CONCENTRATED FORMULA

MV-ONE PLUS

Multivitamin Antioxidant Nutraceutical

MV-ONE PLUS is a novel antioxidative nutraceutical especially formulated for patients with chronic kidney disease (CKD). MV-ONE PLUS has been designed as a supplement to address vitamin D deficiency and chronic inflammation, both commonly associated with CKD. It should not be considered as a general multivitamin supplement to replace the water-soluble vitamins lost during dialysis.

- Designed to be taken at facility only 3 times per week. Greater convenience for patients & caregivers and compliance for providers
- Specifically designed to address oxidative stress and provide high levels of Vitamin D supplementation
- Contains powerful anti-oxidants Vitamin E and Alpha-Lipoic Acid to boost immunity
- Tested and evaluated in large clinical studies

The components found in MV-ONE PLUS have been reported to reduce erythropoietin-stimulating agent (ESA) and intravenous vitamin D analogues.

One tablet of MV-ONE PLUS contains

- 4,000 IU cholecalciferol
- 600 mg gamma-tocopherol
- 800 mg alpha-lipoic acid

One tablet per day, or two tablets everyday per dialysis day or directed by your physician

To order MV-ONE PLUS, call this TOLL-FREE number 1-855-MY MVONE/1-855-696-8663

or

Order MV-ONE PLUS online at www.MV-ONE.com or send an email to: customersupport@MV-ONE.com

Additionally, clinics and dialysis facilities may order through Metro Medical Customer Service.
Call Toll Free at 1-800-768-2002
website: www.metromedical.com

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Medically speaking . . .

Measurements of the biomarkers of C-reactive protein indicate that chronic inflammation is a serious and systemic condition that is found in up to 65% of people who have CKD
(Stenvinkel et al. 1999).

Inflammation and oxidative stress are mediated by a complicated series of interactions between cytokines,which cause common symptoms such as fatigue and flu-like aches and pains that lead to a poorer quality of life. When inflammation is left untreated, it increases morbidity and mortality. In patients with CKD, oxidative stress has been linked to several surrogate markers
of atherosclerosis such as endothelial dysfunction and intima-media thickness.

Patients with CKD have a higher risk of cardiovascular disease, which can be further increased by inflammation (Krasniak et al. 2007, Dursun et al. 2008).

The factors that play a role range from hemodialysis itself, catheter placement, infections, and ischemia. Goldstein et al. (2009)has suggested that the placement of catheters is associated with inflammation and is a risk factor for increased morbidity, independent of infection.

The Dialysis Outcomes and Practice Patterns Study (DOPPS) group reported that in an analysis of 2,500 patients on dialysis, those with inflammation clearly had higher requirements for ESAs. The authors concluded that intervention could lead to a lower ESA dose (Smith et al. 2010). Several investigators have postulated that inflammation inhibits erythropoiesis because of the reduced availability of iron and the shorter life span of red blood cells. More recently, it has been suggested that protein-energy wasting and inflammation (malnutrition-inflammation complex) were independent and significant markers of poor responsiveness to ESAs (Rattanasompattikul et al. 2013).

Further, it has been reported that vitamin D deficiency can cause an inflammatory cytokine cascade that results in an increase in hepcidin synthesis and functional iron deficiency, which can lead to reduced responsiveness to ESAs (Icardi et al. 2013).

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Practically Speaking . . .

The continued decrease in the prospective payment scheme for Medicare patients and changes in the Food and Drug Administration's label on the use of ESAs in CKD suggests that giving the lowest possible ESA dose while avoiding transfusions has created a clinical environment that makes it difficult to achieve and maintain good clinical outcomes.

Nutraceuticals are foods or food products that provide health benefits and are different from dietary supplementsin that there is often a scientific rationale suggesting clinical benefits. A number of commonly used vitamins, like those in MV-ONE PLUS, have been identified as having anti-inflammatory properties, and this has raised the exciting possibility that it might be possible to cost-effectively treat inflammation in people with CKD. Further well-designed, randomized, controlled clinical trials are required to establish thefull potential of antioxidants to make a substantive difference in clinical practice. MV-ONE PLUS, a specially designed nutraceutical, has been shown to be useful in addressing some of the clinical burden resulting from inflammation and oxidative stress, which are key contributors to poor clinical outcomes.

The Scientific Rationale for MV-ONE PLUS. . .

Despite the lack of large epidemiological studies, it is generally accepted that oxidative stress is a nontraditional risk factor that increases with the rate of progression of CKD. The Cochran Collaboration recently published a meta-analysis on antioxidative therapies that reported evidence of beneficial effects in reducing the risk of CKD but not an overall reduction in cardiovascular outcomes (Jun et al. 2012).

On the basis of some promising findings, the use of antioxidants has recently been suggested as a possible therapeutic approach in patients with CKD (Del Vecchio et al. 2011). The safety of the long-term use of antioxidant supplements in patients on dialysis has been studied, and no detrimental effects have been reported (Delanaye et al. 2013).

