

MEDICAL LIQUID NITROGEN LEAFLET
Revision: 10/2023
Liquefied gas for dermatology and cryoconservation



Symbol	Explanation	Symbol	Explanation
	Authorized representative in the European Community		Caution, consult accompanying documents
	CE certified		Manufacturing date
	Medical Device		Expiry date
	Unique Device Identifier		The instruction manual must be read
	Name and address of manufacturer		Breathing hazard
	Batch code		This medical device is not sterile
	Catalog number		Warning

1. WHAT IS LIQUID MEDICAL NITROGEN AND WHAT IS IT USED FOR?

Liquid medical nitrogen is a class IIa medical device under MDR (EU) 2017/745.
It is intended for the following applications:

- **Dermatology**
For the treatment of
- **Cryoconservation**
For the

Read all of this leaflet carefully before using this product.

It contains important information on its use.

If you have other questions, if you have any doubts, ask your supplier for more information.

2. INFORMATION NEEDED BEFORE USING LIQUID NITROGEN:

Precautions for use

Before any use or intervention, make sure that the product used is medical device nitrogen (CE 0476 marked).

Special precaution should be taken in patients with following cold-related diseases: Cryoglobulinemia,

Raynaud's disease, cold intolerance, cold urticaria and cryofibrinogenemia.

As infection is a possible complication, immunosuppression is a special warning including use of immunosuppressive drugs and diseases triggering immune system disorders such as agammaglobulinemia and multiple myeloma.

Furthermore, when treating patients with valvular hearts disease or cardiac valve prostheses, prophylactic antibiotics should be considered to counter any risk of post-cryotherapy infection leading to endocarditis. To minimize risk of infection, cryoprobes should be disinfected and the canister cleaned between each patient.

Due to risk of haemorrhage of cryotherapy, platelet deficiency, the use of anticoagulant and blood dyscrasias of unknown origin should be considered with precaution.

In patients with collagen disease, treatment of ear, eyelid and nasal lesions may lead to cartilage necrosis and distortion of shape.

The treatment of area with superficial nerves may lead to nerve damage. Ballooning of tissue over vulnerable areas is recommended to prevent this complication. It can be done manually squeezing the tissue together over the vulnerable area or by injecting lidocaine under the lesion to be frozen. Ballooning lesions over bony prominences such as the dorsum of the hand could be helpful also to prevent extensor tendon rupture.

Spraying over broken skin can occasionally lead to insufflation of the underlying tissues with nitrogen gas, resulting in subcutaneous emphysema. It can concern previous biopsy site but also malar and periobital areas of the face.

Previous curetted and biopsy sites are at risk of nitrogen emphysema and haemorrhage. Nitrogen emphysema can be prevented by starting with only gentle spraying directed at an angle or use pressure rings or cones. Risk of haemorrhage is reduced by use of topical haemostatic treatments.

Individuals with high Fitzpatrick skin type face the highest risk of prominent hypopigmentation. Whatever the patient skin type, sun protection is essential until complete healing in sun-exposed area. Furthermore, feathering of the freeze margin (lighter freeze area) enables to reduce the extent of pigmentary changes.

A special warning concerns also melanoma, as well as lesions that can evolve into melanoma such as lentigo maligna and melanocytic nevi. These types of lesions require a definitive histologic diagnosis by biopsy before cryotherapy treatment is undertaken. Furthermore, atypical histologic features following cryotherapy could make the differentiation of benign from malignant melanocytic lesions difficult.

Liquid nitrogen and the associated cold vapours can induce injuries like a thermal burn, as well as frostbite when cold exposure is prolonged or cooling of skin tissues is rapid.

Very brief exposure to liquid nitrogen or associated cold vapours, with no effect on the skin, can alter fragile tissues such as ocular tissues and cause the occurrence of frostbite leading to irreversible damage or even blindness.

Some cases of gastric distention and/or perforation were reported in the literature. These occur in a context of ingestion of a beverage, which was prepared with liquid nitrogen. When heated to body temperature, nitrogen instantly expands 700 times, predictably leading to gastric rupture. Cases of gastric perforation are also linked to pneumothorax and subcutaneous emphysema, leading to a barotrauma.

Accidental inhalation of cold nitrogen vapour or aerosol causes lesions such as irritation, oedema and "burns" in the oral cavity, pharynx, bronchi and lungs.

In patients, accidental exposure on normal skin may happen in case of liquid nitrogen runoff. This situation may occur when spray is directed at one spot without interruption, and with cotton-tipped applicators. Drapes or tapes normally used for minor surgical procedure are a hindrance, since this allows liquid nitrogen to accumulate at their borders causing an injury that may go unnoticed until the end of the procedure.

This product is strictly for medical use only.

Warnings

This product is not sterile.

Do not ingest.

For **use in dermatology**, it is advisable, in order to reduce any risk of contamination: to transfer the volume of liquid nitrogen into an appropriate container, never to pour this volume back into the storage container and to use only one applicator per intervention.

