

Renal Nutrition Forum

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Feature Article

Eating Disorder Counseling in the Hemodialysis Population: A Perspective Summary

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This article has been approved for 2 CPE units. The online CPEU quiz and certificate of completion can be accessed in the Members Only section of the RPG web site via the My CPEU link. This CPE offering is available to current RPG members only and the expiration date is November 11, 2010.

Members without internet access can request a copy of the quiz and certificate of completion from Megan Sliwa, RNF Assistant Editor, Address: 425 North Front Street, Apartment 424, Columbus, Ohio 43215. Please provide your name, ADA number, and phone number.

Introduction

What are you afraid of? Maybe snakes, or like me, spiders, or maybe like my five year-old daughter, monsters in the closet or under the bed. Whatever that fear is, however irrational or rational it may be, it is real to you. Fear can cause panic-like symptoms, rapid or irregular heart rate, chest pain, difficulty breathing, dizziness and/or vertigo. Try to close your eyes and imagine facing your fear. You may feel all of those symptoms and as a response want to run

away. Without tapping into that kind of fear, it is very difficult to understand and treat a person with an eating disorder (ED). ED patients may deal with an intense fear of gaining weight along with attachment and dependency issues. They can often become overwhelmed by emotions such as rejection, guilt and shame (1).

On the other side of the coin, how do you handle stress, good or bad? When life doesn't happen the way we plan, outlets are needed for disappointments or stresses. Charles R. Swindoll wrote, "Life is 10% what happens to you and 90% how you react to it." While some pound emotions out with exercise or talk with friends, loved ones, or therapists, others choose the less beneficial route of alcohol, drugs and other legal but addictive substances. If you are unable to understand that side of the coin, whether it is from experience or empathetic experience, it is very difficult to understand and treat a person with an ED.

One of the disheartening manifestations and what sets an ED apart from other addictions is the moral view of accomplishment attached by the ED patient to achieving control over their body (2). Another difference that sets an ED apart from typical addictive behavior is that one can live without an addictive substance, but one cannot live without food.

Eating disorders are rare conditions in chronic renal failure. It has been estimated that only 0.8 cases per million occur, resulting in approximately 220 cases at any one time (3,4). Several case studies have been published on ED in end stage renal disease (ESRD) (5,6). It has been postulated that diet and fluid restrictions

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From the Editor's Desk

Stacey C. Phillips, RD

Editor



As I was contemplating the content of the next letter from the editor, I came across a quote of which you may possibly identify with as a dietitian. Margaret

Meade wrote, "Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it is the only thing that ever had." Approximately a year ago at this time, many of you working with renal patients in the outpatient setting were expected to understand the Centers for Medicare and Medicaid Services Interpretive Guidelines and Measurement Assessment Tool. While an immediate reaction was to feel overwhelmed by this task, think of where you are now, only a short twelve months later. Not only do you better understand the guidelines, but you are also able to use them as required in your documentation.

During this transitional period, it was also key to keep patient care a primary focus of your work. As dietitians it is our role to educate, identify needs and form relationships with individuals in an attempt to promote the option of a healthier lifestyle. Although our time with each individual may be short, depending on if they are a regular dialysis patient or having nutrition issues in an acute care setting, it is our responsibility to make as big of an impact as possible in the time that we are given. An ongoing goal of the Renal Dietitians Dietetics Practice Group (RPG) Editorial Board has been to continue to provide you with thought-provoking articles covering not only the changes within nephrology nutrition, but also in areas which may surface in your everyday practice.

This issue of the Forum offers several different topics which will hopefully be of interest. Within the renal population, it is not uncommon to see patients struggling with severe malnutrition and failure to thrive. The feature article, offering 2 CPEUs and written by Dana Kiker, MA, MS, RD, LD, gives insight into working with a difficult group of patients—those

suffering from renal disease and also an eating disorder such as anorexia nervosa or bulimia. Specific suggestions, supported by research, are provided in the nutritional assessment, as well as goals and treatment for these individuals. Additionally, the provided nutrition tool can help identify particular areas that should be considered when providing care to this population.

On a different note, mistakes are made in medicine, but in some instances such as our case study, not all errors are harmful. In the case study, "An Accidental Overdose of Ergocalciferol," author Ray Campbell, RD, LD, describes the profile of an individual who mistakenly was supplemented with a high dose of ergocalciferol in place of a moderate supplementation of cholecalciferol. While not an ideal situation, it is interesting to see how the body responds to the large dose of vitamin D during the accidental supplementation. Completion of reading this article and answering the quiz questions provides 1 additional CPEU.

As found in the last several editions of the *Renal Nutrition Forum*, the series Nephrology Nutrition and the Nutrition Care Process continues with an article, offered as 1 CPEU credit, entitled "Documenting Follow-Up Care After Initial Assessment." In a previous article, a case study was used to demonstrate the nutrition care process in an initial assessment note. Co-authors Maureen McCarthy, MPH, RD, CSR, LD and Denise Asbell, RD, LD revisit with the original case study patient and provide guidance through the process of completing accurate documentation during a reassessment period.

I hope that as you read through this edition of the Forum, ideas will form in your mind as to areas you would like to see more information about, or perhaps an area of which you would feel comfortable writing about in order for other readers to expand their knowledge. As a member of RPG, we encourage you to take the opportunity and voice your thoughts. Please feel free to contact any member of the editorial team with ideas or suggestions for future editions! ♦

Stacey C. Phillips, RD

Feature Article....

necessary for osteodystrophy management and healthy nutritional outcomes may potentially trigger ED in susceptible individuals (5). In caring for ESRD patients that present with low body weight and vomiting, organic causes must be ruled out. If no organic diagnosis is found, ED must be considered. In addition, patients with a history of an ED may present with ESRD secondary to the ED when no other reason for renal disease can be found. In the cases that have been documented, chronic hypokalemia was the prevalent link between ED and ESRD (7). Other potential causes may be chronic dehydration and a chronic low protein intake, causing a decrease in glomerular filtration rate (4).

The American Dietetic Association position on the nutrition intervention in the treatment of ED stipulates that the registered dietitian (RD) is integral in providing medical nutrition therapy as part of the interdisciplinary team, possibly consisting of a therapist, psychiatrist and primary care physician (8). The RD's role is to assess nutrition status, provide nutritional counseling, formulate dietary recommendations, and communicate with the interdisciplinary team. It is imperative that a person with or suspected of an ED be seen by a therapist, preferably one that has experience with ED patients. It is also key that the RD understands the boundaries and roles that each team member provides. Dietitians should help provide a collaborative approach with the patient and interdisciplinary team.

ED patients present with a wide array of common clinical features, which includes low motivation to change behaviors, denial of illness, perfectionism, inflexibility, mood intolerance, and core low self-esteem (9,10). ED patients are typically very untrusting, possibly due to intrusive, controlling or abusive past relationships, yet they have a strong inclination to seek approval (1,11). Dietitians are often viewed as an enemy or intruder. You may be greeted with severe hostility, anger, and hopelessness during consultations (1). The first step in successful treatment of an ED is when the individual admits that their behavior is a problem.

Nutritional Assessment

Nutritional assessment for an ED individual may be somewhat different from what you currently are utilizing as an assessment tool with renal patients. Attachment 1 is helpful in identifying specific areas for assessment when working with ED patients. The necessity of weighing a dialysis patient before and after treatment presents some difficulty amongst ED patients. Discussing the weighing of a patient backwards with your interdisciplinary team, so that their weight cannot be seen, is one option. This may be necessary to cultivate adherence with the goal of edema-free weight restoration and to assist in the prevention of stress and triggers for the patient associated with weight changes. This

method of weighing may also prevent purposeful fluid overload to misrepresent edema-free weight restoration.

Being knowledgeable about psychopharmacological medications utilized in the treatment of psychiatric disorders that additionally plague some ED patients is necessary. It is important to understand how dialysis may or may not affect the uptake of these medications. Many of the antidepressant medication interventions are ineffective in a starvation state due to the central nervous system depletion of serotonin, making substrate availability reuptake impossible (1). Other medications are highly protein bound and many ED patients are severely protein malnourished, making the medication useless.

Nutrition Goals

Nutritional goals include, but are certainly not limited to: normalizing eating patterns, restoration of weight and satiety signals, and assisting in the change of detrimental compensatory behaviors such as calorie counting, eating rituals, purging by vomiting, laxatives, diuretics, weight loss medications and supplements, amphetamines and/or strenuous exercise (12). The primary goal of promoting a healthy lifestyle must always be in focus and remain consistent. By assessing an ED patient and through communications with their therapist, you will find how to individualize the treatment plan. For instance, some ED patients that suffer with obsessive-compulsive disorder would not benefit from knowing ideal body weight ranges and quantitative caloric needs. A successful approach would be to look at oral intake. If intake is sub-optimal, counseling techniques should be focused on how and where to add foods that are considered "safe" but necessary, and cause the least amount of stress to the patient. The intent is that as therapy progresses less "safe" foods may be added or eating at regular intervals may be suggested. Some patients utilize alarms to assist in this behavior change. Others slowly add variety or eat a sufficient serving size. Engaging in social situations that include food and people may also be helpful. For others, moving away from regimented behaviors such as grocery shopping, food preparation and consumption is beneficial. One behavioral change at a time is encouraged, allowing the patient to make the decision on which behavior to focus. The end result will be a more normal and healthy relationship with food. As treatment progresses, constant reassurance may be necessary to quell the intense fear of gaining weight by reminding the patient that the focus is their health.

Nutrition Counseling

Nutritional counseling may include education about false beliefs regarding food and supplements. It may also include

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Attachment 1

Nutrition Assessment Considerations for ED Patients

Name: _____ Age: _____ Ht: _____ Wt: _____

Therapist: _____ Physician: _____ Psychiatrist: _____

Name: _____

Address: _____

Phone: _____

Have you ever worked with a dietitian/nutritionist? No _____ If Yes, whom _____

Current medications: _____

Vitamin/mineral/herbal supplements: _____

How often do you weigh yourself? _____

Are you on birth control pills? Yes _____ No _____

Approximate date of last menstrual cycle? _____

Has your cycle ever ceased? Yes _____ at what weight _____ No _____

Do you experience problems with:

- a) Constipation? No _____ Yes _____ Describe: _____
- b) Diarrhea? No _____ Yes _____ Describe: _____
- c) Nausea? No _____ Yes _____ Describe: _____
- d) Feeling Bloated? No _____ Yes _____ Describe: _____

Circle any of the following that describes your eating patterns:

- a) Eat 3 meals each day i) Binge followed by diuretics
- b) Eat a 'normal' amount of food j) Binge followed by exercise
- c) Eat 3 meals with snacks k) Vomit without binging
- d) Restrict intake of food l) Use laxatives
- e) Binge without purging m) Use diuretics
- f) Binge followed by vomiting n) Exercise excessively
- g) Binge followed by restriction
- h) Binge followed by laxatives

Current Exercise Program: _____

Past History with Exercise: _____

Eating Pattern History: _____

24-Hour Recall: _____

Purgings

Vomiting	How _____	How often _____	Use Ipecac Yes _____ No _____
Laxatives	Type _____	How many _____	How often _____
Enemas	Type _____	How many _____	How often _____
Diet pills	Type _____	How many _____	How often _____
Diuretics	Type _____	How many _____	How often _____
Amphetamines	Type _____	How many _____	How often _____

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Fluid intake: _____ Alcohol intake: _____ Caffeine: _____

Chew Gum: _____ Smoke: _____ Food allergies: _____

Food Intolerances: _____

Eating Out: _____

Additional Information:

Profession: _____ Place of Employment: _____

Marital Status: Single _____ Married _____ Divorced _____ Partnered _____

Children/Siblings: No _____ Yes _____ Name _____ Age _____
Name _____ Age _____ Name _____ Age _____ Name _____ Age _____

Living situation: _____

Who knows about current eating patterns:

Any members of family with eating disorders:

Any members of family alcohol/drug abusers:

Plan:

Recovery Weight Range: _____

Recovery Kcal Needs:

Women: $655.1 + (9.6 \times \text{wt}) + (1.8 \times \text{ht}) - (4.7 \times \text{age}) = \text{BEE} \times 1.3$

Men: $66.5 + (13.8 \times \text{wt}) + (5 \times \text{ht}) - (4.7 \times \text{age}) = \text{BEE} \times 1.3$

Weight in kilograms, Height in centimeters

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explaining differences between preferences versus elimination of foods or groups of foods based on false information for weight control and health. Counseling should include genuine care, support and the fostering of a trusting relationship that promotes dietary adherence. Enhancing motivation to change is key in effectively treating ED patients (13). Motivating an individual to change may require discussing the perceived benefits and actual detriments of continuing the unhealthy behavior. Promoting the potential beneficial outcomes of changing to a healthier behavior should also be included.

