

Inestom® LEVOCARNITINE

Oral solution single dose 1g/10ml
Solution for injection 1g / 5ml amp.

NAME OF THE MEDICINAL PRODUCT: Inestom® COMPOSITION:

- **Active ingredient:** Levocarnitine (L-carnitine).
- **Excipients for the Oral Solution:** Malic acid, Methylparaben, Propylparaben, Sodium saccharin dihydrate, Orange flavour, Purified water.
- **Excipients for the Solution for injection:** Hydrochloric Acid 10%, Water for Injection.

DRUG FORMULATION:

Oral Solution single dose and Solution for injection.

CONCENTRATION OF THE ACTIVE INGREDIENT:

1. **Oral solution single dose:** Each vial contains Levocarnitine 1g.
2. **Solution for injection:** Each ampoule contains Levocarnitine 1g.

PRESENTATION:

1. **Oral Solution single dose:** Box containing 10 vials of 10 ml each placed in a carton box.
2. **Solution for injection:** Carton Box containing a plastic case with 5 ampoules of 5 ml each.

THERAPEUTIC CATEGORY:

Amino Acids and derivatives (Alimentary tract & metabolism products).

MARKETING AUTHORISATION HOLDER:

HELP S.A. - 10 Valaoritou str., GR 144 52 Metamorfosi, Attiki, Greece,
Tel.: +30 210 2815353.

MANUFACTURED BY:

HELP S.A. – Pedini Ioanninon, GR 455 00 Ioannina, Greece.

WHAT YOU SHOULD KNOW ABOUT THE MEDICINE YOUR DOCTOR HAS PRESCRIBED

INDICATIONS:

1. Oral Solution single dose

Indicated for the treatment of primary and secondary carnitine deficiency in adults and children over 12 years of age.

2. Solution for injection

Indicated 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.

CONTRAINDICATIONS:

Inestom® is contraindicated in patients with known hypersensitivity to any of the constituents of the product.

SPECIAL PRECAUTIONS AND WARNINGS DURING USE:

While improving glucose utilisation, the administration of L-carnitine to diabetic patients receiving either insulin or hypoglycaemic oral treatment may result in hypoglycaemia. Plasma glucose levels in these subjects must be monitored regularly in order to adjust the hypoglycaemic treatment immediately, if required. The safety and efficacy of oral L-carnitine has not been evaluated in patients with renal insufficiency. Chronic administration of high doses of oral L-carnitine in

patients with severely compromised renal function or in end stage renal disease (ESRD) patients on dialysis may result in an accumulation of the potentially toxic metabolites, trimethylamine (TMA) and trimethylamine-N-oxide (TMAO), since these metabolites are usually excreted in the urine. This situation has not been observed following intravenous administration of L-carnitine.

PREGNANCY AND LACTATION:

Reproductive studies were performed in rats and rabbits. There was no evidence of a teratogenic effect in either species. In the rabbit but not in the rat, there was a statistically insignificant greater number of post-implantation losses at the highest dose tested (600mg/kg daily) as compared with control animals. The significance of these findings in man is unknown.

There is no experience of use in pregnant patients with primary systemic carnitine deficiency.

Taking into account the serious consequences in a pregnant woman who has primary systemic carnitine deficiency stopping treatment, the risk to the mother of discontinuing treatment seems greater than the theoretical risk to the foetus if treatment is continued. Levocarnitine is a normal component of human milk. Use of levocarnitine supplementation in nursing mothers has not been studied.

INTERACTION WITH OTHER DRUGS OR SUBSTANCES:

Very rarely, an increase in the International Normalized Ratio (INR) has been reported in patients receiving L-carnitine and coumarin anticoagulants at the same time. The INR – or other appropriate coagulation markers – should be checked weekly until stabilized and then monthly in patients receiving such anticoagulants with L-carnitine.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

None known.

UNDESIRABLE EFFECTS:

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very rare side effects (affecting less than 1 in 10,000 patients):

- Vomiting
- Nausea
- Diarrhoea
- Abdominal pain
- Body odour
- Increase in International Normalised Ratio*

* Very rarely an increase in the International Normalised Ratio (INR) has been reported in patients taking L-carnitine and coumarin anticoagulants (acenocoumarol and warfarin) at the same time - see paragraph "SPECIAL PRECAUTIONS AND WARNINGS DURING USE" and "INTERACTION WITH OTHER DRUGS OR SUBSTANCES".

Mild myasthenia-like disorders have been reported in uremic patients. Tolerance to the drug should be checked during the first week of administration and after each dose increase.

