Could Your End Stage Renal Disease Patient be Carnitine Deficient?

CARNITOR®
levocarnitine
injection USP 1 g/5 mL

Indication

CARNITOR® (levocarnitine) Injection is indicated for the prevention and treatment of carnitine deficiency in patients with end stage renal disease who are undergoing dialysis.

Please see complete Important Safety Information on page 2 of this brochure or please see Full Prescribing Information at www.carnitor.com.

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Indication

CARNITOR® (levocarnitine) Injection is indicated for the prevention and treatment of carnitine deficiency in patients with end stage renal disease who are undergoing dialysis.

CARNITOR® (levocarnitine) Injection is also indicated for the acute and chronic treatment of patients with an inborn error of metabolism which results in secondary carnitine deficiency.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, laryngeal edema, and bronchospasm have been reported following CARNITOR® administration, mostly in patients with end stage renal disease who are undergoing dialysis. Some reactions occurred within minutes after intravenous administration of CARNITOR®.

If a severe hypersensitivity reaction occurs, discontinue CARNITOR® treatment and initiate appropriate medical treatment. Consider the risks and benefits of re-administering CARNITOR® to individual patients following a severe reaction. If the decision is made to re-administer the product, monitor patients for a reoccurrence of signs and symptoms of a severe hypersensitivity reaction.

Drug Interactions

Reports of INR increase with the use of warfarin have been observed. It is recommended that INR levels be monitored in patients on warfarin therapy after the initiation of treatment with levocarnitine or after dose adjustments.

ADVERSE REACTIONS

Neurologic Reactions: Seizures have been reported to occur in patients, with or without pre-existing seizure activity, receiving either oral or intravenous levocarnitine. In patients with pre-existing seizure activity, an increase in seizure frequency and/or severity has been reported.

Gastrointestinal Reactions: Transient nausea and vomiting have been observed. Less frequent adverse reactions are body odor, nausea, and gastritis. An incidence for these reactions is difficult to estimate due to the confounding effects of the underlying pathology.

Hypersensitivity reactions: Anaphylaxis, laryngeal edema and bronchospasm (see Warnings and Precautions).

To report SUSPECTED ADVERSE REACTIONS, contact Leadiant Biosciences, Inc. at 1-888-393-4584 or by email at drugsafety@leadiant.com or contact the FDA at 1-800-FDA-1088 or www.fda.gov/safety/medwatch.

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It's important to understand why your ESRD patient may be carnitine deficient.

The importance of carnitine

Carnitine is a naturally occurring amino acid derivative and transports molecules essential for fatty acid and energy metabolism. It facilitates long-chain fatty acid transportation into the mitochondria, which is necessary for β-oxidation and chemical energy production (ATP) the body needs to function.[1]

The importance of testing for carnitine deficiency in ESRD patients

End-stage renal disease (ESRD) patients on maintenance hemodialysis often have low plasma carnitine concentrations and an increased ratio of acylcarnitine or carnitine.[1]

Three causes of carnitine deficiency for patients on hemodialysis are currently recognized:

Carnitine removal during the dialysis process

- The decrease of carnitine in the body during dialysis occurs due to[1,2,3]:
  - Carnitine is a low molecular weight compound that is highly and efficiently removed in the dialysis process.

Dietary restrictions

- 75% of the body's need for carnitine is met by diet
- Foods that contain primary sources of carnitine, such as red meat and dairy products, are often restricted in the diet of patients on hemodialysis

Impaired synthesis

- 25% of the body's need for carnitine is met by biosynthesis
- The kidney and the liver are primary sources of carnitine synthesis
- Patients on hemodialysis often have impaired kidney or liver functions that may impair carnitine synthesis

Total carnitine levels have been reported to decrease as much as 70% with a single hemodialysis treatment.[4]

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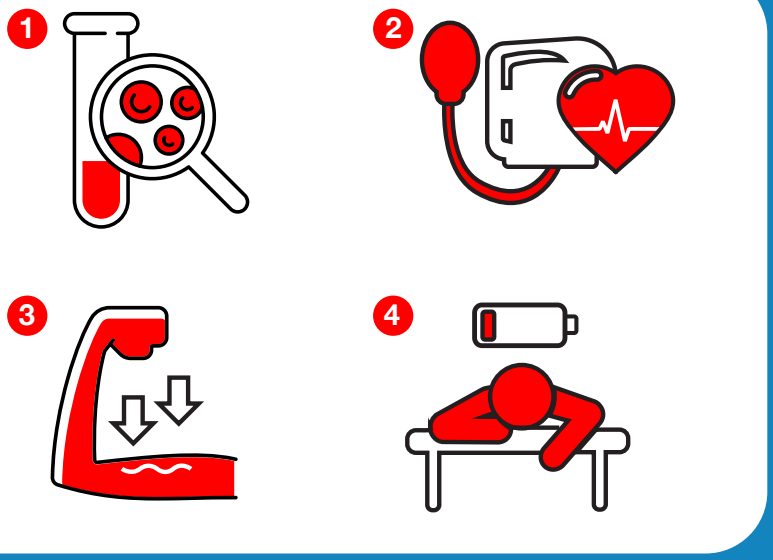