The use of an operating drape or spray cones protecting healthy skin is recommended.

For **cryoconservation**, tissue storage devices must not be damaged and must be compatible with the low

temperature of nitrogen. Manufacturers recommendations should be followed.

Respect the hygiene rules for usage to limit the risk of transmission of pathogens between cryopreserved cell samples.

Paediatric population

There is no contraindication to use liquid nitrogen in paediatric populations. However, topical application of lidocaine tape or lidocaine/prilocain cream is recommended to help children tolerate the procedure better.

Pregnant women

Liquid nitrogen for dermatology is useful in pregnant women and can be performed without anesthesia, with a low risk of infection and with minimal wound care but local analgesia can be required.

Despite the fact that hundreds of thousands of women have been treated with cryotherapy, extensive data reviewing the impact of this therapy on fertility and pregnancy outcome do not exist. However, data gathered show there is no evidence that cryotherapy has a negative impact either on fertility or pregnancy outcome.

Because liquid nitrogen is a nontoxic gas that is unlikely to appear in breastmilk or be absorbed by the infant, it is considered safe to use during breastfeeding. No special precautions are required.

Instructions for use, handling

Nitrogen is considered to be non-toxic due to its inert nature. Liquid nitrogen boiling point is -192°C and easily vaporizes at room temperature. The major risks are potential frostbite/cold burns and asphyxia when manipulating liquid nitrogen and overpressure when storing liquid nitrogen.

Asphyxia

A small amount of liquid nitrogen can vaporize rapidly to large volumes of nitrogen (a litre of liquid nitrogen will produce about 0.7 m^3 of gaseous nitrogen) and sudden evaporation of liquid nitrogen in a limited space can lead to oxygen depletion in the air. As the cold vapour is heavier than air, the vapours spread out along the floor pushing away the breathing air from the bottom at the same time, thus creating the risk of asphyxiation in case of loss of consciousness and fall.

If the oxygen concentration of atmosphere drops below 10%, a human becomes unconscious immediately and unable to rescue oneself from asphyxia.

Hypoxia is a decrease in the supply of oxygen in the tissues. It can be gradual or fast. Presence of symptoms depends on the patient's age, presence of concomitant disease and level of health. Early signs of hypoxia are anxiety, confusion and agitation; if not corrected, hypotension will develop.

Clinical symptoms of hypoxia are (but not limited to):

- Dyspnea
- Hyperventilation
- Cyanosis (late sign)
- Tremors, lack of muscle coordination
- Decreased level of consciousness (confusion, stupor, loss of consciousness)
- Agitation
- Euphoria
- Cold and moist skin
- Tachycardia or bradycardia
- Tachypnea
- Hypotension (late sign)

The onset of symptoms of hypoxia can be insidious. Cognitive disorders may appear more or less quickly: idea of slowdown, memory disorders, delayed reaction time, errors in judgment, etc.

The occurrence of clinical signs of hypoxia is also dependent of the oxygen level in the air. Two breaths in a low-oxygen atmosphere may be enough to cause loss of consciousness and death may occur within minutes.

Being colourless and odourless in the gaseous state, nitrogen does not cause irritant or warning symptoms. Given that exchange of CO_2 continues to occur freely, there is no hypercapnic response

elicited by medullary chemoreceptors that would evoke the traumatic sensation of suffocation. The oxygen chemoreceptors do not have a significant response to hypoxia until PaO₂ reaches below 55 mmHg. An individual may experience loss of consciousness and subsequent death with few to no warning symptoms.

Cold burns

The use of liquid nitrogen for cryotherapy is due to its extremely low temperature causing destruction and necrosis of cells when it is in contact with tissue.

Liquid nitrogen and the associated cold vapours can produce on the epidermis, dermis and subcutaneous tissues similar to a thermal burn, as well as frostbite when cold exposure is prolonged or cooling of the skin tissues is rapid. While this cold effect is desired for patients in cryotherapy, such effect is considered as untoward medical occurrence for users.

The complications due to cold burn are the same for users as for patients (see section undesirable effects below)

To avoid any incident, it is essential to respect the following instructions:

- User personnel must be trained in the handling of liquid/cryogenic gases, in the risks of liquid/gaseous cryogenic gases and in the safety best practices.

Following best practices are recommended:

- User has to wear PPE and manipulate liquid nitrogen carefully; it is recommended that two people work together when manipulating cryogenic gases
- Never use a container that is tightly closed or not equipped with a safety valve for transporting or storing liquid nitrogen
- Install an oxygen sensor and an alarm that triggers at an oxygen threshold of 19%
- Evacuate the room when the oxygen is less than 19% and prohibit access without a self-contained breathing apparatus when the oxygen content is too low
- Control of the oxygen level of the room by using mechanical ventilation (by continuous fresh air supply of 6 volumes per hour) coupled with rate detection of oxygen in the local atmosphere
- Periodically check the proper functioning of the cryogenic equipment and oxygen sensor.
- Design premises so that the nitrogen does not disperse in the building
- Transport containers containing liquid nitrogen on a suitable trolley and use the elevator without any passengers and having a "priority mode" feature.
- Follow all safety procedures written by the users and the SOP shall be visible to all users