Cases of convulsions have been described in patients with or without a history of convulsive episodes receiving oral L-carnitine or intravenous L-carnitine.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

DOSAGE AND ADMINISTRATION:

• ORAL SOLUTION: FOR ORAL ADMINISTRATION ONLY

The Oral Solution can be drunk directly or diluted further in water or fruit juices.

Adults and children over 12 years of age:

It is advisable to monitor therapy by measuring free and acyl carnitine levels in both plasma and urine.

The management of inborn errors of metabolism:

The dosage required depends upon the specific inborn error of metabolism concerned and the severity of presentation at the time of treatment. However, the following can be considered as a general guide. An oral dosage of up to 200mg/kg/day in divided doses (2 to 4) is recommended for chronic use in some disorders, with lower doses sufficing in other conditions. If clinical and biochemical symptoms do not improve, the dose may be increased on a short-term basis. Higher doses of up to 400mg/kg/day may be necessary in acute metabolic decompensation or the i.v. route may be required.

Haemodialysis - maintenance therapy:

If significant clinical benefit has been gained by a first course of intravenous **Inestom**[®] then maintenance therapy can be considered using 1g per day of **Inestom**[®] orally. On the day of the dialysis oral **Inestom**[®] has to be administered at the end of the session.

• SOLUTION FOR INJECTION: INTRAVENOUS USE

Adults, children, infants and neonates:

For slow intravenous administration over 2-3 minutes.

It is advisable to monitor therapy by measuring free and acyl carnitine levels in both plasma and urine.

The management of inborn errors of metabolism:

The dosage required depends upon the specific inborn error of metabolism concerned and the severity of presentation at the time of treatment. However, the following can be considered as a general guide.

In acute decompensation, dosages of up to 100 mg/kg/day in 3-4 divided doses are recommended.

Higher doses have been used although an increase in adverse events, primarily diarrhoea, may occur.

Secondary carnitine deficiency in haemodialysis patients:

It is strongly recommended that, before initiating therapy with **Inestom**[®], plasma carnitine is measured. Secondary carnitine deficiency is suggested by a plasma ratio of acyl to free carnitine of greater than 0.4 and/or when free carnitine concentrations are lower than 20 µmol/litre. A dose of 20mg per kg should be administered as an intravenous bolus at the end of each dialysis session (assuming three sessions per week). The duration of intravenous treatment should be at least three months, which is the time usually required to restore normal muscle levels of free carnitine. The overall response should be assessed by monitoring plasma acyl

to free carnitine levels and by evaluating the patient's symptoms. When carnitine supplementation has been stopped there will be a progressive decline in carnitine levels. The need for a repeat course of therapy can be assessed by plasma carnitine assays at regular intervals and by monitoring the patient's symptoms.

Haemodialysis - maintenance therapy:

If significant clinical benefit has been gained by the first course of intravenous **Inestom®** then maintenance therapy can be considered using 1g per day of **Inestom®** orally. On the day of the dialysis, oral **Inestom®** has to be administered at the end of the session.

MANAGEMENT OF OVERDOSAGE:

There have been no toxic effects from L-carnitine overdosage. Large doses of L-Carnitine can cause diarrhoea. Stop taking the medicine and contact your doctor.

EXPIRY DATE OF THIS PRODUCT:

Do not use the product after the date written in the inside and external packaging.

STORAGE INSTRUCTIONS FOR THIS PRODUCT:

Do not store above 25°C. Protect from light.

DATE OF LAST REVISION OF THIS DATA SHEET:

SEPTEMBER 2022.

INFORMATION ON THE RATIONAL USE OF MEDICINES

- This medicine has been prescribed by your doctor only for your specific medical problem.
- You should not give it to other individuals or use it for any other condition, without previous consultation with your doctor.
- If during your therapy there is any problem with the medicine, you should notify your doctor or pharmacist.
- If you have any questions about the information concerning the drug you are taking or if you need more information about your medical problem, do not hesitate to ask your doctor or pharmacist.
- To be effective and safe the prescribed drug should be used according to the

instructions given to you.

- For your health and safety you must read carefully all the information regarding the drug you have been prescribed.
- Do not store medicines in bathroom cupboards; heat and moisture may alter them and make them hazardous to your health.
- Do not keep medicines you do not need any more, or those that have expired.
- For greater safety keep all medicines out of the reach of children.

THIS MEDICINE IS TO BE TAKEN ONLY BY DOCTOR'S PRESCRIPTION.