

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Medical Liquid Oxygen 100%, medicinal gas, cryogenic

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxygen 100% v/v (-183 °C), with a minimum purity of 99.5 % v/v
There are no other ingredients

3 PHARMACEUTICAL FORM

Medicinal Gas, cryogenic
Light blue cryogenic liquid of about -183 °C contained within a closed vacuum insulated vessel. The liquid rapidly evaporates to form oxygen gas.
Oxygen gas is a colourless, odourless and tasteless gas.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Medical Liquid Oxygen is vaporised to oxygen gas before administration to a patient
Clinical indications are as follows:

- Use in clinical practice to provide a basis for most modern anaesthetic techniques including pre and post-operative management
- To restore tissue oxygen tension towards normal by improving oxygen availability on a wide range of conditions such as
 - Cyanosis of recent origin as a result of cardio-pulmonary disease
 - Surgical trauma, chest wounds and rib fracture
 - Shock, severe haemorrhage and coronary occlusion
 - Carbon monoxide poisoning
 - Hyperpyrexia
- Major trauma (i.e. road traffic accidents and gunshot wounds)
 - In the management of sudden cardiac and respiratory arrest due to drugs or trauma
- Aid in the resuscitation of critically ill patients, when circulation is impaired
- Aid in neo-natal resuscitation
- In the treatment of acute severe headache in adults with an established diagnosis of cluster headache

4.2 Posology and method of administration

Posology

Oxygen should be prescribed to achieve a target saturation of 94-98% for most acutely ill patients, or 88-92% for those at risk of hypercapnic respiratory failure.

Oxygen is used in the care of patients who present with medical emergencies and is given by inhalation to correct three main indications:

- To correct hypoxaemia
- To prevent hypoxaemia
- To alleviate breathlessness

The purpose of oxygen therapy is to ensure the partial arterial oxygen pressure (P_aO_2) is not less than 8.0 kPa (60 mmHg) or the oxygen saturation of haemoglobin in the arterial blood is not less than 90% by adjusting the fraction of oxygen in inspired gas (FiO_2).

If oxygen is administered diluted in another gas the oxygen concentration in the inspired air (FiO_2) must be at least 21%.

The concentration, flow and duration of the treatment will be determined by the condition that is being treated. The dosage must be regulated according to the needs of the individual patient.

The general recommendation is always to use the lowest possible effective oxygen concentration in the inspired air, that is the lowest dose (FiO_2) to achieve the required therapy (P_aO_2).

Regular monitoring of arterial oxygen tension (P_aO_2) or arterial oxygen saturation (SpO_2) and clinical signs is necessary to evaluate the oxygen therapy.

Higher concentrations should be administered for as short a time as possible with close monitoring of blood gas values.

High concentration oxygen therapy, with concentration up to 60% for short term oxygen therapy is safe for conditions like pneumonia, pulmonary thrombo-embolism and fibrosing alveolitis.

Low concentration (controlled) oxygen therapy (long term) is used in patients with ventilator failure due to chronic obstructive airways disease and other causes. The concentration should not exceed 28%; in some patients 24% may be excessive.

Oxygen may be administered at concentrations of up to and including 100% although most delivery systems reduce this to a maximum inspired concentration of 60% in adults (80% in children) and concentrations higher than this are unlikely to be achieved.

In practice, 30% is usually used as the lower limit with an allowance for a safety margin and is adapted to the patient on the basis of the clinical course of the illness and generally ranges from 1 to 10 litres of gas per minute. Oxygen at 100% concentration will only be inspired if the oxygen supply exceeds the patient's peak inspiratory flow rate (around 25 to 35 l/m for a typical adult at rest) or if a reservoir bag and an air tight mask is used (analogous to an anaesthetic circuit). Conventional oxygen mask flow meters only deliver up to 15 l/m and thus cannot provide patients with 100% inspired oxygen. The peak inspiratory rate flow rate of an infant is more easily matched, so the limiting factors can be more easily overcome: however the above arguments are equally applicable to the paediatric population.

Systems for longer term oxygen therapy rely on a mixture of air and additional oxygen being supplied. Care should be taken to prevent patients from rebreathing expired carbon dioxide. The use of vented face masks and flow rates over 4 litres per minute rarely result in the rebreathing of expired carbon dioxide.

In the treatment of cluster headache, oxygen is administered by a close-fitting facemask at an oxygen flow of about 7 – 10 litres per minute. Oxygen therapy should be initiated as early as possible after the onset of an attack and should last for about 15 minutes or until the pain has disappeared/vanished.

Paediatric population

The posology is the same in adults and children.

Method of administration

For inhalation use

Medical Liquid Oxygen is administered by vaporising the liquid to a gas at ambient temperatures and delivered for inhalation through the lungs.

