

Position Statement:

Use of Replavite/Renavite in Adult Chronic Kidney Disease Patients

For the purpose of this discussion chronic kidney disease (CKD) refers to non-dialysis patients.

It is the position of the British Columbia Renal Dietitians Practice Group (RPG) that Replavite/Renavite renal vitamin formulations are appropriate for use in people with CKD.

Consideration should be given to involving a CKD Renal Dietitian to assess a patient's overall nutritional requirements and indication for vitamin supplementation.

Background

The British Columbia Provincial Renal Agency Pharmacy and Formulary Committee requested guidelines from RPG on appropriate use of renal vitamin supplements in the CKD population. This review was completed to assure safe practice in light of the April 2010 Journal of the American Medical Association (JAMA) report with high dose B vitamins. ¹

Rationale

CKD patients are at high risk of developing nutrient deficiencies. This is due, in part, to dysgeusia, anorexia and diet restrictions which limit high biological value protein foods such as meat, poultry, fish, eggs and dairy products including milk, cheese and yogurt. If potassium and/or phosphorus restrictions are necessary then the intake of fruits and vegetables, whole grains, legumes, nuts and seeds must also be limited which, in turn, limits the intake of micronutrients.

Specifically:

- Protein foods are a source of B vitamins such as thiamin, riboflavin, niacin, vitamin B6, vitamin B12 as well as iron and zinc.
- Fruits and vegetables are rich sources of vitamin C, folate and fibre.
- Whole grains, legumes, nuts and seeds also provide B vitamins, fibre, iron, zinc and magnesium.
- Dairy products are a source of calcium and vitamin D.

Restriction of these foods can lead to nutrient deficiencies and, therefore, appropriate vitamin supplementation is important to maintain a patient's nutritional status and to minimize risk of illness and infection.

Rationale

Nutritional analysis of three meal plans ([Appendix 1](#)) tailored for CKD patients revealed that those consuming less than 1500 kcal per day do not meet the recommended intakes for the following vitamins and minerals:

- vitamins B1 (thiamin), B2 (riboflavin), B3 (niacin), B6 (pyridoxine)
- folic acid and pantothenic acid
- iron, magnesium and zinc
- calcium and vitamin D

B vitamins play an instrumental role as coenzymes in many cellular metabolic pathways in the body.

The following table outlines symptoms associated with a deficiency of each vitamin.

Vitamin	Symptoms of Deficiency ²
B1 (Thiamin)	Weakness, loss of appetite, irritability, nervous tingling throughout the body, poor arm and leg coordination and deep muscle pain in the calves (Beriberi)
B2 (Riboflavin)	Early symptoms: inflammation of the mouth and tongue
B3 (Niacin)	Reddened inflammation of the skin, diarrhea, dementia and hallucinations (Pellagra)
B6 (Pyridoxine)	Adverse affect on overall cell synthesis (involved in over 50 enzymes which metabolize protein, fat and carbohydrate)
Folate	Inflammation of the tongue, diarrhea, poor growth, mental confusion and problems in nerve function (Megaloblastic anemia)
Vitamin B12	Weakness, sore tongue, back pain, apathy and tingling in the extremities (Pernicious anemia)

It is also important to note that the three meal plans analyzed were found to provide vitamin C in excess of the Recommended Dietary Allowances (RDAs) but below the tolerable upper intake levels (ULs).

Vitamin C is a water-soluble vitamin that should not be supplemented in large doses due to the possibility of ascorbic acid metabolizing to oxalate.^{3,4} High plasma oxalate concentrations could lead to precipitation in the kidney, possibly causing further renal impairment.

There is a wide selection of over-the-counter (OTC) vitamin preparations available, but many provide higher doses of vitamins A, B and C than are recommended for this patient population. Similarly, the doses of folic acid, vitamin B12 and vitamin B6 in the JAMA report¹ were also much greater than those included in Replavite/Renavite. In addition, many OTC multivitamins contain minerals such as potassium and phosphorus which are not indicated for most CKD patients. Replavite/Renavite do contain vitamin C; however, when compared to many OTC multivitamins and B vitamin formulations, they more closely reflect the overall daily vitamin needs of CKD patients.

Appendix 2 highlights the Dietary Reference Intakes (DRIs) for adult males and females. It also outlines the daily supplemental amounts in Replavite/Renavite and the specific amounts of vitamins recommended for CKD patients. Accurate data on the biotin content of foods is not available and is therefore not included⁶.

