SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Medical Liquid Oxygen

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxygen Ph. Eur. 100 %
There are no other ingredients

3 PHARMACEUTICAL FORM

Inhalation gas
Light blue cryogenic liquid of about -180 deg C contained within a closed container/vessel (see section 6.5). The liquid rapidly evaporates to form oxygen gas

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

*Normobaric oxygen therapy:*
- 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 propellant gas in nebuliser therapy.
- Treatment of acute attack in patients with an established diagnosis of cluster headache

*Hyperbaric oxygen therapy:*
For treatment of decompression sickness, air/gas embolisms of other genesis and carbon monoxide poisoning.
- In carbon monoxide poisoning hyperbaric oxygen therapy is indicated in patients that are or have been unconscious, that have shown neurological signs, cardiovascular dysfunction or severe acidosis and in pregnant females all irrespective of COHb.
- As adjunctive treatment for osteoradionecrosis and clostridial myonecrosis (gas gangrene).

4.2 Posology and method of administration

*Method of administration*
Oxygen is administered via the inspiratory air.
Oxygen can also be administered through a so-called oxygenator directly to the blood in, among other things, heart surgery with a cardio-pulmonary bypass system, and in other conditions that require extracorporeal circulation.

Oxygen is (preferably) administered via special equipment. With this equipment, oxygen is administered with the inspiratory air, and on exhalation the exhaled gas with any oxygen excess leaves the patient and is mixed with the surrounding air (non-rebreathing system).

For anaesthesia, special equipment is often used, when the exhaled gas is recirculated and can be rebreathed (circular system with rebreathing).

There are a large number of devices intended for administration of oxygen.

**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 oxygen concentration that is not influenced – diluted by the surrounding air, e.g. Venturi mask with fixed oxygen flow in order to give a fixed oxygen concentration in the inspiratory air.

**Hyperbaric oxygen therapy**

(HBO) is given in a specially constructed pressure chamber designed for hyperbaric oxygen treatment, in which pressures up to 3 times atmospheric pressure can be maintained. HBO can also be administered within the chamber via a very closely fitting facemask, a hood that closes around the head, or through a tracheal tube.

**Posology**

The purpose of oxygen therapy is to ensure that the partial arterial oxygen pressure (PaO₂) is not less than 8.0 kPa (60 mmHg) or the oxygen saturation of haemoglobin in arterial blood is not less than 90 %, by adjusting the fraction of oxygen in inspired gas (FIO₂).

The dosage must be regulated according to the patient’s need. The oxygen fraction must be adjusted according to each individual patient’s unique requirement, taking account of the risk of oxygen intoxication. (See 4.9.)

The general recommendation is that the lowest dose – FiO₂ – to achieve the desired result of therapy, a safe PaO₂, must be the aim. In severe hypoxia, oxygen fractions that may involve a risk of oxygen intoxication may be indicated.

The therapy must be evaluated continuously and the effect of treatment measured with PaO₂ or alternatively arterial oxygen saturation (SpO₂).

For short term oxygen therapy, the fraction of oxygen in inspired gas (FIO₂) (avoid FiO₂ > 0.6 % = 60 % O₂ in the inhaled gas mixture) must be kept so that with or without positive end-expiratory airway pressure (PEEP) or continuous positive airway pressure (CPAP), a partial arterial oxygen pressure (PaO₂) > 8 kPa is maintained.
Short term oxygen therapy must be monitored by repeated measurements of arterial blood gases (PaO₂) or by pulse oximetry which provides a numerical value for the haemoglobin oxygen saturation (SpO₂). However, these indices are only indirect measures of tissue oxygenation. Clinical assessment of the treatment is of the utmost importance.

For long term treatment, the need for supplemental oxygen should be determined by obtaining arterial blood gas values. To avoid excessive retention of carbon dioxide, blood gases should be monitored so to adjust oxygen therapy in patients with hypercapnia.

If the oxygen is mixed with other gases, its concentration in the gas mixture inhaled (FiO₂) must be maintained at least at 21 % in the inhaled gas. Oxygen inhaled fraction can be increased up to 100 %.

