gas can be administered by mask, tracheal tube or tracheostomy.

Fresh gas flow during general anaesthesia
During anaesthesia, special anaesthesia equipment is used. Anaesthesia equipment commonly consists of a specially designed breathing circle intended for partial re-breathing. A circle system with a carbon dioxide absorber allowing a portion of the expired gas to be re-circled and inhaled again is often used.

Extracorporeal membrane oxygenation
Oxygen is usually administered via inhalation but can also be administered through a so-called oxygenator directly to the blood e.g. in conjunction with heart surgery (when a heart-lung machine is used) or in patients with severe therapy resistant hypoxia requiring extracorporeal membrane oxygenation/extracorporeal lung assist (ECMO/ECLA).

Hyperbaric oxygen
HBO is given in a specially constructed pressure chamber designed for HBO treatment in which pressures up to three times atmospheric pressure can be maintained. HBO can also be given via a very closely fitting facemask i.e. a hood that closes around the head, or through a tracheal tube.

4.3 Contraindications

Normobaric oxygen
There is no absolute contraindication to oxygen therapy under normobaric conditions.

Hyperbaric oxygen
HBO is contraindicated in patients with an untreated pneumothorax, or other accidentally gas filled spaces with no ability to vent.

4.4 Special warnings and precautions for use

Normobaric oxygen
For instructions of disposal and other handling of the medicinal product, see section 6.6.

As a general rule, high concentrations of oxygen should only be administered for the minimum time required to achieve the desired clinical outcome. The inspired oxygen concentration should be reduced as soon as possible to the lowest concentrations needed. The patient should be monitored by repeated analyses of the PaO_2 or SpO_2 and the concentrations of inhaled oxygen should be titrated to maintain these parameters at an acceptable clinical level.

Prolonged exposure to higher concentrations of oxygen than listed below may generate oxygen species/free radicals and subsequently cause inflammation. Thus the risk for oxygen induced lung dysfunction (e.g. signs or symptoms of acute lung injury/respiratory distress syndrome) shall be acknowledged.
The benefit versus risk for prolonged exposure to high concentrations shall be assessed on an individual basis. Evidence suggests that the risk of oxygen toxicity can be minimised if the treatment follows these guidelines [fraction of inhaled oxygen in the inhaled air/gas mixture (FiO_2)]:

- 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 concentrations > 40% (FiO_2 > 0.4) can potentially cause damage after 2 days.

In cases of high concentrations of oxygen in the inspiratory air/gas, the concentration/pressure of nitrogen is lowered. As a result, the nitrogen concentration in tissues and lung (alveoli) is lowered. If oxygen is taken up from alveoli to the blood faster than additional oxygen is delivered by ventilation, alveoli may collapse, causing atelectasis.
The formation of atelectatic lung areas may impair oxygenation of arterial blood, because there will be no gas exchange in the atelectatic area despite perfusion. As a consequence there will be a ventilation/perfusion mismatching and subsequently an increased shunt.

In patients with reduced sensitivity for carbon dioxide pressure in arterial blood, high concentrations of oxygen may cause, respiratory depression subsequently causing carbon dioxide retention, which in extreme cases can lead to carbon dioxide narcosis.

<u>Paediatric population</u>
Special caution should be taken when treating new-born since they have lower levels of defence systems and less active scavenging of free radicals than other populations. Thus the potential negative effects of hyper-oxygenation are increased in the preterm and near term. The absolute lowest concentration, which gives the desired result, should be used in order to minimise the risk of ocular damage, retrolental fibroplasia (ROP), and broncho-pulmonary

dysplasia (BPD) or other potential undesirable effects, which occur with a much lower oxygen concentration/fraction than in other populations.

Hyperbaric oxygen
Hyperbaric oxygen therapy should only be administered by qualified staff and specialized centers aware and equipped for insuring appropriate precautions for hyperbaric use. Compression and decompression should be slow in order to avoid the risk of pressure damage (baro-trauma).

HBO should be used with caution during pregnancy and in females of child bearing potential due to a potential risk of oxidative stress-induced damage in the foetus. The use should be evaluated in each individual patient.

HBO should be used with caution in patients presenting with pneumothorax or other accidentally gas filled spaces with no ability to vent (e.g. the pneumo-pericard) and who are treated with a chest tube and/or patients with a medical history of pneumothorax. The use should be evaluated in each individual patient with regard to the risk of a new (tension) pneumothorax.

Exposure to high oxygen concentrations may result in central nervous system (CNS) effects (see section 4.8). For patients with a history of epilepsy/seizures, or conditions with reduced seizure threshold, such as uncontrolled high fever, the benefit-risk ratio of HBO therapy should be thoroughly evaluated.

Use of greasy substances e.g. cosmetics should be avoided in order to minimise the risk for spontaneous ignition.

Paediatric population
The experience in new-borns, children and adolescents is limited. The benefit-risk should be evaluated in each individual patient.

Risk of fire
Oxygen is an oxidizing product and promotes combustion. Whenever oxygen is used, the increased risk of fire ignition should be taken into account:

- Risk of fire in domestic environment: Patients and caregivers should also be warned about the risk of fire in presence of other sources of ignition (smoking, flames, sparkles, cooking, ovens etc.) and/or highly combustible substances, especially greasy substances (oils, grease, creams, ointments, lubricants etc.). Only water-based products should be used on the hands and face or inside the nose while using oxygen.
- Risk of fire in medical environment: this risk is increased in procedures involving diathermy, defibrillation and electro conversion therapy.
- Fires can occur at valve opening (frictional heating).

Thermal burns have occurred related to accidental fires in presence of oxygen.
For instructions of disposal and other handling of the medicinal product, see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

The pulmonary toxicity associated with high concentrations of oxygen (see special warnings and precautions for use, section 4.4) can be exacerbated by concomitant use of anticancer drugs e.g. bleomycin, cisplatin, and doxorubicin, anti-arrhythmic drugs e.g. amiodarone, antibiotics e.g. furadantin (nitrofurantoin), alcohol deterrents e.g. disulfiram, and chemicals e.g. paraquat.

Paediatric population
There are no known other interactions than those in the adult population.

4.6 Fertility, pregnancy and lactation

Normobaric oxygen
No studies examining the potential toxicity of normobaric hyperoxia on embryo-foetal development or reproduction have been identified in the literature (see pre-clinical safety data, section 5.3).

Pregnancy
Oxygen supplementation has no known negative effects on the foetus. Women of child bearing potential can use oxygen.

Breastfeeding
Oxygen supplementation has no known negative effects on the breastfeeding child. Oxygen can be used during lactation.

Fertility
Oxygen supplementation has no known negative effects on fertility.

Hyperbaric oxygen
HBO treatment during gestation in the mouse, rat, hamster and rabbit led to toxicities (see preclinical safety data, section 5.3).

Pregnancy
HBO should be used with caution during pregnancy and in females of child bearing potential due to a potential risk of oxidative stress-induced damage in the foetus. In severe carbon monoxide intoxication the benefit versus risk for the use of HBO should be evaluated in each individual patient.

Breast-feeding
There are no known adverse effects of HBO on lactation. However, lactation should be avoided during the actual HBO therapy.

Fertility
HBO treatment and effects on fertility has not been studied.

4.7 Effects on ability to drive and use machines

Medicinal oxygen has no or negligible influence on the ability to drive and use machines.In normal circumstances, medicinal oxygen does not interfere with level of consciousness. Patients who require continuous oxygen support should be evaluated on an individual basis, taking their entire medical situation into account for evaluating if it is recommendable to drive and/or operate complex machinery.

4.8 Undesirable effects

Summary of the safety profile
The undesirable effects listed are derived from public domain scientific medical literature and post marketing safety surveillance

The most serious side effects that may occur are severe difficulty in breathing, so called respiratory distress syndrome. Too liberal oxygen administration may also cause respiratory depression in susceptible patients with reduced chemoreceptor sensitivity as seen in e.g. some patients with chronic obstructive pulmonary disease (COPD)

Paediatric population
In the use of oxygen in new-borns the risk for ROP in pre-terms and the development of BPD should be acknowledged. Except for these two risks, there are no other undesirable effects reported than in adults.

Description of selected adverse events
Central nervous toxicity can be observed in HBOT settings. Central nervous toxicity can develop when patients breathe 100% oxygen at pressures above 2 ATA. Early manifestations include blurred vision, peripheral vision decreased, tinnitus, respiratory disturbances, localized muscular twitching especially eyes, mouth, forehead. Continuation of exposure can lead to vertigo and nausea followed by altered behaviour (anxiety, confusion, irritability), and finally generalized convulsions. The hyperoxia-induced discharges are believed to be reversible, causing no residual neurological damage, and disappearing upon reduction of the inspired oxygen partial pressure.