Replavite/Renavite (originally formulated to replace hemodialysis losses)

- Vitamin B1 Thiamin (1.5 mg)
- Vitamin B2 Riboflavin (1.7 mg)
- Vitamin B3 Niacinamide (20 mg)
- Vitamin B6 Pyridoxine (10 mg)
- Folic Acid (1 mg)
- Vitamin B12 (6 mcg)
- Biotin (300 mcg)
- and Vitamin C (100 mg)

Based on current knowledge of nutritional needs of CKD patients, potential nutrient deficiencies associated with disease progression, renal dietary modifications and analysis of three CKD meal plans, it is recommended that the following “Indications for Use” be considered when prescribing Replavite/Renavite for CKD patients.

Indications for Use of Replavite/Renavite for CKD Patients

- Eating less than 50% of meals and/or consuming less than 1500 kcal/day
- Chronically poor or erratic eating habits
- Reduced appetite, nausea, vomiting, taste changes or food aversions
- Undesirable weight loss

“Renal diets are arguably the most restrictive for any patient group and many of the restrictions contradict current recommendations for healthy eating.^{5”} CKD diets frequently contain less than recommended DRIs for certain water-soluble vitamins. In addition, “CKD appears to alter the absorption, metabolism or activity of some vitamins.^{3”}

Summary Opinions of This Committee:

1. A referral to a CKD Dietitian should be considered for diet review, nutrition assessment and for specific recommendations regarding vitamins or nutrition supplements.
2. **Replavite/Renavite supplements are appropriate and safe for many CKD patients with inadequate nutritional intake. However, they may not address all of the nutrient deficiencies of some CKD patients. Therefore, in the future, consideration should be given to reformulation of Replavite/Renavite to meet these needs.**

References:

1. House, A., Eliasziw, M., Cattran, D. et al.: Effect of B-Vitamin Therapy on Progression of Diabetic Nephropathy. JAMA. 303(16): 1603-1609, 2010.
2. Wardlaw, G., Insel, P.: Perspectives in Nutrition. 2nd ed. Saint Louis, MO: Mosby 1993.
3. Mitch, W. and Ikizler, T.: Handbook of Nutrition and the Kidney. 6th ed. Philadelphia, PA: Lippincott William and Wilkins, 2010.
4. Broad, D., Carolan, E., Damji, G., Larratt-Smith, R., McKerracher, M., Roet, M. eds.: CAND Essential Guide for Renal Dietitians. 3rd ed. Nanaimo, Canada: Dietitians of Canada, 2010.
5. Hollingdale, R., Sutton, D., Hark, K.: Facilitating Dietary Change in Renal Disease: Investigating Patients' Perspective. J Ren Care 34: 136-142, 2008.
6. Staggs, C.G., Sealy, W.M., McCabe B.J., Teague, A.M., Mock, D.M.: Determination Of The Biotin Content Of Select Foods Using Accurate And Sensitive Hplc/Avidin Binding. Food Compost Anal. Dec:17(6): 767-776, 2004.
7. Kopple, Joel D., Massry, Shaul G. eds.: Nutritional Management of Renal Disease. 2nd ed. Philadelphia, PA: Lippincott Williams and Wilkins, 2003, Chapter 23: pp 379-414.

Appendix 1: CKD Meal Plans

Small Appetites	Moderate Appetites	Large Appetites
BREAKFAST		
1 poached egg 1 slice of white or 60% whole wheat bread 1 tsp margarine ½ cup berries 1 cup tea 1 tsp sugar ½ cup cranberry juice	1 poached egg 2 slices white or 60% whole wheat bread 2 tsp margarine 1 tsp honey ½ cup blueberries 1 cup herbal tea ½ cup cranberry juice	1 poached egg 2 slices white or 60% whole wheat bread 3 tsp margarine 1 cup berries 1 cup coffee 1 tsp sugar 1 tbsp light coffee cream
LUNCH		
Turkey sandwich: 30 g (1oz) turkey 1 tbsp cream cheese 1 oz cucumber 1 slice white or 60% whole wheat bread ½ cup red pepper sticks ½ cup rice milk	Turkey sandwich: 30 g (1 oz) turkey 1 tbsp cream cheese 2 slices white or 60% whole wheat bread ½ cup cucumber ½ cup red pepper sticks ½ cup rice milk	Turkey sandwich: 30 g (1 oz) turkey 1 tbsp cream cheese 2 slices white or 60% whole wheat bread 1 cup red pepper sticks 1 cup skim milk
DINNER		
56 g Salmon fillet baked with lemon and dill (1 tsp) ½ cup steamed white rice ½ cup green beans boiled 1 tsp margarine 1 cup lettuce 2 tsp Italian dressing	75 g Salmon fillet baked with lemon and dill (1 tsp) ¾ cup steamed white rice ½ cup green beans boiled ½ cup lettuce 1 tbsp Italian dressing ½ dinner roll 1 tsp margarine 1 cup 2% milk	85 g Salmon fillet baked with lemon and dill (1 tsp) 1 cup steamed white rice 3 tsp margarine ½ cup green beans boiled 1 cup lettuce 1 tbsp Italian dressing 1 dinner roll 1 cup rice milk
SNACK		
½ cup pears canned in juice ¾ cup warm 2% milk honey (2 tsp)	½ cup canned pears in juice 1 cup rice milk 2 gingersnap cookies	1 cup pears canned in juice 2 gingersnap cookies
TOTAL DAILY		
Calories: ~ 1200 Protein: 42.5 g Potassium: ~ 1500 mg Phosphorous: ~ 650 mg	Calories: ~ 1500 Protein: 62 g Potassium: ~ 1800 mg Phosphorous: ~ 900 mg	Calories: ~ 1900 Protein: 71 g Potassium: ~ 2300 mg Phosphorous: ~ 1100 mg