Transfer :

- The low temperature of liquid nitrogen (-196°C) can cause skin burns. During any transfer operation from one capacity to another, the use of a **safety visor** , **cryogenic gloves** , **safety shoes** is **compulsory** , as well as the wearing of covering clothing (long sleeves, trousers) protecting any part of the body from possible projections.
- Wearing an oxygen meter is recommended in order to effectively control the risk of under-oxygenation.
- The equipment must be in good condition and used according to the manufacturer's recommendations.
- Containers must be handled with all the necessary precautions, paying particular attention to the risk of the container falling and the nitrogen spilling.
- Transferring Liquid Medical Nitrogen to another suitable container should be done outdoors. Cryogenic containers must always be placed upright on a flat surface.

Driving and using machines

A container of liquid nitrogen must be secured during transport and any movement.

Do not transport a container of liquid nitrogen in an unventilated vehicle, even for a seemingly short journey. Transport time is a critical parameter, sometimes difficult to control, due to the natural vaporization of nitrogen and the risk of anoxia.

For transport, the tanks must comply with the international regulations applicable to the transport of hazardous materials by land (ADR), air (IATA) and rail (RID).

If an elevator is used to transport a container of liquid nitrogen, no one should be in the elevator.

Use appropriate means of handling.

Do not introduce or use a container containing liquid nitrogen in a place or public transport without first ensuring that it is possible to do so.

Undesirable effects

Local complications

- Pain
- Erythema
- Itching
- Oedema or swelling
- Erosion and ulceration
- Bulla/blister/exudation
- Nitrogen emphysema
- Haemorrhage
- Sensory impairment
- Pigmentation changes
- Undesirable tissue necrosis
- Excessive scarring
- Infection

Other complications

- Urticaria
- Headache
- Vaso-vagal syncope
- Asphyxia

3. HOW TO USE LIQUID MEDICAL NITROGEN?

On a person, liquid nitrogen can only be used externally. Do not ingest.

4. WHAT ACTIONS TO TAKE IN THE EVENT OF AN ACCIDENT?

An atmosphere containing less than 19% oxygen becomes dangerous. An atmosphere saturated with nitrogen presents **risks of loss of consciousness** and then of asphyxiation. Gaseous nitrogen coming from the evaporation of liquid nitrogen tends to **accumulate in low points** (at low temperatures, nitrogen is heavier than air).

In the event of a spill or leak:

- Evacuate the room
- Call for help
- Under no circumstances enter the premises before being certain that the oxygen content has risen above 18%: unless you are equipped with self-contained breathing apparatus provided for this purpose.

In case of discomfort

Quickly bring the person back to a normal atmosphere.

Start artificial respiration immediately and contact the emergency services. If necessary, administer oxygen with a respirator or a manual resuscitator.

Continue until a doctor arrives.

In case of projection

- In the eyes: wash the eye thoroughly for at least fifteen minutes and consult a doctor.
- On the skin: do not rub, remove or loosen clothing if necessary. Thaw the affected parts by moderate or gradual warming (in lukewarm water if possible for fifteen minutes; otherwise by placing them against another warm part of the body). See a doctor. The earlier the rewarming with water, the more effective it will be (essentially in the minutes following the lesion).

5. HOW TO STORE LIQUID MEDICAL NITROGEN?

The low temperature weakens many materials. Also, the materials making up the storage or transfer containers are materials for cryogenic use (ferric nickel steel, stable austenitic stainless steel, or aluminum alloys that can be used down to absolute zero).

It is forbidden to use containers or materials other than those recommended by their manufacturer for the storage or use of liquid nitrogen.

The equipment must be in good condition and used according to the manufacturer's recommendations (check that there is no ice on the cap).

For storage, it is mandatory to use non-watertight plugs in order to avoid any risk of overpressure.

Nitrogen storage or use areas must have natural or forced ventilation to the open air, in order to maintain the oxygen content at a value above 19% and to avoid any risk of discomfort or anoxia. In order to alert user personnel, a sign indicating the risks must be installed in a clearly visible manner.

The equipment must be stored in a clean, easily accessible, ventilated place protected from bad weather.

As liquid nitrogen evaporates naturally, it is imperative to regularly monitor the level of liquid nitrogen in the storage tank (absence or excess of nitrogen during filling).

In the context of storage in a fixed tank for the cryoconservation application, the pressure and the level of the tank must remain within the defined limits.

To ensure the delivery of liquid nitrogen, it is imperative to monitor the level of the liquid in the storages and to respect the minimum and maximum pressure instructions in order to guarantee the proper functioning of the equipment connected to the network.

- **Do not leave in sight or reach of children.**
- **Do not smoke**
- **Do not approach a flame.**
- **Do not grease.**

MANUFACTURER

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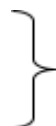
Date of manufacture :



Batch number:



Expiration date :



See batch label