Tabulated summary of adverse reactions

System organ class	**Very common (≥1/10**	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1 000 to 1/100)**	**Rare (≥1/10 000 to 1/1 000)**	**Very rare (<1/10 000)**	**Not known (cannot be estimated from the available data)**
	-	-	-	-	-	
Psychiatric disorders	-	-	-	-	HBO: Anxiety, confusion	
Nervous System disorders	-	-	-	Respiratory depression (chemo-receptor sensitivity) HBO: loss of consciousness, seizures, unspecified		
Eye disorders	-	-		Retrolental fibroplasia in prematures	HBO: Myopia	

Ear and labyrinth disorders	-		HBO: Feeling of pressure in the middle ear, tympanic membrane rupture	-	-	-
Respiratory, thoracic and mediastinal disorders	-	-	Atelectasis, pleuritis	Pulmonary fibrosis. Bronchopulmonary dysplasia HBO: Sinus squeeze	Respiratory distress syndrome.	Worsening of hypercapnia in patients with chronic hypoxia/hypercapnia treated with too much elevated FiO_2: •Hypoventilation, •Respiratory acidosis, •Respiratory arrest
Injury, poisoning and procedural complications					Burns (frostbite) HBO: Baro-trauma	

HBO; Hyperbaric oxygen

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

Normobaric
Initial symptoms of oxygen toxicity are cough and signs and symptoms of pleuritis and subsequently symptoms of respiratory distress.

In case of oxygen overdose, the oxygen concentration should be decreased. Symptomatic therapy should be instituted in order to maintain critical physiology (e.g. in case of respiratory depression, respiratory support should be instituted).

The administration of oxygen is associated with potential risk of baro-/volu-trauma if there is no venting in the delivery system, e.g. when there is no safety pressure reduction valve in the delivery equipment.

Additional information on special populations

In COPD patients with decreased chemoreceptor sensitivity, administration of oxygen may cause respiratory depression and can in extreme cases lead to carbon dioxide narcosis.

Paediatric population
The risk for overdose, because of a too liberal administration of oxygen in new-borns during resuscitation and early part of life, shall be acknowledged. Common guidelines recommend initial resuscitation with air and institution of oxygen supplementation only if the new-born is insufficiently oxygenated.

High oxygen concentration/fraction and fluctuations in oxygenation is considered to contribute to the development of ROP.

Hyperbaric oxygen
The risk of overdose is greater during HBO treatment.

Short exposure to very high partial pressures of oxygen may cause acute cerebral toxicity and related symptoms.

Paediatric population
There is overall limited information available about HBO in the paediatric population.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group:
All other therapeutic products – medical gases, oxygen; ATC code: V03AN01

Normobaric oxygen
The ambient air consists of approximately 21% oxygen. Oxygen is vital to life and must be supplied continuously to all tissues in order to maintain the cells' energy production. The final target for the oxygen is the mitochondria in the individual cells, where oxygen is consumed in an enzymatic chain reaction forming energy. Oxygen is a vital component in the cell's intermediate metabolism for creation of energy i.e. the aerobic adenosine triphosphate (ATP) production in the mitochondria. By increasing the oxygen fraction in the inspired gas mixture, the partial pressure gradient transporting oxygen to the cells is increased. Oxygen speeds up the release of carbon monoxide (CO) that is bound to haemoglobin and other iron-containing proteins, and therefore counteracts the negative blocking effects caused by the binding of carbon monoxide to iron.

Oxygen is vital to maintain cellular metabolism and for the cellular homeostasis. Lack of oxygen rapidly produces an anaerobic cellular situation with malfunction and subsequent cell death. Oxygen is thus vital for the natural cell function. Hyper-oxygenation may cause production of free radicals. If the capacity for handling of reactive oxygen species is exceeded, there is a risk for cellular toxicity, inflammatory reaction caused by the oxygen radicals.

Hyperbaric oxygen
HBO therapy increases the oxygen dissolved in plasma and thus the oxygenation of the blood. The oxygenation of tissues is subsequently improved. The increased oxygenation is of importance in critical hypoxic tissue, e.g. the penumbra of severe necrosis. The increased oxygenation subsequently restore cellular metabolism and thereby improves tissue function, It also facilitates the defence system, and the bacterial killing capacity in tissues, especially in

anaerobic infections. 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.

5.2 Pharmacokinetic properties

Normobaric oxygen

Absorption
Oxygen is administered by inhalation and subsequently transported to the alveoli. The alveolar partial oxygen pressure (P_AO_2) is the driving force for the transport of oxygen from the aerated alveoli through the alveolo-capillary membrane..

Distribution
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
Oxygen delivery is dependent on oxygen content and the cardiac output. Tissue perfusion is dependent on cardiac output, systemic circulation, blood pressure and regional perfusion (content of oxygen: (1.34 x [Hb] x SaO_2) + (PaO_2 x 0.023 mL/dL/kPa).