01 September 2010

Nutrient analysis completed using www.nutritiondata.com , The Food Processor software and www.dietitians.ca

Appendix 2: Meal Plan Analysis and Vitamin/Mineral Comparison

	Small Appetite	Moderate Appetite	Large Appetite	DRIs Males >19 yrs RDA	DRIs Females >19 yrs RDA	Recommended Intake (Kopple & Massry ⁷)	Replavite	Tolerable Upper Intake Levels (UL)
Macronutrients								
Calories (Kcal)	1157	1522	1866					
Protein (g)	42.5	62.3	71	56	46			
Fat (g)	47	46	63	ND ^g	ND ^g			
CHO (g)	116	217	259	130	130			
Fibre (g)	10	13	23	38/30 ^h	25/21 ^h			
Vitamins								
Vit A (IU)	5992	5491	8393	3000	2333	0	0	
Vit C (mg)	207	131	222	90	75	75-90	100	2000
Vit D (IU)	536.5	561	621.8	600/800 ^a	600/800	0	0	4000
Vit E (mg)	4.2	8.4	7	15	15	400-800 IU	0	
Vit B1 (Thiamin) (mg)	0.61	1	1.5	1.2	1.1	1.1-1.2	1.5	ND ^g
Vit B2 (Riboflavin) (mg)	1.1	1.6	1.9	1.3	1.1	1.1-1.3	1.7	ND ^g
Vit B3 (Niacin) (mg)	10	17	22	16	14	14-16	20	35
Vit B6 (Pyridoxine) (mg)	0.97	1.4	1.8	1.3/1.7 ^b	1.3/1.5 ^b	5	10	100
Vit B12 (mcg)	4	6	6	2.4	2.4	2.4	6	ND ^g
Folic Acid (mcg)	203	275	420	400	400	1000	1000	1000
Pantothenic Acid (mg)	3.14	3.8	5.8	5	5	5	10	ND ^g
Biotin (mcg)	no data	no data	no data	30	30		300	ND ^g
Minerals								
Calcium (mg)	453.72	660	721	1000/1200 ^c	1000/1200 ^c			
Iron (mg)	5.98	10	13	8	18/8 ^d			
Magnesium (mg)	114.56	168	217	400/420 ^e	310/320 ^e			
Phosphorus (mg)	647.93	913	1084	700	700			
Potassium (mg)	1506.98	1827	2310	4700	4700			
Zinc (mg)	3.42	5.6	7.4	11	8			

^a Vit D RDA: 600 IU/d (19-70 yrs), 800 IU/d (>70 yrs) for males and females

^b Vit B6: 1.3 mg/d (19-50 yrs), 1.7 mg/d (>51 yrs) males; 1.3 mg/d (19-50 yrs), 1.5 mg/d (>51 yrs) females

^c Calcium RDA: 1000 mg/d (19-50 yrs); 1200 mg/d (>51 yrs), for males and females

^d Iron: 18 mg/d (19-50 yrs); 8 mg/d (>51 yrs) for females

^e Magnesium: 400 mg/d (19-30 yrs), 420 mg/d (>31 yrs) for males; 310 mg/d (19-30 yrs), 320 mg/d (>31 yrs) for females

^f Sodium (Adequate Intakes): 1500 mg/d (19-50 yrs), 1300 mg/d (51-70 yrs), 1200 mg/d (>71 yrs) for males and females

^g ND: Not determined due to lack of suitable data, upper limits could not established. This does not mean that there is no potential for adverse effects resulting from high intakes.

^h Fibre (Adequate Intakes): 38 g/d (19-50 yrs), 30 g/d (>51 yrs) for males; 25 g/d (19-50 yrs); 25 g/d (19-50 yrs), 21 g/d (>51 yrs) for females

ⁱ RDA: Recommended Dietary Allowance