Counseling techniques derived from supportive therapy include: support, acceptance and affection toward the patient or client, emphasizing collaboration rather than lecturing, communicating a hopeful attitude that goals can be achieved, recognizing a patient's defenses and respecting their boundaries, focusing on a patient's strengths, and acknowledging and rewarding accomplishments (2). Supportive therapy utilizes conversational style with active listening; recognizing verbal and nonverbal cues, open questioning, reflection, praise, reassurance, advice, and self-disclosure on a session-by-session basis (2). This means not having a planned agenda before the session. You must have a willingness to be non-judgmental, compassionate, accepting and open to discussing any topic, but focus direction on nutritional parameters (1,14). It is important to remember not to entertain bargaining or pressure to change.

Motivational interviewing (MI) is a technique that was born from the trans-theoretical model for alcohol-dependence treatment. It is defined as "a client-centered, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence" (12). MI has since been found to be an effective intervention technique across a wide range of health-related behaviors (12). Utilizing this technique requires continual attention to the patient's motivation (12). As is true with supportive therapy techniques and cognitive behavioral techniques, collaboration is a core component (12). The guiding principles of MI include expressing empathy and acceptance, showing discrepancy between unhealthy and healthy behaviors by eliciting the patient's own reasons for beneficial change, not opposing resistance but seeing resistance as an opportunity to approach in a different way, and support of self-efficacy (12).

There remain a number of barriers to ED treatment including the clinical manifestations of the disease itself, the high cost of treatment, and the complex medical and psychological dual diagnoses such as depression, anxiety disorders, substance abuse (which can also affect appetite and weight), and personality disorders (1,10). For example, starvation symptoms present clinically very similarly to depressive symptoms (1). In-center hemodialysis

patients present communication difficulties for the RD due to the lack of privacy. It may be beneficial to meet with these individuals privately before or after treatment to foster a more trusting and open relationship.

Conclusion

As health professionals it is imperative that we do no harm, ensure safety, and provide timely and accurate nutritional information, care, and support to our patients. Discussions with patients should be two-way because patients are all individuals, and the goal may be different from our view based on individual morals and values. A recommendation for one person is not going to be applicable to everyone. It is critical to have an open mind to alternative understandings of situations (14). Education should not be limited to verbal modalities. Provision of written materials may assist an individual and their loved ones who process information differently. There is a lack of consensus clinically on the best modality of treatment (10), however, I hope that this article has provided some insight and helpful suggestions if an ED patient presents for nutritional intervention. In addition to ED patients, the aforementioned counseling techniques are likely to be beneficial with renal patients. We must understand as clinicians that ED is not a self-imposed disorder (10). Treatment adherence is only effective if a person is intrinsically motivated to change (11). If all else fails, you must be resigned to provide honest genuineness and focus on quality of life (1). ◆

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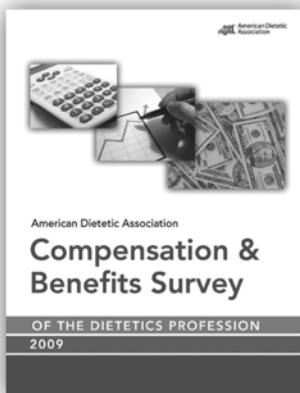
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Advances in Practice

Case Study: An Accidental Overdose of Ergocalciferol

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Introduction

This article examines the case study of an elderly gentleman on hemodialysis who mistakenly took high dose ergocalciferol daily over a two month period of time. This subsequently resulted in a 25(OH) vitamin D level of 307 ng/mL.

Case Study

DW is an 84 year old Caucasian male who was diagnosed with chronic kidney disease (CKD) Stage 5 and started maintenance hemodialysis in late November of 2008. He has a medical history of hypertension, dyslipidemia, type 2 diabetes mellitus (diagnosed 2007), prostate cancer with radiation therapy treatment, gout, dementia, and anemia secondary to CKD (treated with an erythropoiesis-stimulating agent). DW and his spouse are very interested in his medical care. He is generally compliant with his prescribed medications and specialized diet.

Upon admission to the dialysis unit, he underwent a nutrition evaluation by the dietitian. Though DW gardens as a hobby, he was deemed at risk for vitamin D deficiency due to limited sun exposure. While working outdoors, the patient wears full-length trousers and has only minor skin exposure to the sun. The dietitian recommended a start of over-the-counter (OTC) 1,000 IU cholecalciferol given twice daily by mouth. DW preferred the specific prescription information, regarding OTC vitamin D, be sent to his pharmacy, so it was faxed there on December 11, 2008.

This patient was hospitalized from January 22 to January 28, 2009 with a right lower lobe pneumonia. He was treated with antimicrobial therapy. No other major medical events occurred between mid-December 2008 and mid-February 2009.

On February 13, 2009, DW's 25(OH) vitamin D, vitamin D2, and vitamin D3 levels were tested. The total vitamin D level was 307 ng/mL with vitamin D2 of 307 ng/mL and vitamin D3 of < 4 ng/mL. The average level of 25(OH) vitamin D for patients in DW's dialysis unit was 33 ng/mL. It is inconceivable DW could have consumed enough vitamin D2 in his diet alone to achieve these high levels. Additionally, his sun exposure was sparse and would increase vitamin D3 levels, not vitamin D2 levels. After interviewing the patient, the dietitian contacted the head pharmacist at the patient's drug store. The pharmacist reviewed the patient's prescriptions and stated DW had incorrectly received 50,000 IU ergocalciferol tabs in place of the 1,000 IU cholecalciferol tabs.

DW had taken 2 tabs of ergocalciferol daily since mid-December of 2008. That is 100,000 IU ergocalciferol daily for almost two months. His vitamin D supplement was subsequently discontinued.

During this period, DW's calcium levels ranged from 8.8 – 10.0 mg/dL. He was taking a calcium-based phosphate binder, 667 mg calcium acetate, 2 tabs by mouth with meals. The patient did not receive any vitamin D analogs during this period. Table 1 shows the patient's laboratory chemistries with the lightly shaded area indicating the period of his ergocalciferol use.

Discussion

Vitamin D deficiency, a 25(OH) vitamin D level < 30 ng/mL, is widespread among dialysis patients. In a cross-sectional analysis of 825 CKD Stage 5 patients, it was reported 78% of the population suffered from this deficiency (1). Inadequate serum 25(OH) vitamin D has been associated with cardiovascular disease risk factors (2) and increased mortality (1). In the case of deficiency, vitamin D supplementation is the prudent course of action, yet one concern is the safety of this vitamin. In an *American Journal of Clinical Nutrition* 2008 article, Glenville Jones has suggested a vitamin D toxicity threshold of 300 ng/mL 25(OH) vitamin D (3). Additionally, Tokmak et al, examined the effect of high dose cholecalciferol, 20,000 IU, on a randomized treatment group of hemodialysis patients over fifteen months in comparison with a control group who were supplemented for only nine months. They found no negative effects of the high dose supplementation suggesting that increased levels may be needed to replenish vitamin D levels (4).

If hypercalcemia is the chief criterion for vitamin D toxicity (5), then DW did not achieve a harmful level of 25(OH) vitamin D. Dr. Reinhold Vieth, a leading researcher of vitamin D has noted "Vitamin D toxicity is the result of excessive levels of 'free' 1,25-(OH)₂D displaced from its carrier protein, vitamin

Advances in Practice....

Table 1
DW's Laboratory Values

	Lab Norm	12/1/08	12/16/08	1/6/09	1/20/09	2/3/09	2/17/09	3/3/09	3/17/09
Calcium (mg/dL)	8.5-10.5	9.8	8.8	9.4	10	9.9	9.8	9.1	9.3
Corrected Calcium (mg/dL)	8.4-10.2	9.8		9.4		10		9.3	
Albumin (g/dL)	3.5-4.7	4.3		4.0		3.9		3.7	
Intact PTH (ng/L)	150-300	66		66		30		70	
Alkaline Phosphatase (U/L)	38-126	36		35		36		30	
Creatinine (mg/dL)	0.7-1.5	3.91		3.74		5.36		8.09	
Hemoglobin (g/dL)	11-12	11.1	11.3	12.1	11.7	12.5	13.2	12.8	12.4
Epoetin Dose (units)	hemoglobin dependent	7700				6600	5500	HOLD	

*lab norms may vary by facility.

D-binding protein, when there is a vast excess of other vitamin D metabolites" (6).

1,25-(OH)₂ vitamin D (calcitriol) and vitamin D analogs have an exponentially greater effect upon serum calcium levels than 25(OH) vitamin D, though circulating levels of the latter are approximately 1,000 fold greater than that of the former. Calcitriol is a potent agent for increasing intestinal calcium absorption which can lead to hypercalcemia. ESRD patients convert very little 25(OH) vitamin D to 1,25-(OH)₂ vitamin D at the endocrine level. However, these patients will continue to use 25(OH) vitamin D as a substrate for 1,25-(OH)₂ vitamin D production at the autocrine and/or paracrine level with influence by the parathyroid hormone (7).

Given the diminished ability of CKD Stage 5 patients to produce 1-alpha-hydroxylase at the endocrine level, the tolerable upper level of vitamin D in this population may be higher than that of the general population. A study by Frohling et al, which involved administration of 600,000 IU ergocalciferol weekly over several months, concluded that patients with renal impairment handle high doses of vitamin D differently than normal subjects (8).

Conclusion

In our patient, a gradual high intake of ergocalciferol over two months did not appear to cause toxicity. Given the relative safety of this vitamin, the ease of monitoring toxicity via bimonthly calcium testing, and its potential for reduction of mortality and comorbidity rates, 25(OH) vitamin D levels should be tested annually in the CKD Stage 5 population. Vitamin D supplementation, a relatively inexpensive intervention, for those with 25(OH) vitamin D levels < 30 ng/mL, should be recommended. ♦

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Important Treatment Considerations

Renvela® (sevelamer carbonate) is indicated for the control of serum phosphorus in patients with chronic kidney disease (CKD) on dialysis • Renvela is contraindicated in patients with bowel obstruction • Caution should be exercised in patients with dysphagia, swallowing disorders, severe gastrointestinal (GI) motility disorders including severe constipation, or major GI tract surgery • Uncommon cases of bowel obstruction and perforation have been reported • Serum bicarbonate and chloride levels should be monitored • Vitamins D, E, K (coagulation parameters), and folic acid levels should be monitored • The most frequently occurring adverse reactions in a short-term study with sevelamer carbonate tablets were nausea and vomiting • In a short-term study of sevelamer carbonate powder dosed three times daily, adverse events were similar to those reported for sevelamer carbonate tablets • In long-term studies with sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, the most common adverse events included: vomiting, nausea, diarrhea, dyspepsia, abdominal pain, flatulence, and constipation • Cases of fecal impaction and, less commonly, ileus, bowel obstruction, and bowel perforation have been reported • Drug-drug interactions may occur with some medications and should be taken into consideration when instructing patients how to take Renvela • Patients should be informed to take Renvela with meals and to adhere to their prescribed diets

Please see Brief Summary of Prescribing Information on adjacent page.

Reference: 1. Renvela [package insert]. Cambridge, MA: Genzyme Corp; 2009.



sevelamer carbonate

[se vel' a mer]

See package insert for full prescribing information.

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Renvela® (sevelamer carbonate) is indicated for the control of serum phosphorus in patients with chronic kidney disease (CKD) on dialysis.

DOSAGE AND ADMINISTRATION

Because of the rapid reaction with the hydrochloric acid in the stomach, the dosing of Renvela powder or tablet is anticipated to be similar to that of the sevelamer hydrochloride salt or tablet.

General Dosing Information

Patients Not Taking a Phosphate Binder: The recommended starting dose of Renvela is 0.8 to 1.6 g, with meals based on serum phosphorus level. Table 1 provides recommended starting doses of Renvela for patients not taking a phosphate binder.

Table 1. Starting Dose for Dialysis Patients Not Taking a Phosphate Binder

SERUM PHOSPHORUS	RENVELA® 800 MG	RENVELA POWDER
> 5.5 and < 7.5 mg/dL	1 tablet three times daily with meals	0.8 g three times daily with meals
> 7.5 mg/dL	2 tablets three times daily with meals	1.6 g three times daily with meals

Switching from Sevelamer Hydrochloride Tablets: For patients switching from sevelamer hydrochloride tablets to sevelamer carbonate tablets or powder, use the same dose in grams. Further titration may be necessary to achieve desired phosphorus levels. The highest daily dose of sevelamer carbonate studied was 14 grams in CKD patients on dialysis.