Biotransformation
Oxygen diffuses from the blood in the peripheral capillary bed; it reaches the cells where it is part of the internal metabolism, aerobic energy production. The net effect of the aerobic metabolism is energy production [adenosine trisphosphate (ATP)], carbon dioxide and water.

Elimination
Carbon dioxide will be, following transport from the cells by the blood, exhaled by the lungs. Water from energy production will be eliminated by the renal route.
Oxygen that has not taken part in the intermediate metabolism will reach the lungs and thus be exchanged in the alveolar gas exchange.

Hyperbaric oxygen
HBO therapy speeds up the release of carbon monoxide at a greater rate than that achievable by breathing 100% oxygen at normal pressure.

5.3 Preclinical safety data

Normobaric oxygen
Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Non-clinical studies have shown that prolonged continuous inhalation of pure oxygen may have harmful effects. Tissue injury can be induced in the lung, eye and central nervous system. Marked variability occurs between the time of onset of pathological changes among different species and among animals of the same species.

Hyperbaric oxygen
Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.
HBO treatment during gestation in mice, rats, hamsters and rabbits led to increased resorption, foetal abnormalities, and decreased foetal body weight.

Environmental Risk Assessment (ERA)

Oxygen constitutes a natural part of the atmospheric air. The risk for explosive fire whenever the oxygen concentration is increased should be acknowledged (see Special precautions for disposal and other handling, section 6.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

Oxygen is an oxidiser that facilitates fire. Avoid any oil, grease or other chemicals that may ignite during use of high pressure oxygen Increased oxygen concentrations in the ambient air increase the risk for explosive fires. Oxygen can react with flammable substances.

6.3 Shelf life

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

6.4 Special precautions for storage

This medicinal product does not require any special storage instructions with regard to temperature other than those that apply for gas containers and gas under pressure (see below).

Do not smoke or use a naked flame in areas where medicinal gases are stored
Vessels should be stored in a locked and well-ventilated area reserved for the storage of medicinal gases (does not apply to a home environment).
Vessels should be stored under cover, kept dry and clean, kept free from oil and grease, free from combustible material
Must not be exposed to strong heat
If at risk of fire – move to a safe place.
Precautions should be taken to prevent blows or falls.
Vessels containing different types of gases should be stored separately.
Full and empty vessels should be stored separately.
Store and transport upright with valves closed

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 following sizes are used:

Mobile cryogenic vessels from 10 500 to 30 000 litres (8 400 to 27 000 m^3 gas).
Mobile cryogenic vessels from 196 to 627 litres (170 to 530 m^3 gas).
Mobile cryogenic vessels fitted with a dosing device for regulation of the flow to the patient 10, 12, 15, 20, 21, 26, 30, 31, 32, 36, 37, 40, 41, 45, 46 and 55 litres.

Not all pack sizes may be marketed.

The table below gives indicative volume of gas in litre at reference state 1 bar 15°C:

Vessels in litres	10	15	20	30	40	55
Litres of gas	8400	13000	17000	25000	34000	46000

6.6 Special precautions for disposal and other handling

The vessels must not be disposed, but returned to the supplier.

General precautions

- Medicinal gases must only be used for medicinal purposes.
- Do not smoke or use a naked flame in areas where medicinal gases are administered
- Never place a mask or nasal prongs directly on textiles while treatment is being carried out since fabrics that become saturated with oxygen can be highly flammable and cause a risk of fire. If this should occur, thoroughly shake and air the textiles.
- 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.
- Use of greasy substances e.g. hand-cream should be avoided during treatment with HBO
- In case of cleaning of vessels or attached equipment, do not use combustible products and especially not oil-based material. In case of doubt, verify compatibility.
- As medicinal liquid oxygen is a very cold liquid, there is a risk of frostbite injury whenever medicinal liquid oxygen is handled
- Prior to any use, ensure sufficient quantity of product remains to allow completion of the planned administration of oxygen.
- Use only standard devices designed for administration of oxygen
- When delivered from the manufacturer, the vessels should have an intact tamper evident seal

Preparation for use

- Remove the seal from the outlet before use.

Use of vessel

- Parts of the vessel/valve can become cold when in use. This will be evident by ice forming on the cold sections and care should be taken not to touch these areas.
- Close down the apparatus in the event of fire or if it is not being used.

Transportation of vessels

- During transport in vehicles the cryogenic vessels must be secured to prevent them from falling.

7. MARKETING AUTHORISATION HOLDER

Linde Gas
BOX 30193
10425 Stockholm
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

18862

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2005-08-04 / 2010-08-04

10. DATE OF REVISION OF THE TEXT

2026-03-13