Symptoms of carnitine deficiency

Do your patients with ESRD on hemodialysis exhibit any of these symptoms?[5]

1. Anemia
2. Intradialytic hypotension
3. Muscle weakness
4. Malaise

Testing for carnitine deficiency

It's important to test patients with possible symptoms for carnitine deficiency. Dialysis-related carnitine deficiency is defined as a pre-dialysis (trough) plasma concentration of free carnitine < 40 µmol/L. [1]

CARNITOR dosing in ESRD patients on hemodialysis

- The recommended starting dose is 10-20 mg/kg dry body weight as a slow 2-3 minute bolus injection into the venous return line after each dialysis session. [1]
- Initiation of therapy may be prompted by trough (pre-dialysis) plasma levocarnitine concentrations that are below normal (40-50 µmol/L).
- Dose adjustments should be guided by trough (pre-dialysis) levocarnitine concentrations, and downward dose adjustments (e.g. to 5 mg/kg after dialysis) may be made as early as the third or fourth week of therapy.[1]

Indication

CARNITOR® (levocarnitine) Injection is indicated for the prevention and treatment of carnitine deficiency in patients with end stage renal disease who are undergoing dialysis.

Consider testing your patients for carnitine deficiency to see if Carnitor injection may be right for them.

NCA - Levocarnitine for End Stage Renal Disease

(CAG-00077N) - Decision Memo (CMS)[4]

This decision memorandum announces our intention to issue a national coverage determination for the use of levocarnitine in ESRD patients. Intravenous levocarnitine will only be covered in ESRD patients who have been on dialysis for a minimum of three months for one of the following indications:

Patients must have documented carnitine deficiency, as noted by a pre-dialysis (trough) plasma free carnitine level < 40 micromol/L, along with signs and symptoms of:

1. Erythropoietin-resistant anemia (persistent hematocrit < 30% with treatment) that has not responded to standard erythropoietin dosage with iron replacement, and for which other causes have been investigated and adequately treated; or
2. Hypotension on hemodialysis that requires intervention and is unresponsive to all usual management measures (e.g., fluid management) and interferes with dialysis. Such episodes of hypotension must have occurred during at least 2 dialysis treatments in a 30-day period.

Continued use of levocarnitine will not be covered if improvement has not been demonstrated within 6 months of initiation of treatment.

All other indications for levocarnitine are noncovered in the ESRD population.

Levocarnitine Injection CMS Coverage Checklist

Patient Name:_____ **Date:**_____

Carnitine injection checklist derived from CMS guidelines

Identification of erythropoietin-resistant anemia (ERA)

1. Has the patient been on dialysis for a minimum of 3 months? Yes☐ No☐

2. Does the patient have a persistent hematocrit <30 percent? Yes☐ No☐

3. Has the patient not responded to standard erythropoietin dosage (that which is considered clinically appropriate to treat the particular patient)? Yes☐ No☐

4. Is the patient on iron therapy? Yes☐ No☐

5. Have other causes of ERA been investigated and adequately treated? Yes☐ No☐

6. Does the patient have a documented carnitine deficiency, defined as a plasma free carnitine level <40 micromol/L (determined by a professionally accepted method as recognized in current literature)? Yes☐ No☐

If the answers to the above questions are "Yes," the patient may qualify for CMS coverage for ERA

Identification of intradialytic hypotension (IDH)

1. Has the patient been on dialysis for a minimum of 3 months? Yes☐ No☐

2. Does the patient have episodes of hypotension on Hemodialysis that interfere with the delivery of the intended dialysis despite application of usual measures deemed appropriate (e.g., fluid management)? Yes☐ No☐

3. Have such episodes of hypotension occurred during at least 2 dialysis treatments in a 30-day period? Yes☐ No☐

4. Does the patient have a documented carnitine deficiency, defined as a plasma free carnitine level <40 micromol/L (determined by a professionally accepted method as recognized in current literature)? Yes☐ No☐

If the answers to the above questions are "Yes," the patient may qualify for CMS coverage for IDH

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To order Carnitor, please go through your preferred wholesaler or contact our customer service line at 888-276-2217.

For information about Patient Assistance Programs, please contact our Rare Care Team at 877-534-9627.

Please refer to Carnitor® Injection Full Prescribing Information.

Please see End-Stage Renal Disease (ESRD) CMS Guidelines here.

References:

1. Carnitor® (levocarnitine) Injection Package Insert. Date of Issue: 04/18 VPI-15.
2. Hoppel C. The role of carnitine in normal and altered fatty acid metabolism. Am J Kidney Dis. 2003 Apr;41(4 Suppl 4):S4-12.
3. Evans AM, Faull R, Fornasini G, Lemanowicz EF, Longo A, Pace S, Nation RL. Pharmacokinetics of L-carnitine in patients with end-stage renal disease undergoing long-term hemodialysis. Clin Pharmacol Ther. 2000 Sep;68(3):238.
4. Extract from CMS levocarnitine for End Stage Renal Disease 2023.
5. Eknoyan, G, Latos DL, Lindberg J, Willis K. Practice recommendations for the use of L-carnitine in dialysis related carnitine disorder. Am J Kidney Dis. 2003;41(4):868–876.