Switching between Sevelamer Carbonate Tablets and Powder: Use the same dose in grams. Further titration may be necessary to achieve desired phosphorus levels.

Switching from Calcium Acetate: In a study in 84 CKD patients on hemodialysis, a similar reduction in serum phosphorus was seen with equivalent doses (approximately mg for mg) of sevelamer hydrochloride and calcium acetate. Table 2 gives recommended starting doses of Renvela based on a patient's current calcium acetate dose.

Table 2. Starting Dose for Dialysis Patients Switching From Calcium Acetate to Renvela

CALCIUM ACETATE 667 MG (TABLETS PER MEAL)	RENVELA® 800 MG (TABLETS PER MEAL)	RENVELA POWDER
1 tablet	1 tablet	0.8 g
2 tablets	2 tablets	1.6 g
3 tablets	3 tablets	2.4 g

Dose Titration for All Patients Taking Renvela: Titrate the Renvela dose by 0.8 g TID with meals at two-week intervals as necessary with the goal of controlling serum phosphorus within the target range.

Sevelamer Carbonate Powder Preparation Instructions

The entire contents of each 0.8 or 2.4 g packet should be placed in a cup and mixed thoroughly with the amount of water described in Table 3.

Table 3. Sevelamer Carbonate Powder Preparation Instructions

RENVELA POWDER PACKET STRENGTH	MINIMUM AMOUNT OF WATER FOR DOSE PREPARATION (EITHER OUNCES, mL, OR TEASPOON/TABLESPOON)		
	ounces	mL	tsp/tbsp
0.8 g	1	30	6 teaspoons/2 tablespoons
2.4 g	2	60	4 tablespoons

Multiple packets may be mixed together with the appropriate amount of water. Patients should be instructed to stir the mixture vigorously (it does not dissolve) and drink the entire preparation within 30 minutes or resuspend the preparation right before drinking.

Based on clinical studies, the average prescribed daily dose of sevelamer carbonate is approximately 7.2 g per day.

DOSAGE FORMS AND STRENGTHS

Tablets: 800 mg white oval, film-coated, compressed tablets imprinted with "RENVELA 800".

Powder: 0.8 g and 2.4 g pale yellow powder packaged in an opaque, foil lined, heat sealed packet.

CONTRAINDICATIONS

Renvela is contraindicated in patients with bowel obstruction.

WARNINGS AND PRECAUTIONS

Use Caution in Patients with Gastrointestinal Disorders. The safety of Renvela has not been established in patients with dysphagia, swallowing disorders, severe gastrointestinal (GI) motility disorders including severe constipation, or major GI tract surgery. Uncommon cases of bowel obstruction and perforation have been reported.

Monitor Serum Chemistries: Bicarbonate and chloride levels should be monitored.

Monitor for Reduced Vitamins D, E, K (clotting factors) and Folic Acid Levels. In preclinical studies in rats and dogs, sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, reduced vitamins D, E, and K (coagulation parameters) and folic acid levels at doses of 6–10 times the recommended human dose. In short-term clinical trials, there was no evidence of reduction in serum levels of vitamins. However, in a one-year clinical trial, 25-hydroxyvitamin D (normal range 10 to 55 ng/mL) fell from 39 ± 22 ng/mL to 34 ± 22 ng/mL ($p<0.01$) with sevelamer hydrochloride treatment. Most (approximately 75%) patients in sevelamer hydrochloride clinical trials received vitamin supplements, which is typical of patients on dialysis.

ADVERSE REACTIONS

Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

There are limited data on the safety of Renvela. However, based on the fact that it contains the same active ingredient as the hydrochloride salt, the adverse event profiles of the two salts should be similar. In a cross-over study in hemodialysis patients with treatment durations of eight weeks each and no washout the adverse reactions on sevelamer carbonate tablets were similar to those reported for sevelamer hydrochloride. In another cross-over study in hemodialysis patients, with treatment durations of four weeks each and no washout between treatment periods, the adverse reactions on sevelamer carbonate powder were similar to those reported for sevelamer hydrochloride.

In a parallel design study of sevelamer hydrochloride with treatment duration of 52 weeks, adverse reactions reported for sevelamer hydrochloride ($n=99$) were similar to those reported for the active-comparator group ($n=101$). Overall adverse reactions among those treated with sevelamer hydrochloride occurring in > 5% of patients included: vomiting (22%), nausea (20%), diarrhea (19%), dyspepsia (16%), abdominal pain (9%), flatulence (8%), and constipation (8%). A total of 27 patients treated with sevelamer and 10 patients treated with comparator withdrew from the study due to adverse reactions.

Based on studies of 8–52 weeks, the most common reason for withdrawal from sevelamer hydrochloride was gastrointestinal adverse reactions (3–16%).

In one hundred and forty-three peritoneal dialysis patients studied for 12 weeks using sevelamer hydrochloride, most adverse reactions were similar to adverse reactions observed in hemodialysis patients. The most frequently occurring treatment emergent serious adverse reaction was peritonitis (8 reactions in 8 patients [8%] in the sevelamer group and 2 reactions in 2 patients [4%] on active-control). Thirteen patients (14%) in the sevelamer group and 9 patients (20%) in the active-control group discontinued, mostly for gastrointestinal adverse reactions. Patients on peritoneal dialysis should be closely monitored to ensure the reliable use of appropriate aseptic technique with the prompt recognition and management of any signs and symptoms associated with peritonitis.

Postmarketing Experience: Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or to establish a causal relationship to drug exposure.

The following adverse reactions have been identified during post-approval use of sevelamer hydrochloride, which has the same active moiety as sevelamer carbonate: pruritis, rash, abdominal pain, fecal impaction, and uncommon cases of ileus, intestinal obstruction, and intestinal perforation. Appropriate medical management should be given to patients who develop constipation or have worsening of existing constipation to avoid severe complications.

DRUG INTERACTIONS

Sevelamer carbonate has been studied in human drug-drug interaction studies with warfarin and digoxin. Sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, has been studied in human drug-drug interaction studies with ciprofloxacin, digoxin, warfarin, enalapril, metoprolol, and iron.

Ciprofloxacin: In a study of 15 healthy subjects, a co-administered single dose of 2.8 grams of sevelamer hydrochloride decreased the bioavailability of ciprofloxacin by approximately 50%.

Digoxin: In 19 healthy subjects receiving 2.4 grams of sevelamer hydrochloride three times a day with meals for 2 days, sevelamer did not alter the pharmacokinetics of a single dose of digoxin. In 18 healthy subjects receiving 9.6 grams of sevelamer carbonate once daily, sevelamer did not alter the pharmacokinetics of a single dose of digoxin.

Warfarin: In 14 healthy subjects receiving 2.4 grams of sevelamer hydrochloride three times a day with meals, sevelamer did not alter the pharmacokinetics of a single dose of warfarin. In 14 healthy subjects receiving 9.6 grams of sevelamer carbonate once daily with meal, sevelamer did not alter the pharmacokinetics of a single dose of warfarin.

Enalapril: In 28 healthy subjects a single 2.4 gram dose of sevelamer hydrochloride did not alter the pharmacokinetics of a single dose of enalapril.

Metoprolol: In 31 healthy subjects a single 2.4 gram dose of sevelamer hydrochloride did not alter the pharmacokinetics of a single dose of metoprolol.

Iron: In 23 healthy subjects, a single 2.8 gram dose of sevelamer hydrochloride did not alter the absorption of a single oral dose of iron as 200 mg excipient ferrous sulfate tablet.

Other Concomitant Drug Therapy: There are no empirical data on avoiding drug interactions between Renvela and most concomitant drugs. During postmarketing experience, very rare cases of increased thyroid stimulating hormone (TSH) levels have been reported in patients co-administered sevelamer hydrochloride and levothyroxine. Monitor TSH levels and signs of hypothyroidism in patients receiving both medications.

When administering an oral medication where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, there is no information suggesting a dosing regimen that would be universally appropriate for all drugs. One may, however, administer the drug one hour before or three hours after Renvela, and when important, monitor blood levels of the drug. Patients taking anti-arrhythmic medications for the control of arrhythmias and anti-seizure medications for the control of seizure disorders were excluded from the clinical trials.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. Sevelamer products should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The effect of sevelamer hydrochloride on the absorption of vitamins and other nutrients has not been studied in pregnant women. Requirements for vitamins and other nutrients are increased in pregnancy. In pregnant rats given doses of sevelamer hydrochloride during organogenesis, reduced or irregular ossification of fetal bones, probably due to a reduced absorption of fat-soluble vitamin D, occurred at a dose approximately equal to the maximum clinical trial dose of 13 g on a body surface area basis. In pregnant rabbits given oral doses of sevelamer hydrochloride by gavage during organogenesis, an increase of early resorptions occurred at a dose approximately twice the maximum clinical trial dose on a body surface area basis. (See *NONCLINICAL TOXICOLOGY* (13.2)).

Labor and Delivery: No sevelamer hydrochloride treatment-related effects on labor and delivery were seen in animal studies. (See *NONCLINICAL TOXICOLOGY* (13)). The effects of sevelamer carbonate on labor and delivery in humans is unknown.

Pediatric use: The safety and efficacy of Renvela has not been established in pediatric patients.

Geriatric use: Clinical studies of Renvela did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range.

OVERDOSAGE

Sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, has been given to normal healthy volunteers in doses of up to 14 grams per day for eight days with no adverse effects. In CKD patients on dialysis, the maximum dose studied was 14 grams of sevelamer carbonate and 13 grams of sevelamer hydrochloride. There are no reports of overdose with sevelamer carbonate or sevelamer hydrochloride in patients. Since sevelamer is not absorbed, the risk of systemic toxicity is low.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Standard lifetime carcinogenicity bioassays were conducted in mice and rats. Rats were given sevelamer hydrochloride by diet at 0.3, 1, or 3 g/kg/day. There was an increased incidence of urinary bladder transitional cell papilloma in male rats of the high dose group (human equivalent dose twice the maximum clinical trial dose of 13 g). Mice received dietary administration of sevelamer hydrochloride at doses of up to 9 g/kg/day (human equivalent dose 3 times the maximum clinical trial dose). There was no increased incidence of tumors observed in mice.

In an *in vitro* mammalian cytogenetic test with metabolic activation, sevelamer hydrochloride caused a statistically significant increase in the number of structural chromosome aberrations. Sevelamer hydrochloride was not mutagenic in the Ames bacterial mutation assay.

Sevelamer hydrochloride did not impair the fertility of male or female rats in a dietary administration study in which the females were treated from 14 days prior to mating through gestation and the males were treated for 28 days prior to mating. The highest dose in this study was 4.5 g/kg/day (human equivalent dose 3 times the maximum clinical trial dose of 13 g).

Developmental Toxicity: In pregnant rats given dietary doses of 0.5, 1.5, or 4.5 g/kg/day of sevelamer hydrochloride during organogenesis, reduced or irregular ossification of fetal bones, probably due to a reduced absorption of fat-soluble vitamin D, occurred in mid- and high-dose groups (human equivalent doses approximately equal to and 3.4 times the maximum clinical trial dose of 13 g). In pregnant rabbits given oral doses of 100, 500, or 1000 mg/kg/day of sevelamer hydrochloride by gavage during organogenesis, an increase of early resorptions occurred in the high-dose group (human equivalent dose twice the maximum clinical trial dose).

HOW SUPPLIED/STORAGE AND HANDLING

Tablets: Renvela® 800 mg Tablets are supplied as white oval, film-coated, compressed tablets, imprinted with "RENVELA 800", containing 800 mg of sevelamer carbonate on an anhydrous basis, microcrystalline cellulose, hypromellose, diacylated monoglycerides, sodium chloride, and zinc stearate.

1 Bottle of 30 ct 800 mg Tablets (NDC 58468-0130-2)

1 Bottle of 270 ct 800 mg Tablets (NDC 58468-0130-1)

Powder: Renvela® for Oral Suspension is supplied as opaque, foil lined, heat sealed, packets containing 0.8 g or 2.4 g of sevelamer carbonate on an anhydrous basis, natural and artificial citrus cream flavor, propylene glycol alginate, sodium chloride, sucrose, and ferric oxide (yellow).

1 Box (NDC 58468-0131-2) of 90 ct 2.4 g packets (NDC 58468-0131-1)

1 Box (NDC 58468-0132-2) of 90 ct 0.8 g packets (NDC 58468-0132-1)

1 Sample Box (NDC 58468-0131-4) of 90 ct 2.4 g packets (NDC 58468-0131-3)

STORAGE

Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F).

[See USP controlled room temperature.]

Protect from moisture.

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Nephrology Nutrition and the Nutrition Care Process

A Renal Nutrition Forum Series with Practice-Based Examples of the Nutrition Care Process (NCP): Documenting Follow-Up Care After Initial Assessment

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This article has been approved for 1 CPE unit. The online CPEU quiz and certificate of completion can be accessed in the Members Only section of the RPG web site via the My CPEU link. This CPE offering is available to current RPG members only and the expiration date is November 11, 2010.

Members without internet access can request a copy of the quiz and certificate of completion from Megan Sliwa, RNF Assistant Editor, Address: 425 North Front Street, Apartment 424, Columbus, Ohio 43215. Please provide your name, ADA number, and phone number.

Introduction

Since this series began in the Spring 2008 issue of the *Renal Nutrition Forum*, there have been several requests for a case study demonstrating the use of the Nutrition Care Process (NCP) Model and standardized language (SL) in follow-up notes. This issue will further develop a case study which appeared in the Spring 2009 Forum and which provided sample nutrition notes as part of an initial assessment; this update will include some examples of documentation for subsequent care. The original case study: 1) provided guidance in applying the steps of the NCP to the requirements in the new Conditions for Coverage (CfCs); and 2) demonstrated the importance of including a nutrition diagnosis in nutrition care planning even though the CfCs do not specifically require that step (1,2). As the second step in the NCP, between assessment and intervention, nutrition diagnosis is an essential component of providing nutrition care.

Understanding that different dialysis providers have developed their own forms and/or templates for documentation in compliance with CfC mandates, the purpose of this case study is to continue

to demonstrate how the requirements within the CfCs match the NCP and to suggest some standardized language (SL) terms that are applicable in nephrology nutrition. The topic of reassessing patients to determine and record progress on an original nutrition diagnosis(es) and goal(s) is also presented in an article in *Support Line*, the bi-monthly newsletter for Dietitians In Nutrition Support Dietetic Practice Group (3). Renal dietitians may find it helpful to review this article which includes an overview of the NCP and a variety of notes, including brief notes reassessing initial goals.

Conditions for Coverage—Standards for Reassessment

For stable patients, the CfCs mandate a comprehensive reassessment as part of the cycle of accurate and timely care within three months after the initial comprehensive interdisciplinary patient assessment and annually thereafter. This is described in the Interpretive Guidelines (IG) tag V517 (4). This reassessment should refer back to the original individualized plan of care (POC), evaluating progress on the services and outcomes that were identified in the initial assessment. The same topics that are mandated in the initial assessment must be addressed in reassessments.

For CfC §494.80 on patient assessments, IG tag V509 lists parameters that must be included in the nutrition assessment (4). §494.90 establishes requirements for the POC. IG tags V540 to V542 discuss the POC and the role of the interdisciplinary team (IDT) in developing that plan; tags V543 to V559 explain aspects of care that must be reviewed in completing a POC (4). All of these CfC standards apply to the initial and to follow-up assessments. Lastly, the dietitian may address other topics beyond those in IG tag V509, such as adequacy, as part of the facility's team working together to plan and implement an individualized POC at initial assessment and reassessments.

Case Study—Background Information

The full description of the individual in this case study at the time of admission to an outpatient hemodialysis (HD) unit patient appears in a previous article (1). Briefly, and to update this case study example, this patient is a 53-year-old female who is now completing her third month as an in-center HD patient. At initial presentation, she had a diagnosis of Diabetes Mellitus Type 2 (DM2) but it appeared that she had stopped all medications for glucose management and was not monitoring glucose levels at home. End-stage renal disease (ESRD) was secondary to diabetic nephropathy.

At the end of the initial assessment she was determined to be a stable patient in keeping with the IG definition (4). In compliance with the CfCs, the IDT members, including the dietitian, are completing her 3 month reassessment at this time.

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Table 1

Pertinent New Data from Month(s) 0 to 3 on HD

53 yr old female with ESRD due to DM2.

CLINICAL DATA: Summary of data between months 0 and 3 on HD: Vascular access surgery 2 months ago; started using left upper arm arteriovenous fistula last week. Laser surgery on left eye planned in 3 weeks.

Dialysis Prescription: 3x/week on Optiflux 180NRE dialyzer, 240 minutes, 2 K* and 2.5 Ca* baths

Over-the-counter (OTC) meds: Adult Aspirin, Centrum Silver multivitamin (1/day), Slo-Fe (1/day)

Prescription meds with nutrition significance: 9000 units EPOGEN 3x/week, 80 mg furosemide 2x/day; 40 mg/day Lipitor; Novolin

70/30 (65 units before breakfast; 40 units before supper); 2 PhosLo/meal; 50 mg Venofer every week; 2000 IU cholecalciferol daily

Has had two visits with an endocrinologist who is managing DM2; just got a glucometer and checks capillary blood glucose (CBG) before breakfast 5-6x/week.

FOOD AND NUTRITION HISTORY: No nausea or vomiting. Can identify high potassium foods; stated compliance with low potassium diet until recent weeks—strawberries too tempting; eating more beans, too. Still describes good appetite, though never has eaten much meat or poultry; does not like fish. 24-hour recall shows protein intake ~60 gm per day.

ANTHROPOMETRICS: Height 167.6 cm, target weight 73 kg for Body Mass Index (BMI) 26. Was 74.5 kg at month 0 for BMI 26.2. Weight after last HD = 72.5 kg. 2% weight loss in last three months as target weight has been adjusted.

BIOCHEMS	Results at 3 Months	Lab/Unit Norm	BIOCHEMS	Results at 3 Months	Lab/Unit Norm
Potassium	5.8 mEq/L	3.5-5.5	Phosphorus	6.5 mEq/L	3.5-5.5
CO2	22.0 mmol/L	22-30	Corrected Ca x Phos*	59	≤ 55
BUN	74 mg/dL	60-100	iPTH*	155 ng/L	150-300
Creatinine	5.51 mg/dL	0.5-1.3	Kt/V*	1.86	>1.2
Albumin	3.6 g/dL	goal 4.0	URR*	75%	>65
Glucose, non-fasting	289 mg/dL	70-110	Hgb A1c	9.4% (10% at Month 1)	≤ 7%
Calcium	9.1 mg/dL	8.4-10.2	Cholesterol	156 mg/dL	<200
Adj. Calcium	9.4 mg/dL	8.4-10.2	Hemoglobin	10.9 g/dL	11-12

Month 0 hemoglobin A1c = not known

*K=potassium; Ca=calcium; Phos=phosphorus; iPTH=intact parathyroid hormone; Kt/V=a measure of dialysis adequacy; URR=urea reduction ratio

NUTRITIONAL PHYSICAL FINDINGS: No gastrointestinal complaints. Appears pale – but color improved. No edema. Skin warm, no evident ulcers or sores.

(see reference 5 for further information about some anthropometric and biochemical terms and K/DOQI standards in the case study)

Case Study—Reassessment

In reassessing patients, the renal dietitian looks at new data since the prior evaluation includes, but is not limited to, data specific to outcomes identified in that earlier assessment. Table 1 presents a summary of new data within the first 3 months of HD for

this case study. The next step is a review of this information from the perspective of the outcome indicators and criteria established in the POC at the initial assessment (see Table 2). For example, in our case study:

- Serum potassium and phosphorus both exceed goals at

Nutrition Care Process....

- month 3 (potassium was within goal during months 1 and 2; phosphorus has been elevated in 2 of last 3 months). The patient demonstrates knowledge but has relapsed regarding dietary potassium. Improved overall oral intake has included high phosphorus foods, but she does describe adherence to the prescribed phosphorus binder.
- While glucose control is not optimal and the patient has not met the goal of checking CBG twice a day, hemoglobin A1c has shown some improvement. Initially she was overwhelmed and unable to participate in self-management of DM2; at month 3 she has taken a step toward the goal in the initial nutrition assessment as she is being followed by an endocrinologist and now has a new glucometer.
 - The patient has made progress by eliminating duplicate multivitamins (MVs). She was previously taking 2 Centrum Silver and 2 One-A-Day vitamins. However, she has not yet changed to a renal-specific MV. Other nutrition issues have been stable or improved with the exception of serum albumin which dropped from 3.8 at month 0.

Case Study—Nutrition Diagnosis(es)

The next step after reassessment in the NCP is nutrition diagnosis (6). See Table 2 for the diagnoses that were included in the initial assessment for this patient. At the time of the three month reassessment, the dietitian judged that there was improved knowledge of dietary sources of potassium and phosphorus. The major nutrition diagnosis related to serum potassium and phosphorus control now changes from *knowledge deficit* to *excessive intake (altered nutrition-related labs)* is another possible diagnosis. This diagnosis directs intervention to strategies to help the patient anticipate and control excess intake, as well as to educate the patient about the hazards of excess intake. On the other hand, the *self-monitoring deficit* continues to be an active diagnosis, despite improved patient behaviors in this area. Lastly, *excess vitamin and mineral intake* may still be an active diagnosis, though it is not as serious as upon presentation to HD when the patient was consuming 400% and more of the DRI for vitamin C and fat-soluble vitamins through multiple MVs (the patient expressed “more is better” as her motive for consuming multiple supplements and was initially very resistant to reducing them). However, *inadequate protein intake* is a new diagnosis (*inadequate oral food/beverage intake* and *inadequate protein-energy intake* are two other diagnoses that might be considered, depending on specific assessment findings of why serum albumin is declining). There are many other possible scenarios when serum albumin drops, including contributions that might come from an infection or other aspects of the malnutrition inflammatory syndrome, in which case a diagnosis such as *increased protein needs* could be a more accurate nutrition diagnosis (7).

Case Study—Nutrition Intervention and Monitoring & Evaluation

As already mentioned, the intervention for the outcome indicator related to dietary potassium and phosphorus changes from *comprehensive nutrition education* about dietary sources of each to *comprehensive nutrition education* about strategies to avoid foods high in those minerals and a clear understanding of the hazards to the patient with excessive serum levels of potassium and phosphorus. A renal dietitian with counseling skills may choose the intervention of *nutrition counseling*, perhaps applying the transtheoretical model/stages of change framework and using motivational interviewing as a counseling strategy (6).

Since the diagnosis *self-monitoring deficit* is still active in this case (see Table 3), the dietitian must consider if a change is needed in the initial intervention to improve glucose control within the goals accepted for ESRD patients (7). At this time, the dietitian is observing that the patient is finally making some progress toward acknowledging that her glucose control is not acceptable, moving her closer to self-monitoring of CBGs. Since the patient is more receptive than in the past, it appears appropriate to continue the same intervention and even to continue monitoring the same outcomes.

Initially there was concern about excess vitamin and mineral intake with the patient’s use of several MVs at double doses due to her perception of the MVs as “extra health insurance.” By month 3, she has cut back to 1 MV per day. Her renal dietitian recognizes that some progress has been made in an issue with some emotional content to the patient, her commitment to multiple daily MVs. The goal is to transition the patient to a renal MV.

In the meantime, however, *inadequate protein intake* has moved into the three top nutrition diagnosis priorities since serum albumin has dropped in the first three months on HD and since the dietitian has assessed that the patient’s food preferences exclude some high quality protein sources. Appropriate intervention here will include an in-depth discussion of acceptable protein sources in foods acceptable to the patient. It is conceivable that *coordination of care: referral to community agencies/programs* might be an active intervention at some point if the dietitian finds that the patient is lacking resources to obtain food.

Summary

Renal dietitians, many of whom work with chronic dialysis patients over the space of years, have unique opportunities to practice the continuing cycle of assessment and reassessment, followed by diagnosis, planning interventions, and conducting monitoring and evaluation. In computerized medical records, nutrition care that is documented with SL is much more amenable to tabulation and analysis of effectiveness and efficiency of services provided (interventions) for various diagnoses. ◆

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Table 2

Nutrition Diagnosis, Outcome Indicators and Criteria from Initial POC (1)

DIAGNOSES (Problem—Etiology—Signs and Symptoms or PES)	
1. Problem (or Diagnosis): Nutrition-related knowledge deficit related to Etiology: lack of in-depth education on appropriate food choices as evidenced by Signs and symptoms: high potassium and phosphorus foods in 24-hour diet recall.	
2. Problem (or Diagnosis): Self-monitoring deficit related to Etiology: feeling overwhelmed by progression of kidney disease as evidenced by Signs and symptoms: patient not checking CBG and patient unaware of medications for DM2.	
3. Problem (or Diagnosis): Excess vitamin and mineral intake related to Etiology: patient unaware of special needs in ESRD, as evidenced by Signs and symptoms: taking double doses of 2 different multivitamins.	
MONITORING AND EVALUATION	
Outcome Indicator	Criteria
1. Potassium and phosphorus intake	1. Will limit high potassium foods to 1 serving/day and will limit dairy to 1 serving/day. Serum potassium and phosphorus will be within goal next month.
2a. Preprandial capillary blood glucose	2a. Will record CBGs at least 1-2 times a day, before and 2 hours after meals by the next monthly labs.
2b. Medication Use	2b. Will consult with primary care provider about blood glucose management, meds.
4. Vitamin and mineral intake	3. Will replace current MVI's with a renal-specific MVI within the next 2-4 weeks.

