IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Medical Oxygen a compressed medical gas (100% Oxygen Ph. Eur., from Industrial Pressure Testing Ltd on 29th May 2015. Medical Oxygen is used to treat the following conditions:

At high concentrations in the treatment of acute severe asthma, pulmonary thrombo-embolism, pneumonia and fibrosing alveolitis.

At low concentrations in the treatment of ventilatory failure due to chronic obstructive airways disease and other causes.

For the treatment of carbon monoxide poisoning.

To reduce the volume of air trapped in body cavities, as for example, in patients with pneumothorax (collapsed lung), air embolism and decompression sickness. Inhalation of air containing a high concentration of oxygen (and hence low concentration of nitrogen) enhances removal of trapped oxygen.

Pulmonary oedema.

As a diluent or carrier gas in anaesthesia.

Other indications include cystic fibrosis, shock, severe anaemia, sleep apnoea, cluster headaches and anaerobic infections.

This application for a marketing authorisation was submitted in accordance with Article 10a of Directive 2001/83/EC and is referred to as a 'well established medical use' application. This means that the Marketing Authorisation Holder for Medical Oxygen is not required to submit any new clinical trials to support its use.

Medical Oxygen is a prescription only medicinal product to be promoted only to the medical profession.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at http://www.hpra.ie/.

Name of the product	Medical Oxygen 100% v/v Inhalational Gas
Name(s) of the active substance(s) (INN)	OXYGEN
Pharmacotherapeutic classification (ATC code)	V03 AN01
Pharmaceutical form and strength(s)	100% v/v Inhalational Gas
Marketing Authorisation Number(s) in Ireland (PA)	PA22852/001/001
Marketing Authorisation Holder	Air Liquide Healthcare Ireland Limited

II. QUALITY ASPECTS

II.1. Introduction

This application is Medical Oxygen medicinal gas.

II.2 Drug substance

The active substance is oxygen, an established active substance described in the European Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The product is entirely composed of oxygen, there are no other ingredients.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)

There are no excipients in the formulation.

P.5 Control of Finished Product

The Finished Product Specification is based on the relevant pharmacopoeial monograph for medicinal gases and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of the product.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance has been available on the European/Irish market for more than fifty years. Preclinical data have been superseded by clinical experience and therefore no preclinical assessment report is available.

IV. CLINICAL ASPECTS

IV.1 Introduction

Medical Oxygen is a well known active substance with established efficacy and tolerability. The application for a marketing authorisation was made under Regulation EC 1084/2003 Article 10a on the basis of well established medical use.

IV.2 Pharmacokinetics

The uptake of oxygen by the blood in the lungs and discharge to the tissues is determined by the blood/oxygen dissociation curve. At tensions between 5kpa (40mm Hg) and 2kpa (15mm Hg) the oxygen carried in the blood can readily be delivered to the tissues.

The uptake from the lungs is rapid because blood flow through the capillaries, where the exchange takes place, occurs in about 0.5 seconds. The uptake of oxygen is facilitated by the simultaneous loss of carbon dioxide which is then excreted in the expired air.

IV.3 Pharmacodynamics

High concentration oxygen therapy, with concentrations up to 60% for short periods is safe for conditions like acute severe asthma, pulmonary thrombo-embolism, pneumonia and fibrosing alveolitis. Low concentration oxygen therapy should be used in patients with ventilatory failure due to chronic obstructive airways disease and other causes. The concentration should not exceed 28%.

Oxygen may be administered at concentrations of up to and including 100% although with most delivery systems concentrations over 60% (80% in children) are unlikely to be achieved. In practice 24% is usually taken as the lower limit, with allowance for a safety margin. The dosage 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.

Systems for longer-term oxygen therapy usually rely on a mixture of air and additional oxygen being supplied. Masks, nasal cannulae, etc. can provide fixed or variable mixtures depending on their design. In circumstances where oxygen is not being mixed with air, but is mixed with other gases (e.g. anaesthetics and analgesics) then it is essential that the proportion of oxygen in the inspired mixture never falls below the concentration in air. In practice 30% is usually taken as a lower limit.

IV.4 Clinical Efficacy

No new clinical trials have been conducted in support of the application and none are required. This is because of the basis of the application – well established medical use – under which it is considered that the medicinal properties of the substance are sufficiently understood as to not require further demonstration by means of clinical studies.

IV.5 Clinical Safety

As above.

IV.6 Discussion on the clinical aspects

Please see section IV.4

V. OVERALL CONCLUSIONS

The Marketing Authorisation Holder has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted, considered that Medical Oxygen demonstrated adequate evidence of efficacy for the approved indication(s) as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

November 2019