



Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Levocarnitine 1 g Solution for Injection

Levocarnitine

PL 46052/0003

Cenoté Pharma Limited

LAY SUMMARY

Levocarnitine 1 g Solution for Injection Levocarnitine

This is a summary of the Public Assessment Report (PAR) for Levocarnitine 1 g Solution for Injection. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Levocarnitine Injection in this lay summary for ease of reading.

For practical information about using Levocarnitine Injection, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Levocarnitine Injection and what is it used for?

This product is a generic medicine. This means that this medicine is the same as, and considered interchangeable with, a reference medicine already authorised, called Carnitor 1 g Solution for Injection.

Levocarnitine Injection is used to treat primary and secondary carnitine deficiency in adults, children, infants and newborn children. It can also be used to treat secondary carnitine deficiency in haemodialysis patients.

How does Levocarnitine Injection work?

Levocarnitine injection contains the active ingredient levocarnitine, which is a type of protein. Carnitine deficiency occurs when the body has a shortage of levocarnitine. Levocarnitine injection makes up for the lack of levocarnitine in the body and helps give the body more energy.

How is Levocarnitine Injection used?

The pharmaceutical form of this medicine is a solution for injection and the route of administration is intravenous (into a vein).

The patient's doctor will carefully calculate the amount of Levocarnitine injection that the patient should be given and may vary it depending on the patient's response to the treatment. The doctor may take blood and urine samples to check the amount of the drug in the patient's body.

The patient's doctor will give the injection slowly into a vein (intravenous injection) over a period of 2-3 minutes.

Primary Carnitine deficiency

The usual dose of Levocarnitine injection is 100 mg per kg of body weight per day. This will be given over 3-4 doses.

Secondary Carnitine deficiency in haemodialysis patients (dialysis of the blood)

A dose of 20 mg per kg of body weight should be given in the same way as above at the end of each dialysis session (assuming three sessions per week). The treatment should last at least three months, which is the time required to restore normal muscle levels of free carnitine. If

significant benefit is seen following the first course of treatment, ongoing therapy using 1g per day of Levocarnitine oral solution may be used. On the day of dialysis, Levocarnitine oral solution should be taken at the end of the dialysis session. If the patient is elderly, they do not need special precautions or modifications to Levocarnitine dosage.

For further information on how Levocarnitine Injection is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

What benefits of Levocarnitine Injection have been shown in studies?

Levocarnitine Injection is a generic medicine that fulfils criteria meaning that no additional studies are required. Levocarnitine Injection has been considered a generic medicine of the reference medicine based on a comparison of their physical and chemical characteristics.

What are the possible side effects of Levocarnitine Injection?

For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at <https://yellowcard.mhra.gov.uk> or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Levocarnitine Injection is a generic medicine, its benefits and possible side effects are considered to be the same as for the reference medicine.

Why was Levocarnitine Injection approved?

It was concluded that Levocarnitine Injection has been shown to be comparable to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Levocarnitine Injection?

As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Levocarnitine Injection. The RMP details the important risks of Levocarnitine Injection, how these risks can be minimised, any uncertainties about Levocarnitine Injection (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Levocarnitine Injection.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Levocarnitine Injection are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Levocarnitine Injection

A marketing authorisation for Levocarnitine Injection was granted in the United Kingdom (UK) on 15 April 2025.

The full PAR for Levocarnitine Injection follows this summary.

This summary was last updated in June 2025.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Levocarnitine 1 g Solution for Injection (PL 46052/0003) could be approved.

The product is approved for the following indications:

- For the treatment of primary and secondary carnitine deficiency in adults, children, infants and neonates.
- Secondary carnitine deficiency in haemodialysis patients.
Secondary carnitine deficiency should be suspected in long-term haemodialysis patients who have the following conditions:
 1. Severe and persistent muscle cramps and/or hypotensive episodes during dialysis.
 2. Lack of energy causing a significant negative effect on the quality of life.
 3. Skeletal muscle weakness and/or myopathy.
 4. Cardiomyopathy.
 5. Anaemia of uraemia unresponsive to or requiring large doses of erythropoietin.
 6. Muscle mass loss caused by malnutrition.

The active substance is levocarnitine. Levocarnitine is present as a natural constituent in animal tissues, micro-organisms and plants. In man the physiological metabolic requirements are met both by the consumption of food containing carnitine and the endogenous synthesis in the liver and kidneys from lysine with methionine serving as the methyl donor. Only the L-isomer is biologically active, playing an essential role in lipid metabolism as well as in the metabolism of ketone bodies as branched chain amino acids.