Neonates may be given up to 100% of Oxygen if required. However, careful monitoring should be performed during the treatment. As a common recommendation, oxygen concentrations exceeding 40 % should be avoided on account of the risk of damaging the crystalline lens or lung collapse. The oxygen pressure in arterial blood (PaO₂) should be monitored, and if PaO₂ is kept below 13.3 kPa (100 mmHg) and no major variations in oxygenation is avoided, the risk of damage to the eyes is reduced.

For the indication acute attack of cluster headache, Oxygen is to be delivered by facemask, in a non re-breathing system, with an oxygen flow of about 7 – 10 l/min.

Oxygen therapy should be instituted as early as possible after onset of the attack and should last for about 15 minutes or until pain has disappeared/vanished.

Hyperbaric Oxygen therapy:

Hyperbaric oxygenation (HBO) means delivering 100% oxygen at pressure above 1.4 times the atmospheric pressure at sea level (1 atmosphere = 101.3 kPa = 760 mmHg). For safety reasons the pressure for HBO should not exceed 3 atmospheres.

The duration of a single treatment with HBO at a pressure of 2 to 3 atmospheres is normally between 60 minutes and 4 - 6 hours depending on the indication. Sessions may, if necessary, be repeated 2 to 3 times a day, depending on the indication and the patient’s clinical condition. Multiple sessions are often necessary for treatment of soft-tissue infections and hypoxic wounds that do not respond to the usual conventional treatment.

HBO should be given by staff qualified to give this treatment.

Compression and decompression should be slow in accordance with common routines in order to avoid the risk of pressure damage (barotrauma).

Instructions for handling and use of Medical Liquid Oxygen Equipment

Only use equipment designated for use with Medical Liquid Oxygen.

Hospital pipelines for medical gases should be installed in accordance with the guidance given in HTM 02.

Equipment for use with oxygen must be clean and dry. If necessary, clean only with plain water. Do not use solvents. Use clean, lint free cloths for cleaning and drying off. Use no oil or grease on equipment for use with oxygen.
Do not allow naked flames near the container. Do not smoke when using oxygen.

*Leaks*

Should leaks occur this will usually be evident by a hissing noise.

There are no user serviceable parts associated with Medical Liquid Oxygen containers, do not attempt to correct any problems with leakage.

Sealing or jointing compounds must never be used to cure a leak.

Contact Air Liquide to arrange repair of the faulty container.

*Use of Medical Liquid Oxygen Containers.*

Containers should be handled with care.

Containers must only be moved with an appropriate size and type of trolley.

Smoking and naked flames must not be allowed near containers or pipeline outlets.

Equipment for use with Medical Liquid Oxygen must never be lubricated and must be kept free from oil and grease.

Contact with medical liquid oxygen can cause burns.

Always follow the instructions for use for the equipment.

4.3 **Contraindications**

Patients should not smoke while on oxygen therapy due to increased risk from fire.

4.4 **Special warnings and precautions for use**

As a general rule, high concentrations of Oxygen should only be administered for the minimum time required to achieve the desired result, and should be monitored by repeated analyses of the arterial oxygen pressure (PaO$_2$) or oxygen saturation of the haemoglobin (SpO$_2$) and the inhaled oxygen concentration (FiO$_2$).

There is literature supporting the safety of oxygen fraction:

Oxygen is safely administered in the following concentration during the indicated times:

- Oxygen in concentration up to 100 % (FiO$_2$ 1.0) for less than 6 h
- Oxygen in concentration of 60 – 70 % (FiO$_2$ 0.6 – 0.7) during 24h
- Oxygen in concentration of 40-50 % (FiO$_2$ 0.4 – 0.5) during the second 24 h
- Any Oxygen concentration > 40 % (FiO$_2$ > 0.4) is potentially toxic after 2 days.

Premature infants are excluded from these guidelines because retrolental fibroplasia occurs with a much lower FiO$_2$.

*Special precautions for use*

Special caution should be observed when treating newborn and premature infants. The absolute lowest concentration which gives the desired result should be used in order to minimise the risk of ocular damage, retrolental
fibroplasia, or other potential undesirable effects. The arterial oxygen pressure should be monitored and kept below 13.3 kPa (100 mmHg).