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Nutrition Care Process....

Table 3

Reassessment Documentation

PREVIOUS DIAGNOSES	
1. Problem (or Diagnosis): Nutrition-related knowledge deficit	<input checked="" type="checkbox"/> Resolved at this time <input type="checkbox"/> Partially resolved, continue to address <input type="checkbox"/> No change, continue to address
2. Problem (or Diagnosis): Self-monitoring deficit	<input type="checkbox"/> Resolved at this time <input type="checkbox"/> Partially resolved, continue to address <input checked="" type="checkbox"/> No change, continue to address
3. Problem (or Diagnosis): Excess vitamin and mineral intake	<input type="checkbox"/> Resolved at this time <input checked="" type="checkbox"/> Partially resolved, continue to address <input type="checkbox"/> No change, continue to address
CURRENT DIAGNOSIS AT 3 MONTH REASSESSMENT	
1. Problem (or Diagnosis): Excess phosphorus and potassium intake related to	
Etiology: relapse after acceptable labs and related to availability of seasonal foods as evidenced by	
Signs and symptoms: high phosphorus and seasonal high potassium foods in 24-hour recall.	
2. Problem (or Diagnosis): Self-monitoring deficit related to	
Etiology: still learning how to use glucometer and how to add to daily routines as evidenced by	
Signs and symptoms: just receiving new glucometer last month and only 5-6 CBGs per week.	
3. Problem (or Diagnosis): Inadequate protein intake related to	
Etiology: food preferences, as evidenced by	
Signs and symptoms: patient does not like meat or poultry, and dietary protein below goal.	
PLAN OF CARE: Interventions (Services)	
Nutrition Prescription: 2200 kcal/day (30 kcal/kg), 90-95 g protein (1.2-1.3 g/kg), 2 g sodium, 2 g potassium, 1200 mg phosphorus, consistent carbohydrates (CHO) (5-6 CHO/meal with 15 g CHO per carb serving) (5,8)	
1. Goal: Improved compliance with guidelines for dietary control of potassium and phosphorus to maintain serum levels within goal.	
Intervention: Comprehensive nutrition education re: advanced topic—strategies for better dietary control and hazards of excess serum levels	
2. Goal: Improved compliance with self-management of blood glucose.	
Intervention: Comprehensive nutrition education re: advanced topic—how CBG data can help with glucose control, pattern management	
3. Goal: Patient will improve dietary protein to goal for HD patients.	
Intervention: Comprehensive nutrition education re: advanced topic—alternative sources of protein	
MONITORING AND EVALUATION	
Outcome Indicator	Criteria
1. Potassium and phosphorus intake	1. Will limit high potassium foods to 1 serving/day and will limit dairy to 1 serving/day. Serum potassium and phosphorus will be within goal next month.
2. Preprandial capillary blood glucose	2. Will record CBGs at least 1-2 times a day before meals by the next monthly labs.
3. Protein intake	3. Will identify acceptable foods to add at least 14 gm dietary protein at each of 2 meals/day.
4. Vitamin and mineral intake	4. Discontinue general MVI and initiate daily renal MVI.

Malnutrition-Inflammation Complex Syndrome in Dialysis Patients: Causes and Consequences. *J Am Kidney Dis.* 2003;42:864-881.

8. NKF-K/DOQI. Clinical practice guidelines and clinical prac-

tice recommendations for diabetes and chronic kidney disease. Available at http://www.kidney.org/professionals/kdoqi/guidelines_updates/nut_a09.html. Accessed June 2009.

ZEMPLAR is indicated for the prevention and treatment of secondary hyperparathyroidism (SHPT) associated with chronic kidney disease (CKD) stage 3 and 4 (ZEMPLAR Capsules) and stage 5 (ZEMPLAR Injection)^{1,2}

HELP FIGHT A COMPLICATION OF CKD

Important Safety Information^{1,2}

- ZEMPLAR Capsules and Injection are contraindicated in patients with evidence of vitamin D toxicity, hypercalcemia, or hypersensitivity to any product ingredient.
- Excessive administration of vitamin D compounds can cause over suppression of parathyroid hormone (PTH), hypercalcemia, hypercalciuria, hyperphosphatemia, and adynamic bone disease. High intake of calcium and phosphate concomitant with vitamin D compounds may lead to similar abnormalities, and patient monitoring and individualized dose titration is required. Progressive hypercalcemia due to overdosage of vitamin D may require emergency medical attention. Acute hypercalcemia may exacerbate tendencies for cardiac arrhythmias and seizures and may potentiate the action of digitalis. Use caution when digitalis compounds are prescribed concomitantly with ZEMPLAR. Chronic hypercalcemia can lead to vascular and soft-tissue calcifications. Chronic administration of ZEMPLAR Injection may place patients at risk for hypercalcemia, elevated Ca x P product, and metastatic calcification.

- ZEMPLAR is partially metabolized by CYP3A. Care should be taken while dosing ZEMPLAR with ketoconazole and other strong cytochrome P450 3A inhibitors including atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, neflunavir, ritonavir, saquinavir, telithromycin or voriconazole.
- During ZEMPLAR Capsules therapy withhold pharmacologic doses of vitamin D compounds. PTH, calcium and phosphorus levels should be monitored at least every 2 weeks for 3 months after initiation or following dose adjustments, then monthly for 3 months, and every 3 months thereafter. Patient monitoring and individualized dose titration are required to maintain physiologic targets and optimum reduction/levels of PTH. The dose of ZEMPLAR Capsules should be reduced or interrupted if hypercalcemia or elevated Ca x P is observed.
- During ZEMPLAR Injection therapy withhold phosphate or vitamin D related compounds. PTH should be monitored at least every 3 months and more frequently at initiation and dosage changes. Calcium and phosphorus should be measured at least monthly and

more frequently at initiation or following dosage changes. If clinically significant hypercalcemia develops or an elevated Ca x P product greater than 75 mg²/dL² is noted, the dose should be immediately reduced or interrupted.

- Patients should be informed to adhere to their diet and phosphorus restriction, to take prescribed phosphate binders, and should be knowledgeable about the symptoms of hypercalcemia. While taking ZEMPLAR Capsules patients should be informed to comply with dosage instructions.
- Adverse events reported by at least 5% and at a frequency of at least twice that of placebo were allergic reaction, rash, arthritis, and vertigo for the ZEMPLAR Capsules Stage 3 and 4 treated patients and chills, fever, sepsis, gastrointestinal bleeding, vomiting, edema, light-headedness, and pneumonia for the ZEMPLAR Injection Stage 5 treated patients.



Goal achievement across the treatment continuum

www.zemplar.com



Please see brief summary of Prescribing Information for ZEMPLAR Injection and ZEMPLAR Capsules on following pages.

References: 1. ZEMPLAR (paricalcitol) Capsules [package insert]. North Chicago, IL; Abbott Laboratories. 2. ZEMPLAR (paricalcitol) Injection [package insert]. Lake Forest, IL; Abbott Laboratories.

ZEMPLAR is a trademark of Abbott Laboratories.

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

Zemplar®

(paricalcitol) Capsules

Rx only

INDICATIONS AND USAGE

Zemplar Capsules are indicated for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease (CKD) Stage 3 and 4.

CONTRAINdications

Zemplar Capsules should not be given to patients with evidence of vitamin D toxicity, hypercalcemia, or hypersensitivity to any ingredient in this product (see **WARNINGS**).

WARNINGS

Excessive administration of vitamin D compounds, including Zemplar Capsules, can cause over suppression of PTH, hypercalcemia, hypercalciuria, hyperphosphatemia, and adynamic bone disease. Progressive hypercalcemia due to overdose of vitamin D and its metabolites may be so severe as to require emergency attention. Acute hypercalcemia may exacerbate tendencies for cardiac arrhythmias and seizures and may potentiate the action of digitalis. Chronic hypercalcemia can lead to generalized vascular calcification and other soft-tissue calcification. High intake of calcium and phosphate concomitant with vitamin D compounds may lead to similar abnormalities and patient monitoring and individualized dose titration is required.

Pharmacologic doses of vitamin D and its derivatives should be withheld during Zemplar treatment to avoid hypercalcemia.

PRECAUTIONS

General

Digitalis toxicity is potentiated by hypercalcemia of any cause, so caution should be applied when digitalis compounds are prescribed concomitantly with Zemplar Capsules.

Information for Patients

The patient or guardian should be informed about compliance with dosage instructions, adherence to instructions about diet and phosphorus restriction, and avoidance of the use of unapproved nonprescription drugs. Phosphate-binding agents may be needed to control serum phosphorus levels in patients, but excessive use of aluminum containing compounds should be avoided. Patients also should be informed about the symptoms of elevated calcium (see **ADVERSE REACTIONS**).

Laboratory Tests

During the initial dosing or following any dose adjustment of medication, serum calcium, serum phosphorus, and serum or plasma iPTH should be monitored at least every two weeks for 3 months after initiation of Zemplar therapy or following dose-adjustments in Zemplar therapy, then monthly for 3 months, and every 3 months thereafter.

Drug Interactions

Paricalcitol is not expected to inhibit the clearance of drugs metabolized by cytochrome P450 enzymes CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1 or CYP3A nor induce the clearance of drugs metabolized by CYP2B6, CYP2C9 or CYP3A.

A multiple dose drug-drug interaction study demonstrated that ketoconazole approximately doubled paricalcitol AUC_{0-∞}. Since paricalcitol is partially metabolized by CYP3A and ketoconazole is known to be a strong inhibitor of cytochrome P450 3A enzyme, care should be taken while dosing paricalcitol with ketoconazole and other strong P450 3A inhibitors including atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, neflavir, ritonavir, saquinavir, telithromycin or voriconazole. Dose adjustment of Zemplar Capsules may be required, and iPTH and serum calcium concentrations should be closely monitored if a patient initiates or discontinues therapy with a strong CYP3A4 inhibitor such as ketoconazole.

Drugs that impair intestinal absorption of fat-soluble vitamins, such as cholestyramine, may interfere with the absorption of Zemplar Capsules.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 104-week carcinogenicity study in CD-1 mice, an increased incidence of uterine leiomyoma and leiomyosarcoma was observed at subcutaneous doses of 1, 3, 10 mcg/kg given three times weekly (2 to 15 times the AUC at a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The incidence rate of uterine leiomyoma was significantly different than the control group at the highest dose of 10 mcg/kg. In a 104-week carcinogenicity study in rats, there was an increased incidence of benign adrenal pheochromocytoma at subcutaneous doses of 0.15, 0.5, 1.5 mcg/kg (< 1 to 7 times the exposure following a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The increased incidence of pheochromocytomas in rats may be related to the alteration of calcium homeostasis by paricalcitol. Paricalcitol did not exhibit genetic toxicity *in vitro* with or without metabolic activation in the microbial mutagenesis assay (Ames Assay), mouse lymphoma mutagenesis assay (L5178Y), or a human lymphocyte cell chromosomal aberration assay. There was also no evidence of genetic toxicity in an *in vivo* mouse micronucleus assay. Paricalcitol had no effect on fertility (male or female) in rats at intravenous doses up to 20 mcg/kg/dose (equivalent to 13 times a human dose of 14 mcg based on surface area, mcg/m²).

Pregnancy

Pregnancy category C

Paricalcitol has been shown to cause minimal decreases in fetal viability (5%) when administered daily to rabbits at a dose 0.5 times a human dose of 14 mcg or 0.24 mcg/kg (based on body surface area, mcg/m²), and when administered to rats at a dose two times the 0.24 mcg/kg human dose (based on body surface area, mcg/m²). At the highest dose tested, 20 mcg/kg administered three times per week in rats (13 times the 14 mcg human dose based on surface area, mcg/m²), there was a significant increase in the mortality of newborn rats at doses that were maternally toxic and are known to produce hypercalcemia in rats. No other effects on offspring development were observed. Paricalcitol was not teratogenic at the doses tested. Paricalcitol (20 mcg/kg) has been shown to cross the placental barrier in rats.

There are no adequate and well-controlled clinical studies in pregnant women. Zemplar Capsules should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Nursing Mothers

Studies in rats have shown that paricalcitol is present in the milk. It is not known whether paricalcitol is excreted in human milk. In the nursing patient, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Geriatric Use

Of the total number (n = 220) of patients in clinical studies of Zemplar Capsules, 49% were 65 and over, while 17% were 75 and over. No overall differences in safety and effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Pediatric Use

Safety and efficacy of Zemplar Capsules in pediatric patients have not been established.

ADVERSE REACTIONS

The safety of Zemplar Capsules has been evaluated in three 24-week (approximately six-month), double-blind, placebo-controlled, multicenter clinical studies involving 220 CKD Stage 3 and 4 patients. Six percent (6%) of Zemplar Capsules treated patients and 4% of placebo treated patients discontinued from clinical studies due to an adverse event. All reported adverse events occurring in at least 2% in either treatment group are presented in Table 3.

Table 3. Treatment - Emergent Adverse Events by Body System Occurring in ≥ 2% of Subjects in the Zemplar-Treated Group of Three, Double-Blind, Placebo-Controlled, Phase 3, CKD Stage 3 and 4 Studies; All Treated Patients

Body System ^a COSTART V Term	Number (%) of Subjects	
	Zemplar Capsules (n = 107)	Placebo (n = 113)
Overall	88 (82%)	86 (76%)
Body as a Whole		
Accidental Injury	49 (46%)	40 (35%)
Pain	10 (9%)	8 (7%)
Viral Infection	8 (7%)	7 (6%)
Allergic Reaction	6 (6%)	2 (2%)
Headache	5 (5%)	5 (4%)
Abdominal Pain	4 (4%)	2 (2%)
Back Pain	4 (4%)	1 (1%)
Infection	4 (4%)	4 (4%)
Asthenia	3 (3%)	2 (2%)
Chest Pain	3 (3%)	1 (1%)
Fever	3 (3%)	1 (1%)
Infection Fungal	3 (3%)	0 (0%)
Cyst	2 (2%)	0 (0%)
Flu Syndrome	2 (2%)	1 (1%)
Infection Bacterial	2 (2%)	1 (1%)
Cardiovascular		
Hypertension	27 (25%)	19 (17%)
Hypotension	7 (7%)	4 (4%)
Syncope	5 (5%)	3 (3%)
Cardiomyopathy	3 (3%)	1 (1%)
Congestive Heart Failure	2 (2%)	5 (4%)
Myocardial Infarct	2 (2%)	0 (0%)
Postural Hypotension	2 (2%)	0 (0%)
Digestive		
Diarrhea	29 (27%)	31 (27%)
Nausea	7 (7%)	5 (4%)
Vomiting	6 (6%)	4 (4%)
Constipation	6 (6%)	5 (4%)
Gastroenteritis	4 (4%)	4 (4%)
Dyspepsia	3 (3%)	3 (3%)
Gastritis	2 (2%)	2 (2%)
Rectal Disorder	2 (2%)	4 (4%)
Hemic and Lymphatic System		
Hemolytic Anemia	4 (4%)	10 (9%)
Hypervolemia	2 (2%)	4 (4%)
Ecchymosis	2 (2%)	4 (4%)

(Continued..)

Body System ^a COSTART V Term	Number (%) of Subjects	
	Zemplar Capsules (n = 107)	Placebo (n = 113)
Overall	88 (82%)	86 (76%)
Metabolic and Nutritional Disorders		
Edema	24 (22%)	34 (30%)
Uremia	7 (7%)	5 (4%)
Gout	4 (4%)	6 (5%)
Dehydration	3 (3%)	1 (1%)
Acidosis	2 (2%)	1 (1%)
Hyperkalemia	2 (2%)	3 (3%)
Hyperphosphatemia	2 (2%)	4 (4%)
Hypoglycemia	2 (2%)	4 (4%)
Hypokalemia	2 (2%)	1 (1%)
Musculoskeletal		
Arthritis	12 (11%)	9 (8%)
Leg Cramps	5 (5%)	1 (1%)
Myalgia	2 (2%)	5 (4%)
Nervous		
Dizziness	18 (17%)	12 (11%)
Vertigo	5 (5%)	4 (4%)
Depression	5 (5%)	0 (0%)
Insomnia	3 (3%)	2 (2%)
Neuropathy	2 (2%)	1 (1%)
Respiratory		
Pharyngitis	26 (24%)	25 (22%)
Rhinitis	11 (10%)	12 (11%)
Bronchitis	5 (5%)	4 (4%)
Cough Increased	3 (3%)	2 (2%)
Sinusitis	3 (3%)	1 (1%)
Epistaxis	2 (2%)	1 (1%)
Pneumonia	2 (2%)	0 (0%)
Skin and Appendages		
Rash	17 (16%)	10 (9%)
Pruritus	6 (6%)	3 (3%)
Skin Ulcer	3 (3%)	0 (0%)
Skin Hypertrophy	2 (2%)	0 (0%)
Vesiculobullous Rash	2 (2%)	1 (1%)
Special Senses		
Amblyopia	9 (8%)	11 (10%)
Retinal Disorder	2 (2%)	0 (0%)
Urogenital System		
Urinary Tract Infection	10 (9%)	10 (9%)
Kidney Function Abnormal	3 (3%)	1 (1%)

a. Includes all patients with events in that body system.

Potential adverse effects of Zemplar Capsules are, in general, similar to those encountered with excessive vitamin D intake. The early and late signs and symptoms of hypercalcemia associated with vitamin D overdoses include:

Early: Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, and metallic taste.

Late: Anorexia, weight loss, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, puritus, hyperthermia, decreased libido, elevated BUN, hypercholesterolemia, elevated AST and ALT, ectopic calcification, hypertension, cardiac arrhythmias, somnolence, death, and, rarely, overt psychosis.

OVERDOSE

Excessive administration of Zemplar Capsules can cause hypercalcemia, hypercalciuria, and hyperphosphatemia, and over suppression of PTH (see **WARNINGS**).

Treatment of Overdosage

The treatment of acute overdosage of Zemplar Capsules should consist of general supportive measures. If drug ingestion is discovered within a relatively short time, induction of emesis or gastric lavage may be of benefit in preventing further absorption. If the drug has passed through the stomach, the administration of mineral oil may promote its fecal elimination. Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion, and assessment of electrocardiographic abnormalities due to hypercalcemia should be obtained. Such monitoring is critical in patients receiving digitalis. Discontinuation of supplemental calcium and institution of a low-calcium diet are also indicated in accidental overdosage. Due to the relatively short duration of the pharmacological action of paricalcitol, further measures are probably unnecessary. If persistent and markedly elevated serum calcium levels occur, there are a variety of therapeutic alternatives that may be considered depending on the patient's underlying condition. These include the use of drugs such as phosphates and corticosteroids, as well as measures to induce an appropriate forced diuresis.

Ref: 03-5368-R1

Revised: May, 2005

05E-131-J612-2 MASTER

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

Zemplar®

(paricalcitol) Injection

Fliptop Vial

Rx only

INDICATIONS AND USAGE

Zemplar is indicated for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5.

CONTRAINDICATIONS

Zemplar should not be given to patients with evidence of vitamin D toxicity, hypercalcemia, or hypersensitivity to any ingredient in this product (see **WARNINGS**).

WARNINGS

Acute overdose of Zemplar may cause hypercalcemia, and require emergency attention. During dose adjustment, serum calcium and phosphorus levels should be monitored closely (e.g., twice weekly). If clinically significant hypercalcemia develops, the dose should be reduced or interrupted. Chronic administration of Zemplar may place patients at risk of hypercalcemia, elevated Ca x P product, and metastatic calcification.

Treatment of patients with clinically significant hypercalcemia consists of immediate dose reduction or interruption of Zemplar therapy and includes a low calcium diet, withdrawal of calcium supplements, patient mobilization, attention to fluid and electrolyte imbalances, assessment of electrocardiographic abnormalities (critical in patients receiving digitalis), hemodialysis or peritoneal dialysis against a calcium-free dialysate, as warranted. Serum calcium levels should be monitored frequently until normocalcemia ensues.

Phosphate or vitamin D-related compounds should not be taken concomitantly with Zemplar.

PRECAUTIONS

General

Digitalis toxicity is potentiated by hypercalcemia of any cause, so caution should be applied when digitalis compounds are prescribed concomitantly with Zemplar. A dynamic bone lesions may develop if PTH levels are suppressed to abnormal levels.

Information for the Patient

The patient should be instructed that, to ensure effectiveness of Zemplar therapy, it is important to adhere to a dietary regimen of calcium supplementation and phosphorus restriction. Appropriate types of phosphate-binding compounds may be needed to control serum phosphorus levels in patients with chronic kidney disease (CKD) Stage 5, but excessive use of aluminum containing compounds should be avoided. Patients should also be carefully informed about the symptoms of elevated calcium (see **ADVERSE REACTIONS**).

Laboratory Tests

During the initial phase of medication, serum calcium and phosphorus should be determined frequently (e.g., twice weekly). Once dosage has been established, serum calcium and phosphorus should be measured at least monthly. Measurements of serum or plasma PTH are recommended every 3 months. An intact PTH (iPTH) assay is recommended for reliable detection of biologically active PTH in patients with CKD Stage 5. During dose adjustment of Zemplar, laboratory tests may be required more frequently.

Drug Interactions

Paricalcitol is not expected to inhibit the clearance of drugs metabolized by cytochrome P450 enzymes CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A nor induce the clearance of drug metabolized by CYP2B6, CYP2C9 or CYP3A.

Specific interaction studies were not performed with Zemplar Injection.

A multiple dose drug-drug interaction study with ketoconazole and paricalcitol capsule demonstrated that ketoconazole approximately doubled paricalcitol AUC_{0-∞}. Since paricalcitol is partially metabolized by CYP3A and ketoconazole is known to be a strong inhibitor of cytochrome P450 3A enzyme, care should be taken while dosing paricalcitol with ketoconazole and other strong P450 3A inhibitors including azatazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin or voriconazole.

Digitalis toxicity is potentiated by hypercalcemia of any cause, so caution should be applied when digitalis compounds are prescribed concomitantly with Zemplar.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 104-week carcinogenicity study in CD-1 mice, an increased incidence of uterine leiomyoma and leiomyosarcoma was observed at subcutaneous doses of 1, 3, 10 mcg/kg (2 to 15 times the AUC at a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The incidence rate of uterine leiomyoma was significantly different than the control group at the highest dose of 10 mcg/kg.

In a 104-week carcinogenicity study in rats, there was an increased incidence of benign adrenal pheochromocytoma at subcutaneous doses of 0.15, 0.5, 1.5 mcg/kg (<1 to 7 times the exposure following a human dose of 14 mcg, equivalent to 0.24 mcg/kg based on AUC). The increased incidence of pheochromocytomas in rats may be related to the alteration of calcium homeostasis by paricalcitol.

Paricalcitol did not exhibit genetic toxicity *in vitro* with or without metabolic activation in the microbial mutagenesis assay (Ames Assay), mouse lymphoma mutagenesis assay (L5178Y), or a human lymphocyte cell chromosomal aberration assay. There was also no evidence of genetic toxicity in an *in vivo* mouse micronucleus assay. Zemplar had no effect on fertility (male or female) in rats at intravenous doses up to 20 mcg/kg/dose [equivalent to 13 times the highest recommended human dose (0.24 mcg/kg) based on surface area, mg/m²].

Pregnancy

Pregnancy Category C.

Paricalcitol has been shown to cause minimal decreases in fetal viability (5%) when administered daily to rabbits at a dose 0.5 times the 0.24 mcg/kg human dose (based on surface area, mg/m²) and when administered to rats at a dose 2 times the 0.24 mcg/kg human dose (based on plasma levels of exposure). At the highest dose tested (20 mcg/kg 3 times per week in rats, 13 times the 0.24 mcg/kg human dose based on surface area), there was a significant increase of the mortality of newborn rats at doses that were maternally toxic (hypercalcemia). No other effects on offspring development were observed. Paricalcitol was not teratogenic at the doses tested.

There are no adequate and well-controlled studies in pregnant women. Zemplar should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Nursing Mothers

Studies in rats have shown that paricalcitol is present in the milk. It is not known whether paricalcitol is excreted in human milk. In the nursing patient, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

The safety and effectiveness of Zemplar were examined in a 12-week randomized, double-blind, placebo-controlled study of 29 pediatric patients, aged 5-19 years, with end-stage renal disease on hemodialysis and nearly all had received some form of vitamin D prior to the study. Seventy-six percent of the patients were male, 52% were Caucasian and 45% were African-American. The initial dose of Zemplar was 0.04 mcg/kg 3 times per week, based on baseline iPTH level of

less than 500 pg/mL, or 0.08 mcg/kg 3 times a week based on baseline iPTH level of ≥ 500 pg/mL, respectively. The dose of Zemplar was adjusted in 0.04 mcg/kg increments based on the levels of serum iPTH, calcium, and Ca x P. The mean baseline levels of iPTH were 841 pg/mL for the 15 Zemplar-treated patients and 740 pg/mL for the 14 placebo-treated subjects. The mean dose of Zemplar administered was 4.6 mcg (range: 0.8 mcg – 9.6 mcg). Ten of the 15 (67%) Zemplar-treated patients and 2 of the 14 (14%) placebo-treated patients completed the trial. Ten of the placebo patients (71%) were discontinued due to excessive elevations in iPTH levels as defined by 2 consecutive iPTH levels > 700 pg/mL and greater than baseline after 4 weeks of treatment.

In the primary efficacy analysis, 9 of 15 (60%) subjects in the Zemplar group had 2 consecutive 30% decreases from baseline iPTH compared with 3 of 14 (21%) patients in the placebo group (95% CI for the difference between groups –1%, 63%). Twenty-three percent of Zemplar vs. 31% of placebo patients had at least one serum calcium level > 10.3 mg/dL, and 40% vs. 14% of Zemplar vs. placebo subjects had at least one Ca x P ion product > 72 (mg/dL)². The overall percentage of serum calcium measurements > 10.3 mg/dL was 7% in the Zemplar group and 7% in the placebo group; the overall percentage of patients with Ca x P product > 72 (mg/dL)² was 8% in the Zemplar group and 7% in the placebo group. No subjects in either the Zemplar group or placebo group developed hypercalcemia (defined as at least one calcium value > 11.2 mg/dL) during the study.

Geriatric Use

Of the 40 patients receiving Zemplar in the three phase 3 placebo-controlled CKD Stage 5 studies, 10 patients were 65 years or over. In these studies, no overall differences in efficacy or safety were observed between patients 65 years or older and younger patients.

ADVERSE REACTIONS

Zemplar has been evaluated for safety in clinical studies in 454 CKD Stage 5 patients. In four, placebo-controlled, double-blind, multicenter studies, discontinuation of therapy due to any adverse event occurred in 6.5% of 62 patients treated with Zemplar (dosage titrated as tolerated) and 2.0% of 51 patients treated with placebo for 1 to 3 months. Adverse events occurring with greater frequency in the Zemplar group at a frequency of 2% or greater, regardless of causality, are presented in the following table:

Adverse Event Incidence Rates For All Treated Patients In All Placebo-Controlled Studies		
Adverse Event	Zemplar (n=62) %	Placebo (n=51) %
Overall	71	78
Body as a Whole		
Chills	5	0
Feeling unwell	3	0
Fever	5	2
Flu	5	4
Sepsis	5	2
Cardiovascular		
Palpitation	3	0
Digestive System		
Dry mouth	3	2
Gastrointestinal bleeding	5	2
Nausea	13	8
Vomiting	8	4
Metabolic and Nutritional Disorders		
Edema	7	0
Nervous System		
Light-headedness	5	2
Respiratory System		
Pneumonia	5	0

A patient who reported the same medical term more than once was counted only once for that medical term.

Safety parameters (changes in mean Ca, P, Ca x P) in an open-label safety study up to 13 months in duration support the long-term safety of Zemplar in this patient population.

Potential adverse events of Zemplar Injection are, in general, similar to those encountered with excessive vitamin D intake. Signs and symptoms of vitamin D intoxication associated with hypercalcemia include:

Early
Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, and metallic taste.

Late
Anorexia, weight loss, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated BUN, hypercholesterolemia, elevated AST and ALT, ectopic calcification, hypertension, cardiac arrhythmias, somnolence, death, and rarely, overt psychosis.

Adverse events during post-marketing experience: Taste perversion, such as metallic taste, and allergic reactions, such as rash, urticaria, pruritus, facial and oral edema rarely have been reported.

OVERDOSE

Overdosage of Zemplar may lead to hypercalcemia, hypercalciuria, hyperphosphatemia, and/or suppression of PTH. (see **WARNINGS**).

Treatment of Overdosage and Hypercalcemia

The treatment of acute overdosage should consist of general supportive measures. Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion, and assessment of electrocardiographic abnormalities due to hypercalcemia should be obtained. Such monitoring is critical in patients receiving digitalis. Discontinuation of supplemental calcium and institution of a low calcium diet are also indicated in acute overdosage.

General treatment of hypercalcemia due to overdosage consists of immediate suspension of Zemplar therapy, institution of a low calcium diet, and withdrawal of calcium supplements. Serum calcium levels should be determined at least weekly until normocalcemia ensues. When serum calcium levels have returned to within normal limits, Zemplar may be reinitiated at a lower dose. If persistent and markedly elevated serum calcium levels occur, there are a variety of therapeutic alternatives that may be considered. These include the use of drugs such as phosphates and corticosteroids as well as measures to induce diuresis. Also, one may consider dialysis against a calcium-free dialysate.

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Not All Dieting Is Bad

The Relationship Between Dieting and Eating Pathology

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Learning Objectives

After you read this article, you will be able to:

- Describe the evidence supporting a theorized link between dieting and eating disorder symptoms.
- Summarize the data from randomized trials examining caloric reduction and eating pathology.
- Discuss proposed reasons for inconsistent findings from studies on weight loss and disordered eating.

It has been proposed that dieting increases the risk for developing and maintaining eating disorder symptoms (1-3). According to this hypothesis, dieting—defined as an intentional reduction in energy intake below what is needed to maintain energy balance (4)—produces a shift from reliance on physiologic to cognitive mechanisms to control eating (1,2) (often termed dietary restraint). When cognitive control is disrupted, dieters become vulnerable to eating that is out of control (1), a key component of binge eating (5). Once uncontrolled eating (i.e., binge eating) begins, dietary restraint is theorized to increase as a means to offset weight gain, and more severe methods of weight control may emerge. The increased restraint is believed to strengthen the likelihood of recurrent binge eating. The relationship between restraint and binge eating creates the core of the binge-purge cycle outlined in the cognitive behavioral framework of bulimia nervosa developed by Fairburn (6).

The Relationship Between Dieting and Binge Eating

Two areas of evidence support the theorized causal relationship between dietary restraint and eating disorder pathology. The first area arose from experimental eating laboratory studies conducted initially by Herman and Mack (7) and later by Polivy and Herman (8). These studies found that restrained eaters (participants who reported conscious control over their eating for weight control) showed an increase in eating when restraint was

overridden (known as counter-regulatory eating or disinhibition). For example, when given a preload high in calories, restrained participants consumed more food ad libitum following the preload in comparison to the amount of food consumed ad libitum when no preload had been consumed. The investigators theorized that the abstinence-violation effect (9) had occurred and that as restraint was violated, dietary restriction was temporarily abandoned, leading to increased consumption. The increased consumption occurring in these situations was considered to be a laboratory simulation of binge eating. However, in these simulations the two markers of binge eating—eating an amount of food that is definitely larger than most people would eat, and exhibiting a sense of loss of control (5)—did not occur; this study limitation has been acknowledged by Polivy and Herman (1).

The second area of evidence that links dieting and binge eating comes from longitudinal observational studies demonstrating that dieters or adolescent females with elevated dietary restraint were at increased risk for binge eating (10-12) and partial (13,14) as well as full eating disorders (13). Conclusions from these investigations posit that dieting may be a harmful behavior (11). Because of the belief that dieting causes eating pathology, some researchers have stated that all dieting should be stopped (15).

Do Weight Loss Programs with Caloric Limits Produce Binge Eating?

Family-based behavioral pediatric weight control programs produce significant weight loss, approximately 15% to 20% of excess weight (16). These programs involve modifications to the diet, including a daily caloric goal (1,200 kcals/day) and an emphasis on making dietary choices that improve the nutrient quality of the diet. Such dietary modifications fit the definition of “dieting,” because intake falls below energy requirements, producing a negative energy-balance state.

With these types of interventions it might be expected that eating disorder symptoms would increase as children lose weight, due to the increase in dietary restraint required to meet the caloric prescription. Several studies have assessed eating pathology in overweight children (aged 7 to 17 years) receiving these behavioral interventions. Although all of these investigations reported significant weight reductions, indicating significant decreases in energy intake, no increases in eating pathology were found.

For example, one study found a significant decrease in eating disorder pathology (17), and another found no change in pathology (18) at the completion of treatment. Epstein and colleagues (19) followed 8- to 12-year-old children over 2 years, which included 6 months of treatment, and found no change in disordered eating. Braet and Winckel (20) followed children, aged 7 to 17 years, who

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received approximately four months of treatment, over four years and observed no change in emotional eating. This study did find that five children had an elevated score on the Bulimia subscale Eating Disorders Inventory at a 4-year follow-up, but three of the five children with elevated scores had been in the advice-only arm. While these studies did not find increases in eating pathology, it is important to note that they were not designed to test the relationship between dieting and binge eating, but instead were measuring potential changes in eating pathology during participation in a family-based behavioral pediatric weight control intervention.

Randomized Trials on Caloric Reduction and Eating Pathology

To better examine the relationship between objective consistent reductions in energy intake and development of eating disorder symptoms, several randomized trials have involved overweight females (21,22), non-obese females (23), and females with full- and sub-threshold bulimia nervosa (24). Results from all of these studies revealed that significant weight reductions occurred among participants who followed a calorie reduction plan versus control participants who did not follow such a plan. Furthermore, no change or significant reductions in eating pathology occurred in the group receiving the calorie reduction plan compared with the control group.

In one of these trials, Wadden and colleagues (21) examined the influence of different degrees of caloric reduction on development of eating pathology. Obese women were randomly assigned to one of three 40-week interventions: 1) a 1,000 kcal/day diet that included 4 servings/day of a liquid meal replacement for 14 weeks, followed by a 1,200 to 1,500 kcal/day balanced diet consisting of conventional foods (MR); 2) a 1,200 to 1,500 kcal/day balanced diet consisting of conventional foods for 40 weeks (BDD); or 3) a nondieting approach for 40 weeks that discouraged reducing caloric intake and instead encouraged participants to eat every 4 hours, consume whatever foods were desired to eliminate the notion of “bad” foods, stop eating when full (ND). Eating disorder symptoms were assessed using the Eating Disorder Examination administered by practitioners blinded to conditions. Dietary restraint, disinhibition, mood, self-esteem, and body image dissatisfaction also were measured.

Results showed that at week 40, significant weight losses occurred in the MR and BDD groups (-11.5% and -8.4%, respectively), but weight loss was not significant in the ND group (-0.8%). Weight loss outcomes also matched changes in dietary restraint, which significantly increased in the MR and BDD groups but not in the ND group. At week 40, no difference was found

among the three interventions in objective bulimic episodes (eating episodes meeting the quantity of food consumed and loss of control criteria for binge eating). Additionally, subjective bulimic episodes (episodes not meeting quantity of food consumed criterion, but meeting loss of control criterion for binge eating) and objective overeating episodes (episodes meeting quantity of food consumed criterion but not the loss of control criterion for binge eating) did not change over the course of the study. Moreover, disinhibition, poor self-esteem, and negative body image significantly decreased in all groups (MR, BDD, and ND), with no differences noted. In addition, symptoms of depression significantly declined in the MR and BDD groups, but not in the ND group. Thus, participants receiving the MR and BDD interventions lost a significant amount of weight and significantly improved in eating pathology variables, providing

“These studies found that restrained eaters...showed an increase in eating when restraint was overridden.”
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no evidence for a link between dieting that reduces intake enough to produce significant weight loss and development of eating pathology.

Explaining the Mixed Findings

Stice et al (22-25) have proposed several reasons for the inconsistent findings from prospective versus experimental weight loss studies on eating pathology. According to one explanation, the measures of “dieting” and dietary restraint used in the prospective studies do not actually measure an achievement of negative energy balance. Studies examining what self-reported dieting means to adults and adolescent females indicates that “dieting” has many different interpretations (e.g., eating less, increasing fruits and vegetables) to participants (26,27), and it has long been proposed that the main measures of restraint—the Restraint Scale (28), the restraint subscale of the Three Factor Eating Questionnaire (29), and the Dutch Restrained Eating Scale (30)—measure different constructs (31). Furthermore, these tools may not adequately differentiate individuals who are at a negative energy balance (as shown by objective weight loss) from individuals who are eating less than they want to eat but have not reduced intake enough to be in negative energy balance, and are thus in a “perceived deprivation” state—a type of psychological rather than physiological hunger (32).

