For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

CARNISURE™

(Levocarnitine)

COMPOSITION:

CARNISURE™ - 500
Each film-coated tablet contains: Levocarnitine USP ..... 500 mg

COLOUR: Titanium Dioxide IP

CARNISURE™ SYRUP
Each 5 ml contains: Levocarnitine USP ..... 500 mg
in a syrup base ..... q.s.

COLOUR: Carmoisine

CARNISURE™ INJECTION
Each 5 ml ampoule contains: Levocarnitine USP ..... 1 g
Excipients ..... q.s.
Hydrochloric Acid IP
Water for injection IP

CLINICAL PHARMACOLOGY:

CARNISURE™ (Levocarnitine) is a naturally occuring substance required in mammalian energy metabolism. It has been shown to facilitate long-chain fatty acid entry into cellular mitochondria, therefore delivering substrate for oxidation & subsequent energy production. Primary systemic carnitine deficiency is characterised by low plasma, RBC and/or tissue levels.

Secondary Levocarnitine deficiency can be a consequence of inborn error of metabolism. **CARNISURE™** may alleviate the metabolic abnormalities of patients with inborn errors that result in accumulation of toxic organic acids. The resulting impairment in fatty acid metabolism manifests itself as elevated triglycerides & free fatty acids, diminished ketogenesis & lipid infilteration of liver & muscle.

In patients with uraemia who undergo long-term intermittent haemodialysis. It has been shown that serum concentrations of L-Carnitine decreased by 30-90% below those of normal controls. This is possibly because of reduced L-Carnitine synthesis in the kidney & the loss of nutrient into the dialysate. Decreased muscle concentrations of L-Carnitine may contribute to the reported muscle symptoms of cramps & asthenia that may accompany dialysis.

PHARMACOKINETICS:

L-Carnitine is absorbed from the intestine & peak plasma concentration of free carnitine of 48.5 & 69.5 micromoles/lit. have been attained 3.5-5 hours following single oral 500 mg & 2 g doses respectively.

In the bioavailability study of 15 healthy adult males, **CARNISURE™** Injection administered as a slow 3 minutes bolus intravenous injection at a dose of 20 mg/kg, approx, 76% of free L-Carnitine is eliminated in the urine. The mean distribution half-life was 0.585 hrs. & the mean apparent terminal elimination half-life was 17.4 hrs. following a single intravenous dose. The majority of body carnitine is excreted in the urine & faeces.

INDICATIONS & USAGE

CARNISURE™ - 500 Tablets / CARNISURE™ - Syrup are indicated in the treatment of primary systemic carnitine deficiency. Further **CARNISURE™** is useful in the treatment of cardiomyopathy, skeletal myopathy, ischaemic cardiopathy, long-term haemodialysis, oligospermia, hereditary disorders affecting fatty acid metabolism, acute neonatal crisis, failure to thrive, in preterm infants and along with valproate therapy.

CARNISURE™ Injection is indicated in the treatment of secondary carnitine deficiency e.g. in haemodialysis patients.

CONTRAINDICATIONS: None Known

WARNINGS: None

PRECAUTIONS:

Mutagenicity tests performed in Salmonella typhimurium, Saccharomyces cerevisiae and Schizosaccharomyces pombe do not indicate that **CARNISURE™** (Levocarnitine) is mutagenic. Long term animal studies have not been conducted to evaluate the carcinogenicity of the compound.
Administration of high doses of the oral formulations of Levocarnitine for long periods of time is not recommended in patients with severely compromised renal function or in ESRD patients on dialysis due to the fact that major metabolites formed following oral administration (trimethylamine (TMA) and trimethylamine-N-oxide (TMAO) will accumulate since they can not be efficiently removed by the kidneys. This does not occur to the same extent following intravenous administration. TMA accumulation is not desirable since it increases the amount of nitrogenous waste to be removed in the dialysis procedure. In addition, increased levels of TMA in dialysis patients have been reported to be associated with possible neurophysiologic effects. Also, the inefficient removal of TMA may result in the development of 'fishy odor' syndrome. Only the intravenous form of Levocarnitine is indicated for use in ESRD patients on haemodialysis.

USAGE IN PREGNANCY:

Studies have been performed in rats and rabbits using parenteral administration at doses equivalent on a mg/kg basis to the suggested oral adult dosage and have revealed no harm to the foetus due to Levocarnitine. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

NURSING MOTHERS:

Levocarnitine is a normal component of human milk.
Levocarnitine supplementation in nursing mothers has not been studied.

ADVERSE EFFECTS:

Various mild gastrointestinal complaints have been reported during the long-term administration of oral Levocarnitine, these include transient nausea and vomiting, abdominal cramps and diarrhoea.

OVERDOSAGE:

There have been no reports of toxicity from Levocarnitine overdosage. The oral LD_{50} of Levocarnitine in mice is 19.2 g/ kg. Levocarnitine may cause diarrhoea. Overdosage should be treated with supportive care.

DRUG INTERACTIONS:

None known

DOSAGE & ADMINISTRATION:

CARNISURE™ - 500 Tablets / CARNISURE™ - Syrup
Adults: The recommended oral dosage for adults is 990 mg two or three times a day and increased slowly, while assessing tolerance & therapeutic response. With the oral solution the recommended dose is 10-30 mg/kg for a 50 kg subject. Dosage should start at 1 gm/day (10 ml/day) and can be increased depending on the therapeutic response.

Infants & Children: The dose recommended is 50-100 mg/kg/day, and be increased slowly to a maximum of 3 gm/day (30 ml/day).

CARNISURE™ Injection
CARNISURE™ Injection is administered intravenously. The recommended dose is 20-40 mg/kg given as a slow 2-3 minute bolus injection or by infusion.

PRESENTATION:

CARNISURE™ - 500 : Blister of 10 Tablets

CARNISURE™ SYRUP : 30 ml bottle with a dropper

CARNISURE™ INJECTION: Tray of 5 x 5 ml Ampoules.

Marketed by:

TORRENT PHARMACEUTICALS LTD.
Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA