

NATURAL HEALTH PRODUCT

L-CARNITINE

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient.

Notes

- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms and/or statements are synonymous. Either term or statement may be selected by the applicant.

Date

December 18, 2018

Proper name(s), Common name(s), Source material(s)

Table 1. Proper name(s), Common name(s), Source material(s)

Proper name(s)	Common name(s)	Source material(s)
		Common name(s)
<ul style="list-style-type: none"> ▶ (L-3-Carboxy-2-hydroxypropyl)trimethylammonium hydroxide, inner salt ▶ (R)-3-carboxy-2-hydroxy-N,N,N-trimethyl-1-propanaminium hydroxide, inner salt ▶ L-Carnitine ▶ Levocarnitine 	<ul style="list-style-type: none"> ▶ L-Carnitine ▶ Levocarnitine 	<ul style="list-style-type: none"> ▶ L-Carnitine tartrate ▶ L-Carnitine fumarate

References: Proper name: O'Neil 2013, USP 35; Common name: O'Neil 2013, USP 35; Source material: EFSA 2012, Wall et al. 2011, EFSA 2003.

Route of administration

Oral

Dosage form(s)

This monograph excludes foods or food-like dosage forms as indicated in the Compendium of Monographs Guidance Document.

Acceptable dosage forms for the age category listed in this monograph and specified route of administration are indicated in the Compendium of Monographs Guidance Document.

Use(s) or Purpose(s)

L-CARNITINE FUMARATE; L-CARNITINE TARTRATE

- ▶ Antioxidant (Cao et al. 2011; Arkadeb et al. 2008; Gomez-Amores et al. 2007).
- ▶ Workout support/supplement (Wall et al. 2011; Cha et al. 2001; Arenas et al. 1994; Huertas et al. 1992; Arenas et al. 1991; Vecchiet et al. 1990; Marconi et al. 1985).

L-CARNITINE TARTRATE

- ▶ Aids in the muscle recovery process by reducing muscle tissue damage associated with a resistance training regimen (Ho et al. 2010; Spiering et al. 2008; Spiering et al. 2007; Kraemer et al. 2006; Kramer et al. 2003; Volek et al. 2002).
- ▶ Helps support muscle tissue repair in individuals involved in resistance training (Ho et al. 2010; Spiering et al. 2008; Spiering et al. 2007; Kraemer et al. 2006; Kramer et al. 2003; Volek et al. 2002).
- ▶ Helps improve physical performance when used in conjunction with a training regimen (Wall et al. 2011; Cha et al. 2001; Arenas et al. 1994; Huertas et al. 1992; Arenas et al. 1991; Vecchiet et al. 1990; Marconi et al. 1985).
- ▶ Helps delay fatigue during physical activity (Cha et al. 2011; Wall et al. 2011; Karahan et al. 2010).
- ▶ Helps support fat metabolism (Stephens et al. 2007; Karlic and Lohninger 2004; Müller et al. 2002).
- ▶ Helps support fat oxidation (Wall et al. 2011; Stephens et al. 2007; Wutzke and Lorenz 2004; Müller et al. 2002).

The following combined use(s) or purpose(s) is/are also acceptable (L-Carnitine tartrate only):

- ▶ Helps support fat metabolism and oxidation (Wall et al. 2011; Stephens et al. 2007; Karlic and Lohninger 2004; Wutzke and Lorenz 2004; Müller et al. 2002).
- ▶ Workout support/supplement that helps improve physical performance when used in conjunction with a training regimen (Wall et al. 2011; Cha et al. 2001; Arenas et al. 1994; Huertas et al. 1992; Arenas et al. 1991; Vecchiet et al. 1990; Marconi et al. 1985).
- ▶ Workout support/supplement that delays fatigue during physical activity (Wall et al. 2011; Stephens et al. 2007; Karlic and Lohninger 2004; Müller et al. 2002; Cha et al. 2001; Arenas et al. 1994; Huertas et al. 1992; Arenas et al. 1991; Vecchiet et al. 1990; Marconi et al. 1985).



Dose(s)

Subpopulation(s)

Adults 18 years and older

Quantity(ies)

Antioxidant

Not to exceed 4 grams of L-carnitine per day and 2 grams per single dose (Karlic and Lohninger 2004; Benvenha et al. 2001; Ahmet et al. 2000; Harper et al. 1988).

Muscle recovery, Muscle tissue repair, Workout support/supplement

1 - 4 grams of L-carnitine, per day; Not to exceed 2 grams per single dose (Ho et al. 2010; Spiering et al. 2008; Spiering et al. 2007; Kraemer et al. 2006; Kramer et al. 2003; Volek et al. 2002; Benvenha et al. 2001; Ahmet et al. 2000; Harper et al. 1988).

Physical performance, Fatigue, Workout support/supplement combined with Physical performance/Fatigue

2 - 4 grams of L-carnitine, per day; Not to exceed 2 grams per single dose (Wall et al. 2011; Benvenha et al. 2001; Cha et al. 2001; Ahmet et al. 2000; Arenas et al. 1994; Huertas et al. 1992; Arenas et al. 1991; Vecchiet et al. 1990; Harper et al. 1988; Marconi et al. 1985).

Fat metabolism, Fat oxidation

3 - 4 grams of L-carnitine, per day; Not to exceed 2 grams per single dose (Wall et al. 2011; Stephens et al. 2007; Karlic and Lohninger 2004; Wutzke and Lorenz 2004; Müller et al. 2002).

Direction(s) for use

Muscle recovery, Muscle tissue repair, Workout support/supplement, Physical performance, Fatigue

Take 2-4 hours prior to exercise (Harper et al. 1988).

Duration(s) of use

No statement required.



Risk information

Caution(s) and warning(s)

Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are pregnant, breastfeeding or have a seizure disorder (CPS 2008).

Contraindication(s)

No statement required.

Known adverse reaction(s)

No statement required.

Non-medicinal ingredients

Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database.

Storage conditions

No statement required.

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide.
- ▶ The medicinal ingredient must comply with the requirements outlined in the NHPID.

References cited

Ahmet U, Abdurrahman K, Sait B, Ahmet E, Salih D, Mendane S, Ates Y, Fatih B, Necmettin K, Kemal D. L-carnitine therapy in non-alcoholic steatohepatitis. Turkish Journal of Pediatrics 2000;11(3):196-201.

Arenas J, Huertas R, Campos Y, Diaz AE, Villalon JM, Vilas E. Effect of L-carnitine on the pyruvate dehydrogenase complex and carnitine palmitoyl transferase activities in muscle of endurance athletes. FEBS Letters 1994;341:91-93.



Arenas J, Ricoy JR, Encinas AR, Pola P, D'Iddio S, Zeviani M, Didonato S, Corsi M. Carnitine in muscle, serum, and urine of nonprofessional athletes: Effects of physical exercise, training, and L-carnitine administration. *Journal of Muscle & Nerve* 1991;14:598-604.

Arkadeb D, Koushik R, Vijay K. Singh, Vats P, Singh SN, Singh SB. L-carnitine supplementation attenuates intermittent hypoxia-induced oxidative stress and delays muscle fatigue in rats. *Experimental Physiology* 2008;93:1139-1146.

Benvenga S, Ruggeri RM, Russo A, Lapa D, Campenni A, Trimarchi F. Usefulness of Lcarnitine, a naturally occurring peripheral antagonist of thyroid hormone action, in iatrogenic hyperthyroidism: a randomized, double-blind, placebo-controlled clinical trial. *Journal of Clinical Endocrinology and Metabolism* 2001;86(8):3579-3594.

Cao Y, Qu HJ, Li P, Wang CB, Wang LX, Han ZW. Single dose administration of L-carnitine improves antioxidant activities in healthy subjects. *The Tohoku Journal of Experimental Medicine* 2011;224(3):209-213.

Cha Y-S, Choi S-K, Suh H, Lee S-N, Cho D, Lim K. Effects of carnitine coingested caffeine on carnitine metabolism endurance capacity in athletes. *Journal of Nutritional Science and Vitaminology* 2001;47:378-384.

CPS 2008: Compendium of Pharmaceuticals and Specialties: The Canadian Drug Reference for Health Professionals. Ottawa (ON): Canadian Pharmacists Association;2008.

EFSA 2012: SCIENTIFIC OPINION: Scientific Opinion on the safety and efficacy of L-carnitine and L-carnitine L-tartrate as feed additives for all animal species based on a dossier submitted by Lonza Benelux BV. European Food Safety Authority (EFSA), Parma, Italy. [Accessed 2018 September 21]. Available from: <https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/j.efsa.2012.2676>

EFSA 2003: Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) on a request from the Commission related to LCarnitine-L-tartrate for use in foods for particular nutritional uses (adopted on 3 November 2003 by written procedure). European Food Safety Authority (EFSA). Parma. Italy. [Accessed 2018 September 21]. Available from: http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/19.pdf

Gomez-Amores L, Mate A, Miguel-Carrosco J, Jimenez L, Jos A, Camean AM, Revilla E, Santa-Maria C, Vasquez C. L-carnitine attenuates oxidative stress in hypertensive rats. *The Journal of Nutritional Biochemistry* 2007;18(8):533-540.

Harper P, Elwin CE, Cederblad G. Pharmacokinetics of intravenous and oral bolus doses of Lcarnitine in healthy subjects. *European Journal of Clinical Pharmacology* 1988;35:555-562.



Ho JY, Kraemer WJ, Volek JS, Fragala MS, Thomas GA, Dunn-Lewis C, Coday M, Hakkinen K, Maresh CM. L-carnitine L-tartrate supplementation favorably affects biochemical markers of recovery from physical exertion in middle-aged men and women. *Metabolism Clinical and Experimental Journal* 2010;59:1190-1199.

Huertas R, Campos Y, Diaz E, Esteban J, Vechietto L, Montanari G, D'Iddio S, Corsi M, Arenas J. Respiratory chain enzymes in muscle of endurance athletes: Effect of L-carnitine. *Biochemical and biophysical research communications* 1992;188(1):102-107.

Karahan M, Coksevim B, Artis S. The effect of L-carnitine supplementation on 1500 m running performance. *Science, Movement and Health Journal* 2010;10(2):504-507.

Karlic H, Lohninger A. Supplementation of L-carnitine in athletes: Does it make sense? *Journal of Nutrition* 2004;20:709-715.

Kraemer WJ, Spiering BA, Volek JS, Ratamess NA, Sharman MJ, Rubin MR, French DN, Silvestre R, Hatfield DL, Van Heest JC, Vingren JL, Judelson DA, Deschenes MR, Maresh CM. Androgenic responses to resistance exercise: Effects of feeding and L-Carnitine. *Official Journal of the American College of Sports Medicine* 2006;1288-1296.

Kraemer WJ, Volek JS, French DN, Rubin MR, Sharman MJ, Gomez AL, Ratamess NA, Newton RU, Jemiolo B, Craig BW, Hakkinen K. The effects of L-carnitine L-tartrate supplementation on hormonal responses to resistance exercise and recovery. *Journal of Strength and Conditioning Research* 2003;17(3):455-462.

Marconi C, Sassi G, Carpinelli A, Cerretelli P. Effect of L-carnitine loading on the aerobic and anaerobic performance of endurance athletes. *European Journal of Applied Physiology* 1985;54:131-135.

Müller DM, Seim H, Kiess W, Löster H, Richter T. Effects of oral L-carnitine supplementation on in vivo long-chain fatty acid oxidation in healthy adults. *Journal of Metabolism* 2002;51(11):1389-1391.

O'Neil MJ, Smith A, Heckelman PE, Budavari S, editors. *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals*, 15th edition. Whitehouse Station (NJ): Merck & Co., Inc., 2013.

Spiering BA, Kraemer WJ, Hatfield DL, Vingren JL, Fragala MS, Ho J-Y, Thomas GA, Hakkinen K, Volek JS. Effects of L-carnitine L-tartrate supplementation on muscle oxygenation responses to resistance exercise. *Journal of Strength and Conditioning Research* 2008;22(4):1130-1135.

Spiering BA, Kraemer WJ, Vingren JL, Hatfield DL, Fragala MS, Ho J-Y, Maresh CM, Anderson JM, Volek JS. Responses of criterion variables to different supplemental doses of L-carnitine L-tartrate. *Journal of Strength and Conditioning Research* 2007;21:259-264.



Stephens FB, Constantin-Teodosiu D, Greenhaff PL. New insights concerning the role of carnitine in the regulation of fuel metabolism in skeletal muscle. *Journal of Physiology* 2007;581.2:431-444.

USP 35: United States Pharmacopeia and the National Formulary (USP 35 - NF 30). Rockville (MD): The United States Pharmacopeial Convention; 2012.

Vecchiet L, Di Lisa F, Pieralisi G, Ripari P, Menabo R, Giamberardino MA, Siliprandi N. Influence of L-carnitine administration on maximal physical exercise. *European Journal of Applied Physiology* 1990;61:486-490.

Volek JS, Kraemer WJ, Rubin MR, Gomez AL, Ratamess NA, Gaynor P. L-carnitine L-tartrate supplementation favorably affects markers of recovery from exercise stress. *American Journal of Physiology-Endocrinology and Metabolism* 2002;282:E474-E482.

Wall BT, Stephens FB, Constantin-Teodosiu D, Marimuthu K, Macdonald IA, Greenhaff PL. Chronic oral ingestion of L-carnitine and carbohydrate increases muscle carnitine content and alters muscle fuel metabolism during exercise in humans. *The Journal of Physiology* 2011;589.4:963-973.

Wutzke KD, Lorenz H. The effect of L-carnitine on fat oxidation, protein turnover; and body composition in slightly overweight subjects. *Metabolism* 2004;53(8):1002-1006.

References reviewed

Brass EP, Hiatt WR. The role of carnitine and carnitine supplementation during exercise in man in individuals with special needs. *Journal of the American College Nutrition* 1998;17(3):207-215.

Broad EM, Maughan RJ, Galloway S. Carbohydrate, protein, and fat metabolism during exercise after oral carnitine supplementation in humans. *International Journal of Sport Nutrition and Exercise Metabolism* 2008;18:567-584.

Colombani P, Wenk C, Kunz I, Kraehenbul S, Kuhnt M, Arnold M, Frey-Rindova P, Frey W, Langhans W. Effects of L-carnitine supplementation on physical performance and energy metabolism of endurance-trained athletes: a double-blind crossover field study. *European Journal of Applied Physiology* 1996;73:434-439.

Flanagan JL, Simmons PA, Vehige J, Willcox M, Garrett Q. Role in carnitine in disease. *Nutrition and Metabolism* 2010;7(30):1-14.

Hathcock JN, Shao A. Risk assessment for carnitine. *Regulatory Toxicology and Pharmacology Journal* 2006;46(1):23-28.



Malaguarnera M, Cammalleri L, Gargante MP, Vacante M, Colonna V, Motta M. L-carnitine treatment reduces severity of physical and mental fatigue and increases cognitive functions in centenarians : a randomized and controlled clinical trial. *The American Journal of Clinical Nutrition* 2007;86:1738-1744.

Rubin MR, Volek JS, Gomez AL, Ratamess NA, French DN, Sharman MJ, Kraemer WJ. Safety measures of L-carnitine L-tartrate supplementation in healthy men. *Journal of Strength and Conditioning Research* 2001;15(4):486-490.

Stuessi C, Hofer P, Meir C, Boutellier U. L-carnitine and the recovery from exhaustive endurance exercise: a randomized, double-blind, placebo-controlled trial. *European Journal of Applied Physiology* 2005;95:431-435.

Tabibi H, Hakeshzadeh M, Malakoutian T. Effects of L-carnitine supplement on serum amyloid A and vascular inflammation markers in hemodialysis patients: a randomized controlled trial. *Journal of Renal Nutrition* 2011;21(6):485-491.

Wyss V, Ganzit GP, Rienzi A. Effects of L-carnitine administration on VO_{2max} and the aerobicanaerobic threshold in normoxia and acute hypoxia. *European Journal of Applied Physiology* 1990;60:1-6.