Oxygen is administered via inspiratory air.

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

Oxygen is normally administered via a dedicated medical device (face mask, nasal cannulae etc) with inhaled air and on exhalation the exhaled gas with any excess oxygen leaves the patient and is mixed with the surrounding air (“non-rebreathing” system). Masks, nasal cannulae, etc. can provide fixed or variable mixtures depending on their design.

In anaesthesia, special systems can be used when the exhaled gas is recirculated and can be rebreathed (“rebreathing” system).

If a patient cannot breathe independently, artificial breathing support can be provided.

In addition to the administration of oxygen via inhaled air, for example in heart surgery, a metered supply of oxygen can be injected into the bloodstream via an oxygenator of an extracorporeal circulation of a cardio-pulmonary bypass system.

Other systems of administration include face tents, headboxes, cot hoods and supply to a tracheostomy. In severe hypoxia the use of a positive pressure mask may be valuable. This technique should only be supervised by experienced practitioners.

Oxygen levels should be monitored as required in the breath, blood and tissue to ensure that appropriate concentrations are not exceeded.

4.3 Contraindications

There are no absolute contraindications to the use of oxygen, but the inspired concentration should be limited in the case of premature neonates and in those patients with chronic severe airways disease (such as COPD and emphysema)

Medical Liquid Oxygen, whilst non-flammable supports combustion and should be handled with due care. Patients should not smoke while on oxygen therapy because of the fire risks.

4.4 Special warnings and precautions for use

Patients with chronic severe obstructive airways disease rely on hypoxic drive for respiration. When such patients are given oxygen therapy it must be administered at a relatively low concentration and must be accurately metered and titrated against arterial concentrations and clinical observation.

Special caution is required in the treatment of neonates, in these cases the lowest effective dose must be used to achieve adequate oxygenation; fluctuations in oxygen

saturation should be avoided. This is required to minimise the risk of eye damage, retrolental fibroplasia or other potential adverse effects. The inspired concentration should not exceed 40%, the arterial oxygen pressure should be monitored and kept below 13.3kPa (100 mmHg).

In hyperbaric chambers in the management of conditions such as carbon monoxide poisoning, anaerobic infections and acute ischaemic disease, convulsions may occur at 3 atmospheres after a few hours.

Where the patient has been exposed to agents which are toxic to the lungs, such as Paraquat, the use of gases containing more than 21% should be avoided.

Medical Oxygen is non-flammable but strongly supports and accelerates combustion. This means that it makes things burn more easily, more fiercely and with a greater intensity. Do not allow naked flames or other sources of ignition where oxygen is in use.

4.5 Interaction with other medicinal products and other forms of interaction

The pharmacokinetic activity of oxygen is modified by changes in blood carbon dioxide tension, but this has little clinical significance

The use of higher levels of oxygen can increase the risk of pulmonary toxicity in patients who have been administered Bleomycin, Amiodarone and Nitrofurantoin or similar antibiotics. In these cases, oxygen should be administered with caution and at levels kept as low as possible.

Patients with pre-existing oxygen radical damage to the lung may have this 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 Fertility, pregnancy and lactation

There are no contraindications for oxygen therapy during pregnancy or breast-feeding or any effect on fertility that is known

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 and operate machinery. Patients who require continuous oxygen support should be assessed for their ability to drive or operate machinery.

4.8 Undesirable effects

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.

Acute rises and accumulation of serum carbon dioxide in patients with chronic severe airway disease may result in hypercapnia and respiratory acidosis. Patients appear flushed with elevated heart rates, headache and drowsiness, which can progress to confusion and coma.

CNS oxygen toxicity only occurs when the partial pressure of inspired oxygen exceeds 2 atmospheres (203 kPa), as in hyperbaric oxygen therapy. Symptoms of CNS toxicity may include mood changes, nausea, dizziness, twitching, convulsions and loss of consciousness.

Hyperbaric oxygen treatment has been shown in some studies to be linked with hyperbaric oxygen-induced oxidative DNA damage that can lead to gross genetic alterations and chromosome aberrations after hyperbaric oxygen under therapeutic conditions. It has also been shown that a single hyperbaric oxygen exposure induced adaptive protection against further induction of oxidative DNA damage. Cases must be assessed individually and the therapy protocol may consider a shortened treatment before the standard protocol is applied.

Paediatric Population:

In the premature neonate, exposure to excessive oxygen concentrations may be associated with the following conditions: retrolental fibroplasia, bronchopulmonary dysplasia, sub-ependymal and intraventricular haemorrhage and necrotising enterocolitis.

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Oxygen overdose does not occur outside of the intensive care setting.