In cases of high concentrations of oxygen in the inspiratory air/gas, the concentration/pressure of nitrogen are lowered. As a result, the nitrogen concentration in tissue and lung (alveoli) is lowered. If oxygen is taken up from alveoli to the blood faster than additional oxygen is delivered by ventilation, alveoli collapse may occur (atelectases).

The formation of atelectasic lung areas may impair oxygenation of arterial blood because there will be no gas exchange in the atelectasic area despite perfusion, there will be ventilation/ perfusion mismatching – an increased shunt.

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

In hyperbaric oxygen therapy compression and decompression should be slow in order to avoid the risk of pressure damage - barotrauma.

Rebound attacks may be experienced by patients suffering from cluster headaches treated with oxygen.

4.5 Interaction with other medicinal products and other forms of interaction
- Interactions with amiodarone have been reported.
- Relapse of bleomycin-induced lung disease may be associated with a fatal outcome.
- Patients with pre-existing oxygen radical damage to the lung may have damage exacerbated by oxygen therapy, e.g. in the treatment of paraquat poisoning.
- Respiratory depression due to alcohol may potentiate that caused by oxygen.

4.6 Pregnancy and lactation
Oxygen can be used during pregnancy or lactation.

4.7 Effects on ability to drive and use machines
Oxygen therapy at ambient pressure has no adverse effect on the ability of the patient to drive or operate machinery.

4.8 Undesirable effects
Oxygen therapy causes only minor effects on pulmonary and cardiovascular function.

In treatment with high oxygen concentrations and consequently reduced nitrogen pressure in the inspiratory air/gas, the nitrogen concentration in tissue and lung is reduced. This can lead to resorption atelectases caused by a reduced volume in the alveoli in combination with an oxygen-induced effect
on the surfactant. This can lead to a poorer ventilation/perfusion ratio and this to poorer oxygenation. (see 4.4).

Heart rate and cardiac output are reduced when 100 % Oxygen is administered for short periods (< 6 hours) and under normobaric conditions.

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

Vital capacity is seen to decrease slightly after treatment with 100 % Oxygen for prolonged periods (approx. 18 hours). On continued treatment with 100 % oxygen for more than 24 – 48 hours a condition with acute pulmonary failure may develop Acute Respiratory Distress Syndrome (ARDS). Long-term treatment with 100 % Oxygen may also result in toxic effects on other organs.

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

The adverse effects of hyperbaric oxygenation (HBO) are usually mild and reversible. HBO may cause middle ear barotrauma, sinus squeeze, myalgia and central nervous system toxicity varying from nausea, vertigo, anxiety – confusion, muscle twitching to loss of consciousness and epileptic seizures. Those CNS symptoms may occur during HBO treatment at more than two atmospheres lasting more than a few hours. At higher pressures more rapid onset of those symptoms will occur.

Patients should be carefully monitored by competent personnel.

In patients with chronic severe airway disease, who rely on hypoxic drive of respiration, the administration of high levels of oxygen will result in further under-ventilation, and further accumulation of carbon dioxide and acidosis.

**Paediatric Patients**

Retrolental fibroplasia with fibroblastic infiltration of the retina, which can lead to blindness, has been claimed to be associated to oxygen treatment in concentrations greater than 40 % in neonates. Other negative effects of Oxygen therapy in high concentration (FiO2 1.0) in neonates are haemolytic anaemia, pulmonary fibrosis, cardiac, renal and hepatic toxicity.

All ages may be at risk for toxic side effects of high inspired oxygen fractions.

In order to reduce the risk of parenchymal damage, including an effect on the lungs (broncho-pulmonary dysplasia), it is of the utmost importance to continually monitor arterial oxygen pressure (see 4.4.).

### 4.9 Overdose

Oxygen overdose does not occur outside the intensive care setting and the risks of this are greater during hyperbaric treatment.

In case of oxygen toxicity, apart from decreasing the Oxygen concentration, therapy should be instituted in order to maintain critical physiology ( e.g. in case of respiratory depression, institute respiratory support).