Levocarnitine as a factor is necessary in the transport of long-chain fatty acids into the mitochondria - facilitating the oxidation of fatty acids rather than their incorporation into triglycerides. By releasing CoA from its thioesters, through the action of CoA; carnitine acetyl transferase, levocarnitine also enhances the metabolic flux in the Krebs's cycle; with the same mechanism it stimulates the activity of pyruvate dehydrogenase and in skeletal muscle, the oxidation of branched-chain amino acids. Levocarnitine is thus involved, directly or indirectly in several pathways so that its availability should be an important factor controlling not only the oxidative utilisation of fatty acids and ketone bodies but also that of glucose and some amino acids.

This application was approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as a generic medicine of a suitable originator medicinal product, Carnitor 1 g Solution for Injection, that has been licensed for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the application is for a generic medicinal product of a suitable reference product.

A biowaiver was submitted with this application, which was accepted. No bioequivalence study was required and no new clinical studies were provided with this application.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A marketing authorisation for Levocarnitine Injection was granted in the United Kingdom (UK) on 15 April 2025.

II QUALITY ASPECTS

II.1 Introduction

This product consists of a solution for injection. Each 1ml of solution contains 200 mg of levocarnitine. Each 5 ml of solution contains 1 g of levocarnitine.

In addition to levocarnitine, this product also contains the excipients hydrochloric acid 10% (for pH adjustment) and water for injection.

The finished product is packaged in clear, type I glass ampoules, of 5 ml capacity. The ampoules are packed in a white plastic case with capacity to hold 5 ampoules in a carton box.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

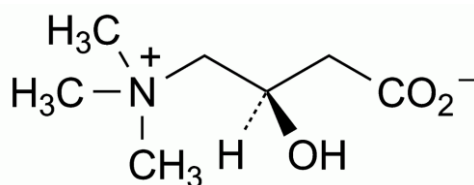
II.2 ACTIVE SUBSTANCE

rINN: Levocarnitine

Chemical Name: (3R)-3-Hydroxy-4-(trimethylazaniumyl)butanoate

Molecular Formula: $C_7H_{15}NO_3$

Chemical Structure:



Molecular Weight: 161.2

Appearance: White or almost white, crystalline powder or colourless crystals, hygroscopic

Solubility: Freely soluble in water, soluble in warm ethanol (96 per cent), practically insoluble in acetone.

Levocarnitine is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development was provided.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis were provided for all excipients.

No excipients of animal or human origin are used in the final products.

This product does not contain or consist of genetically modified organisms (GMO).

Manufacture of the product

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 3 years, with the storage conditions 'This medicinal product does not require any special temperature storage conditions. Keep the ampoules in the outer carton in order to protect from light', is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The grant of a marketing authorisation was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction

As the pharmacodynamic, pharmacokinetic and toxicological properties of levocarnitine are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology

No new pharmacology data were provided, and none were required for this application.

III.3 Pharmacokinetics

No new pharmacokinetic data were provided, and none were required for this application.

III.4 Toxicology

No new toxicology data were provided, and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment

A suitable justification was provided for non-submission of an Environmental Risk Assessment. As the application is for a generic version of an already authorised product, an increase in environmental exposure is not anticipated following approval of the marketing authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects

The grant of a marketing authorisation was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

The clinical pharmacology, efficacy and safety of levocarnitine is well-known. According to the regulatory requirements, the applicant has provided a suitable biowaiver and a bioequivalence study is not required for this product. An overview based on a literature review is, thus, satisfactory.

IV.2 Pharmacokinetics

No new pharmacokinetic data were submitted for this application and none were required.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted for this application and none were required.

IV.4 Clinical efficacy

No new efficacy data were submitted with this application and none were required.

IV.5 Clinical safety

No new safety data were submitted with this application and none were required. The safety profile for this product is considered to be the same as Carnitor 1 g Solution for Injection.

IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects

The grant of a marketing authorisation was recommended for this application.

V USER CONSULTATION

A text version of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation. The applicant has committed to submitting a PIL mock prior to placing the product on the market.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with levocarnitine is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference product.

In accordance with legal requirements, the current approved UK version of the SmPC and PIL for this product are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	Scope	Product information affected	Date of grant	Outcome	Assessment report attached Y/N