Prolonged hyperoxygenation can result in lung injury. Cases must be assessed individually, but experience from healthy volunteers would suggest that prolonged exposure, over periods of months, to concentrations up to 30% whilst producing sub-clinical pathologic changes has not been proven to cause specific lung injury; similarly, for exposures up to 60% 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.

See section 4.8 'Undesirable effects' of over dose in specific patient groups.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group - Medical Gas. ATC Code - V03AN01.

The characteristics of medical liquid oxygen are a light blue cryogenic liquid of about -180° C that evaporates to oxygen gas which is an odourless, colourless, tasteless gas

Oxygen is present in the atmosphere at 21% and is an essential for life. Oxygen must be supplied continuously to all body tissues in order to maintain the cells' energy production. Oxygen is transported via the airways to the lung with the inspired air.

The basal Oxygen consumption in man is about 250ml/min for a body surface of 1.8m². It is reduced by about 10% during anaesthesia and natural sleep and by about 50% for a 10°C fall in body temperature.

Alveolar air contains about 14% oxygen (105mmHg) and the arterial blood has an oxygen tension of 97mmHg. The difference, known as the alveolararterial oxygen tension gradient, increases with age. The difference may be as great as 30mmHg in a healthy, elderly individual.

Gas exchange takes place in the alveoli through the difference in partial pressure from the inspired air/gas mixture to the capillary blood. Oxygen in the blood is mostly combined with haemoglobin. 1.34ml per 9ml to give a maximum capacity of 20ml per 100ml of blood. A small amount, 0.3ml, exists in solution in the same volume of blood.

The oxygen is transported to the capillary bed in tissue where it is transported by the pressure gradient to the difference cells. In the mitochondria in the individual cells the oxygen is consumed in an enzymatic chain reaction forming energy. By increasing the oxygen fraction in inspired air the partial pressure gradient transporting oxygen to the cells is increased

The concept of oxygen availability first described by Richards in 1943 and later elaborated by Freeman and Nunn has been used to quantify the amount of oxygen available to the body. It can be expressed as the product of the cardiac output and the oxygen content of the blood.

Available oxygen = (cardiac output) x Hb conc x 1.34 x (% saturation)

Substituting normal values:

Available oxygen = (5000ml) 15/100 x 1.34 x 95/100 = 950ml

The average healthy individual with a basal oxygen consumption has no more than four minutes supply of oxygen in the blood.

5.2 Pharmacokinetic properties

The uptake of oxygen by the blood in the lungs and discharge to the tissues is determined by the oxygen dissociation curve. The characteristic sigmoid shape ensures that, at tensions between 40 and 15mm Hg, the Oxygen carried in the blood from the lungs can be readily given up to the tissues.

The uptake from the lungs is rapid, because blood flow through the capillaries, where exchange takes place, occurs in about 0.5 seconds.

The uptake of oxygen is favoured the simultaneous loss of carbon dioxide which is then excreted in the expired air. Conversely the entry of carbon dioxide into the blood from the tissues facilitates oxygen transfer to the cells. At rest, mixed venous blood returning to the lungs contains 13-14ml of oxygen p per 100ml, but with severe exercise, the oxygen content may fall to 3-4ml. In very active tissue, almost complete extraction occurs.

5.3 Preclinical safety data

The published toxicological-pharmacological data indicates that medical oxygen is not harmful to humans

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

There are no known incompatibilities with oxygen.

6.3 Shelf life

6 weeks

6.4 Special precautions for storage

Medical Liquid Oxygen containers should be stored in a secure area that is well ventilated, under cover, preferably inside, kept dry and clean (free from debris) and not subjected to extremes of heat or cold.

- Containers should be stored in a secure area
- Containers should be kept out of the reach and sight of children
- Keep container below 50°C and preferably between 10 °C and 30 °C.
- The Medical Liquid Oxygen container will periodically release a small amount of oxygen gas to prevent build-up of pressure within the container, the equipment should be kept in a well-ventilated area
- The Medical Liquid Oxygen container should be stored separately from other medical gases and non-medical gases.
- Do not cover the Medical Liquid Oxygen container with blankets or other fabrics
- Containers should not be stored near clothing or combustible materials or near sources of heat.
- Precautions should be taken to protect containers from theft.
- Warning notices prohibiting smoking or naked lights should be posted clearly. Emergency services should be advised of the location of the storage area for Medical Liquid Oxygen containers.
- Do not smoke near Medical Liquid Oxygen containers

6.5 Nature and contents of container

The container consists of an inner and outer vessel made of stainless steel. The space between the vessels is filled with an insulating material to prevent heat conduction by radiation and evacuated to a very low pressure to decrease heat conduction. The inner and outer vessels are both equipped with bronze safety valves to prevent formation of an excessive pressure inside the vessels.

The vent valve, made of stainless steel and bronze, is used to release gas during filling. When liquid oxygen starts to escape through the vent valve, the container is full. This is at 95% of the nominal water capacity of the container.

The material of construction in contact with the medical liquid oxygen is stainless steel. Gaseous product will also contact aluminium and bronze valve components when oxygen is drawn directly from the container. All materials used are compatible with medical liquid oxygen and low temperatures.

The pack sizes are 30 litres, 32 litres and 35 litres.

Each litre of medical liquid oxygen delivers 840 litres of gaseous medical oxygen at 15 °C and 1 bar.

Container designation	Container volume (litres water capacity) Nominal	Medical Liquid Oxygen Capacity (kg)
<u>Liberator 30</u>	30	34.01
<u>Low Loss 32</u>	32	34.47
<u>EasyMate 2335</u>	35	40.00

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

General

All personnel handling Medical Liquid Containers should have adequate knowledge of:

- the properties of the gas,
- precautions to be taken, actions in the event of any emergency

the correct operating procedures for their use

-

Smoking and naked lights must not be allowed in the vicinity of where Oxygen Therapy is being used.

- Do not smoke near the Medical Liquid Oxygen container

Under no circumstances should oil or grease be used to lubricate any part of the valve or the associated equipment used to deliver the medical gas to the patient. Oxygen may react violently when it comes into contact with hydrocarbons such as oils and greases.

When moving or transporting the unit use the specialised equipment supplied for this purpose, precautions should be taken to ensure that the Medical Liquid Oxygen container does not tip over or fall over as this may cause damage to the Medical Liquid Oxygen container or cause personal injury.

The temperature of Medical Liquid Oxygen is -183 °C and can cause painful cold burns if it comes into contact with skin, care should be taken when handling or using Medical Liquid Oxygen containers.

- Do not touch Medical Liquid Oxygen
- Do not touch frosted parts of the container

Cold (cryogenic) Burns

Unprotected skin can become stuck to very cold metal parts upon contact, which may tear the skin if it is pulled off. Freezing of the skin may cause local pain, or may not cause much pain at all. Frozen skin may have a waxy yellow appearance. When it thaws, this can cause intense pain and may lead to shock.

First Aid for Cold Burns

Do not attempt to pull frozen skin apart from other items or remove clothing frozen to the skin. If the skin is stuck to metal parts, it may be removed by flushing with large amounts of tepid water (no higher than body temperature). Do not use dry heat, such as a hair drier or electric heater. Loosen any tight clothing that may restrict blood flow. Affected skin can be covered with sterile dressings. Do not rub or massage frozen skin and do not apply any creams or ointments. Seek medical attention as soon as possible for anything but the most minor injuries.

Preparation for Use

- Check that hands are clean and free from any oils or grease before handling equipment associated with the use of Medical Liquid Oxygen to prevent contamination.
- Where moisturising creams are required for use by a patient with a facemask or in nasal passages, oil based creams should not be used.
- Where alcohol gels are used to control microbiological cross-contamination ensure that all alcohol has evaporated before handling Medical Liquid Oxygen equipment.
- Medical oxygen can either be supplied directly from the Medical Liquid Oxygen containers or from a portable liquid oxygen unit that has been filled from the Medical Liquid Oxygen container by the user.
- Ensure the correct container has been selected – check that the container contains Medical Liquid Oxygen. (Read the label on the cylinder)
- Ensure that the gas is within its expiry date (this is specified on a separate batch label on the container)
- Ensure that the connections on the Medical Liquid Oxygen container or the associated equipment are dry and clean

Use of Medical Liquid Oxygen Containers

- Containers must not have any markings obscured or labels removed.
- Always keep the Medical Liquid Oxygen container in an upright position.
- Use the Medical Liquid Oxygen container following the manufacturer's instructions.
- Only use the equipment provided for use with the Medical Liquid Oxygen container.
- Check the level of liquid oxygen in the container.
- Check for leakage.
- If using the Medical Liquid Oxygen container to fill a portable oxygen unit, follow the filling instructions provided for the portable unit.

After Use

- Return empty containers to your supplier.
- Any containers that are no longer required should be returned to your supplier.

In the event of a leak

- In the unlikely event of a leak from the Medical Liquid Oxygen container, open windows and doors to ventilate the room and allow the oxygen to disperse.
- Shut off any potential sources of heat such as ovens, heaters etc.
- Stay away from the Medical Liquid Oxygen container.
- Contact the manufacturer immediately using telephone number: 01352 736050

7 MARKETING AUTHORISATION HOLDER

Medical Gas Solutions Ltd
Unit 19 Manor Industrial Estate
Bagillt
Flint. CH6 5UY

8 MARKETING AUTHORISATION NUMBER(S)

PL 17872/0003

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

06/08/2025

10 DATE OF REVISION OF THE TEXT

06/08/2025