Prolonged hyperoxygenation can result in lung injury. Cases must be assessed individually, but experience from healthy volunteers would suggest that prolonged exposure, over a period of months, to concentrations up to 30% whilst producing sub-clinical pathologic changes has not been proven to cause specific lung injury. The same applies for exposure up to 60% oxygen, for up
to one week. However, administration of 100% oxygen for more than 24 to 30 hours will result in substernal chest pain and mild dyspnoea. Symptoms may progress, become systemic and include malaise, nausea and transient paraesthesia.

5  PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

All other therapeutic products, Medical Gases.

ATC class: VO3A

Oxygen constitutes approx. 21% of air. Oxygen is vital to life and must be continuously supplied to all tissues in order to maintain the cells’ energy production. Oxygen is transported via the airways to the lung with the inspired air. In the alveoli a gas exchange takes place through the difference in partial pressure from the inspired air/gas mixture to the capillary blood. The oxygen is transported, mainly bound to haemoglobin, further with the systemic circulation to the capillary bed in tissue where it is transported by the pressure gradient to the different cells. The final target for the oxygen is the mitochondria in the individual cells, where oxygen is consumed in an enzymatic chain reaction forming energy. By increasing the oxygen fraction in inspired air, the inspired gas mixture, the partial pressure gradient transporting oxygen to the cells is increased.

When oxygen is given to a patient at pressure higher than atmospheric (HBO), it greatly increases the amount of oxygen that is transported to the peripheral tissues by the blood. Intermittent hyperbaric therapies generate oxygen transport even within oedematous tissue and tissue with poor perfusion and in this way can maintain cellular energy production and function.

Hyperbaric oxygen therapy (HBO) diminishes in proportion to the pressure that is given with the volume of gas bubbles in the tissues, according to Boyle's law.

Hyperbaric oxygen treatment (HBO) inhibits the growth of anaerobic organisms.

5.2 Pharmacokinetic properties

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

The oxygen is transported, mainly bound to haemoglobin, with the systemic circulation to all tissues in the body. Only a very small proportion is free, dissolved in plasma. During passage through the tissues, a partial pressure-dependent transport of the oxygen to the individual cells takes place. Oxygen is a vital component in the cell’s intermediate metabolism for creation of energy – the aerobic ATP production in the mitochondria.
5.3 **Preclinical safety data**

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.

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

Oxygen taken up in the body is excreted almost entirely as carbon dioxide formed in the intermediary metabolism.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

None

6.2 **Incompatibilities**

Not applicable

6.3 **Shelf life**

6 months

6.4 **Special precautions for storage**

Liquid oxygen containers should be kept out of the reach and sight of children.

Oxygen is non flammable but strongly supports combustion. It is highly dangerous when in contact with oils and greases due to the risk of fire.

The normal precautions required in the storage of medical gas containers as described below are applicable:

Containers should be stored separately from containers containing non-medical gases.

Medical containers containing different medical gases should be segregated and identified within the store.

Full and empty containers should be stored separately.

Containers should be stored under cover, kept dry and clean and not subjected to extremes of temperature.

Containers should not be stored near stocks of combustible materials or sources of heat.

Warning notices prohibiting smoking and naked lights should be clearly posted.

Emergency services should be advised of the location of the Medical Liquid Oxygen store.

Precautions should be taken to protect containers from theft.
6.5 Nature and contents of container
The medical liquid oxygen is packaged in vacuum insulated containers made of stainless steel specifically designed to store cryogenic gases at low temperatures (about -180 °C). The transportable medical liquid oxygen supply vessel – 10 litre, 20 litre, 21 litre, 30 litre, 31 litre, 32 litre, 36 litre, 37 litre, 41 litre, 42 litre, 45 litre, 46 litre, 60 litre, 100 litre, 180 litre, 230 litre, 450 litre, 600 litre, 1000 litre and 23500 litre – is used to fill the medical liquid oxygen storage tank at the customer’s location or is supplied for use at the customer’s location.

6.6 Special precautions for disposal
Contact Linde Gas to arrange refill of the container.
Containers that are no longer required should be returned to Air Liquide.

7 MARKETING AUTHORISATION HOLDER
Air Liquide Limited
Station Road
Coleshill
Birmingham
West Midlands
B46 1JY

8 MARKETING AUTHORISATION NUMBER
PL15929/0009

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
01/11/2006

10 DATE OF REVISION OF THE TEXT
20/07/2010