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Although only limited data on MV-ONE PLUS are available, there is a larger body of evidence on its individual constituents. To date, only one study has been published on the use of MV-ONE PLUS in patients on dialysis (Sharma et al. 2011). However, a larger 12-month clinical study using MV-ONE PLUS in several hundred patients on dialysis was conducted in the United States. MV-ONE PLUS was reported to be well tolerated (data on file). Patients who have continued taking it have not reported any new adverse affects with long term use (private communications).

MV-ONE PLUS contains vitamins whose antioxidative effects are supported by the largest body of scientific evidence.

- Vitamin E (gamma-tocopherol)
- Vitamin E is the most potent fat-soluble antioxidant known in nature.
- Reported benefits include
- Lower levels of low-density lipoproteins (LDLs)
- Fewer episodes of muscle cramps in patients on dialysis
- Less oxidative stress when commonly used stents are coated with vitamin E

Vitamin E works by inhibiting LDL oxidation and limiting cellular response to oxidized LDL. It also reduces levels of LDLs, which researchers have suggested are involved in atherogenesis and are present at high concentrations in patients on hemodialysis (Mafra et al. 2009).

Vitamin E is important in the proper functioning of muscle cells, and vitamin E supplementation has been studied as a treatment for muscle cramps in patients on dialysis (El-Hennawy et al. 2010).

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The findings of a series of small, randomized double-blind studies in patients on hemodialysis have suggested that oral vitamin E supplementation could improve ESA responsiveness and reduce the oxidative stress induced by intravenous iron (Cristol et al. 1997, Roob et al. 2000).

Himmelfarb et al. (2003) reported data showing that the administration of gamma-tocopherol reduced systemic markers of inflammation in patients on hemodialysis. Compared with placebo, a vitamin E combination was reported to reduce intermedial wall thickening and improve brachial artery flow-mediated dilatation (Nanayakkara et al.2007).

Vitamin D (cholecalciferol D3)
Vitamin D is fat-soluble and can be obtained from food or synthesized from sunlight, especially from chole-calciferol, which is eventually converted to the biologically active form of vitamin D in the kidneys. The use of vitamin D supplements is becoming increasingly common in patients with CKD.

The results of vitamin D deficiency are well documented and include

- Increased oxidative stress in patients with CKD
- Bone and mineral diseases in patients with CKD
- Impaired cognitive function in older people
- Increased cardiovascular disease and hypertension

Diabetic complications
Vitamin D3 is converted to the active form—1, 25(OH)2D—in the kidney. While the consequences of vitamin D deficiency have been well documented, its role in inflammation in patients on dialysis in less well known (Ferreira et al. 2008, Mucsi et al. 2010). However, the role of vitamin D continues to evolve, and it has recently been postulated that in addition to its role in the endocrine system, there is a synergistic and beneficial effect on the paracrine and autocrine systems that could help attenuate chronic inflammation (Armas et al. 2011). Other studies have shown that patients have experienced no difficulties taking up to 2,800 IU/day of cholecalciferol on a short-term basis. Matias et al. (2010) reported that oral cholecalciferol supplementation reduced both vitamin D and ESA use. Moreover, when 158 patients on dialysis were followed for one year, their paricalcitol dose decreased from 7.2 ug/week to 6.0 ug/week on average, a statistically significant reduction drop.

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A decrease in the use of phosphate binders was reported as well. ESA use declined from 0.042 to 0.033 ug/kg/week per g/dL of hemoglobin, also a statistically significant drop.

The reason for this decline could have been a decrease in inflammation. The study showed that C-reactive protein levels dropped by nearly 50%, which was statistically significant too (Matias et al. 2010). Similar findings have been reported with vitamin D supplementation in patients on dialysis (Saab et al. 2007, Bucharles et al. 2012).

The supplemental use of vitamin D3 is becoming more common in patients with CKD, and more clinical benefits, such as an improvement in proteinuria, are being reported (Paul et al. 2013). The safety of the long-term use of vitamin D3 has been evaluated, and no adverse effects have been reported (Delanaye et al. 2013).

Alpha-lipoic acid

Alpha-lipoic acid (ALA) is a naturally occurring fatty acid that cells require to produce energy by glucose conversion. It has the unique property of being both fat and water soluble. ALA's antioxidative properties appear to work by recycling other antioxidants such as vitamin C and glutathione once they have been used up naturally by cells.

Reported uses include

- Help in cases of peripheral neuropathy (because of ALA's reported ability to enter all parts of the nerve)
- Prevention of free radical damage (which helps brain function and counteracts the effects of aging)

In a randomized placebo-controlled study, Chang et al. (2007) reported a statistically significant change in asymmetric dimethylarginine (ADMA) levels. ADMA is an endogenous inhibitor of nitric oxide synthase and a predictor of cardiovascular outcomes in patients with end-stage renal disease. Endothelial dysfunction caused by the reduced availability of nitric oxide precedes the development of atherosclerosis. ALA could potentially have a beneficial effect in part by decreasing the level of ADMA in plasma. More recently, similar results were replicated using the same doses of ALA in patients on hemodialysis (Khabbazi et al. 2012).

ALA has also been reported to attenuate lipopolysaccharide-induced kidney injury in animal models by the suppression of apoptosis, inflammation, and renal tubular dysfunction (Suh et al. 2013).

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