Another explanation for the mixed results is that an unmeasured third variable is responsible for the relationship found in the observational studies (25). In contrast to observational studies, randomized experiments are better able to rule out third-variable explanations and draw causal relationships between

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variables, thereby providing the strongest data from which evidence based practices are developed. Therefore, it has been proposed that the observational studies may be measuring a relationship that begins with overconsumption and leads to “dieting” and the potential onset of eating pathology (25). In addition, experimental studies that promote a caloric reduction and consequential weight loss are based on behavioral weight loss interventions that focus on helping participants develop a healthy lifestyle; therefore, the reduction in energy intake is achieved through what are considered to be healthy dietary changes (16,33). Potentially, unhealthy dietary behaviors (e.g., fasting) may drive the relationship between dieting and eating pathology (25).

Finally, the link between dieting and binge eating may be moderated by age or body weight in such a way that it occurs only in normal-weight adolescent females and not in overweight children or adults (25).

“Potentially, unhealthy dietary behaviors (e.g., fasting) may drive the relationship between dieting and eating pathology” (25).

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Summary

Data from randomized trials indicate that providing a calorie goal to help induce a state of negative energy balance and consequential weight loss does not necessarily promote binge eating. In particular, research suggests that for overweight children and adults, reducing energy intake in such a way that can be included and maintained in a healthy lifestyle promotes weight loss and improves some aspects of eating pathology. More research is required to better understand the relationship between “dieting” and binge eating, particularly regarding the moderators and mediators that may be involved in this relationship. ◆

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Sensipar® is indicated for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis.

Important Safety Information

Significant reductions in calcium may lower the threshold for seizures. Secondary hyperparathyroidism (HPT) patients, particularly those with a history of seizure disorder, should be carefully monitored for the occurrence of low serum calcium or symptoms of hypocalcemia.

In Sensipar® postmarketing use, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia were reported in patients with impaired cardiac function. The causal relationship to Sensipar® therapy could not be completely excluded and may be mediated by reductions in serum calcium levels.

Sensipar® lowers serum calcium; therefore, it is important that patients have a serum calcium ≥ 8.4 mg/dL when initiating therapy.

Adynamic bone disease may develop if intact parathyroid hormone (iPTH) levels are suppressed below 100 pg/mL.

Patients with moderate to severe hepatic impairment should be monitored throughout treatment with Sensipar®, as cinacalcet exposure assessed by area under the curve (AUC) was higher than in patients with normal hepatic function.

Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months.

The most commonly reported side effects were nausea, vomiting, and diarrhea.

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Please see brief summary of prescribing information on next page.

Brief Summary**See package insert for full prescribing information****SENSIPAR® (cinacalcet) Tablets****INDICATIONS AND USAGE**

Sensipar® is indicated for the treatment of secondary hyperparathyroidism in patients with Chronic Kidney Disease on dialysis.

CONTRAINDICATIONS

Sensipar® is contraindicated in patients with hypersensitivity to any component(s) of this product.

WARNINGS

Seizures: In three clinical studies of CKD patients on dialysis, 5% of the patients in both the Sensipar® and placebo groups reported a history of seizure disorder at baseline. During the trials, seizures (primarily generalized or tonic-clonic) were observed in 1.4% (9/656) of Sensipar®-treated patients and 0.4% (2/470) of placebo-treated patients. Five of the nine Sensipar®-treated patients had a history of a seizure disorder and two were receiving anti-seizure medication at the time of their seizure. Both placebo-treated patients had a history of seizure disorder and were receiving anti-seizure medication at the time of their seizure. While the basis for the reported difference in seizure rate is not clear, the threshold for seizures is lowered by significant reductions in serum calcium levels. Therefore, serum calcium levels should be closely monitored in patients receiving Sensipar®, particularly in patients with a history of a seizure disorder (see PRECAUTIONS, Hypocalcemia).

Hypotension and/or Worsening Heart Failure: In postmarketing safety surveillance, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia have been reported in patients with impaired cardiac function, in which a causal relationship to Sensipar® could not be completely excluded and which may be mediated by reductions in serum calcium levels. Clinical trial data showed hypotension occurred in 7% of Sensipar®-treated patients and 12% of placebo-treated patients, heart failure occurred in 2% of both Sensipar®- and placebo-treated patients.

PRECAUTIONS**General**

Hypocalcemia: Sensipar® lowers serum calcium, and therefore patients should be carefully monitored for the occurrence of hypocalcemia. Potential manifestations of hypocalcemia include paresthesias, myalgias, cramping, tetany, and convulsions. Sensipar® treatment should not be initiated if serum calcium is less than the lower limit of the normal range (8.4 mg/dL). Serum calcium should be measured within 1 week after initiation or dose adjustment of Sensipar®. Once the maintenance dose has been established, serum calcium should be measured approximately monthly (see DOSAGE AND ADMINISTRATION). If serum calcium falls below 8.4 mg/dL but remains above 7.5 mg/dL, or if symptoms of hypocalcemia occur, calcium-containing phosphate binders and/or vitamin D sterols can be used to raise serum calcium. If serum calcium falls below 7.5 mg/dL, or if symptoms of hypocalcemia persist and the dose of vitamin D cannot be increased, withhold administration of Sensipar® until serum calcium levels reach 8.0 mg/dL, and/or symptoms of hypocalcemia have resolved. Treatment should be re-initiated using the next lowest dose of Sensipar® (see DOSAGE AND ADMINISTRATION). In the 26-week studies of patients with CKD on dialysis, 66% of patients receiving Sensipar® compared with 25% of patients receiving placebo developed at least one serum calcium value < 8.4 mg/dL. Less than 1% of patients in each group permanently discontinued study drug due to hypocalcemia. Sensipar® is not indicated for CKD patients not on dialysis. In CKD patients with secondary HPT not on dialysis, the long-term safety and efficacy of Sensipar® have not been established. Clinical studies indicate that Sensipar®-treated CKD patients not on dialysis have an increased risk for hypocalcemia compared to Sensipar®-treated CKD patients on dialysis, which may be due to lower baseline calcium levels. In a phase 3 study of 32 weeks duration and including 404 subjects (302 cinacalcet, 102 placebo), in which the median dose for cinacalcet was 60 mg at the completion of the study, 80% of Sensipar®-treated patients experienced at least one serum calcium value < 8.4 mg/dL compared to 5% of patients receiving placebo.

Adynamic Bone Disease: Adynamic bone disease may develop if iPTH levels are suppressed below 100 pg/mL. One clinical study evaluated bone histomorphometry in patients treated with Sensipar® for one year. Three patients with mild hyperparathyroid bone disease at the beginning of the study developed adynamic bone disease during treatment with Sensipar®. Two of these patients had iPTH levels below 100 pg/mL at multiple time points during the study. In the three 6-month, phase 3 studies conducted in CKD patients on dialysis, 11% of patients treated with Sensipar® had mean iPTH values below 100 pg/mL during the efficacy-assessment phase. If iPTH levels decrease below the NKF-K/DOQI recommended target range (150–300 pg/mL)* in patients treated with Sensipar®, the dose of Sensipar® and/or vitamin D sterols should be reduced or therapy discontinued.

Hepatic Insufficiency: Cinacalcet exposure as assessed by AUC_{0-48h} in patients with moderate and severe hepatic impairment (as indicated by the Child-Pugh method) were 2.4 and 4.2 times higher, respectively, than that in normals. Patients with moderate and severe hepatic impairment should be monitored throughout treatment with Sensipar® (see CLINICAL PHARMACOLOGY, Pharmacokinetics and DOSAGE AND ADMINISTRATION). **Information for Patients:** It is recommended that Sensipar® be taken with food or shortly after a meal. Tablets should be taken whole and should not be divided.

Laboratory Tests: Patients with CKD on Dialysis with Secondary Hyperparathyroidism:

Serum calcium and serum phosphorus should be measured within 1 week and iPTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®.

Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months (see DOSAGE AND ADMINISTRATION). All iPTH measurements during the Sensipar® trials were obtained using the Nichols IRMA. In patients with end-stage renal disease, testosterone levels are often below the normal range. In a placebo-controlled trial in patients with CKD on dialysis, there were reductions in total and free testosterone in male patients following six months of treatment with Sensipar®. Levels of total testosterone decreased by a median of 15.8% in the Sensipar®-treated patients and by 0.6% in the placebo-treated patients. Levels of free testosterone decreased by a median of 31.3% in the Sensipar®-treated patients and by 16.3% in the placebo-treated patients.

The clinical significance of these reductions in serum testosterone is unknown. **Drug Interactions and/or Drug/Laboratory Test Interactions:** See CLINICAL PHARMACOLOGY, Pharmacokinetics and Drug Interactions. Effect of Sensipar® on other drugs: Drugs metabolized by cytochrome P450 2D6 (CYP2D6): Sensipar® is a strong in vitro, as well as in vivo, inhibitor of CYP2D6. Therefore, dose adjustments of concomitant medications that are predominantly metabolized by CYP2D6 (e.g., metoprolol and carvedilol) and particularly those with a narrow therapeutic index (e.g., flecaïnide, vinblastine, thioridazine and most tricyclic antidepressants) may be required. Desipramine: Concurrent administration of cinacalcet (90 mg) with desipramine (50 mg) increased the exposure of desipramine by 3.6 fold in CYP2D6 extensive metabolizers. Amitriptyline: Concurrent administration of 25 mg or 100 mg cinacalcet with 50 mg amitriptyline increased amitriptyline exposure and nortriptyline (active metabolite) exposure by approximately 20% in CYP2D6 extensive metabolizers. Midazolam: There were no significant differences in the pharmacokinetics of midazolam, a CYP3A4 and CYP3A5 substrate, in subjects receiving 90 mg cinacalcet once daily for 5 days and a single dose of 2 mg midazolam on day 5 as compared to those of subjects receiving 2 mg midazolam alone. This suggests that cinacalcet would not affect the pharmacokinetics of drugs predominantly metabolized by CYP3A4 and CYP3A5. Effect of other drugs on Sensipar®: Sensipar® is metabolized by multiple cytochrome P450 enzymes, primarily CYP3A4, CYP2D6, and CYP1A2. Ketoconazole: Sensipar® is metabolized in part by CYP3A4. Co-administration of ketoconazole, a strong inhibitor of CYP3A4, increased cinacalcet exposure following a single 90 mg dose of Sensipar® by 2.3 fold. Dose adjustment of Sensipar® may be required and PTH and serum calcium concentrations should be closely monitored if a patient initiates or discontinues therapy with a strong CYP3A4 inhibitor (e.g., ketoconazole, erythromycin, itraconazole; see DOSAGE AND ADMINISTRATION).

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Carcinogenicity:

Standard lifetime dietary carcinogenicity bioassays were conducted in mice and rats. Mice were given dietary doses of 15, 50, 125 mg/kg/day in males and 30, 70, 200 mg/kg/day in females (exposures up to 2 times those resulting with a human oral dose of 180 mg/day based on AUC comparison). Rats were given dietary doses of 5, 15, 35 mg/kg/day in males and 5, 20, 35 mg/kg/day in females (exposures up to 2 times those resulting with a human oral dose of 180 mg/day based on AUC comparison). No increased incidence of tumors was observed following treatment with cinacalcet. **Mutagenicity:** Cinacalcet was not genotoxic in the Ames bacterial mutagenicity assay or in the Chinese Hamster Ovary (CHO) cell HGprt forward mutation assay and CHO cell chromosomal aberration assay, with and without metabolic activation or in the *in vivo* mouse micronucleus assay. **Impairment of Fertility:** Female rats were given oral gavage doses of 5, 25, 75 mg/kg/day beginning 2 weeks before mating and continuing through gestation day 7. Male rats were given oral doses 4 weeks prior to mating, during mating (3 weeks) and 2 weeks post-mating. No effects were observed in male or female fertility at 5 and 25 mg/kg/day (exposures up to 3 times

those resulting with a human oral dose of 180 mg/day based on AUC comparison). At 75 mg/kg/day, there were slight adverse effects (slight decreases in body weight and food consumption) in males and females. **Pregnancy Category C:** In pregnant female rats given oral gavage doses of 2, 25, 50 mg/kg/day during gestation no teratogenicity was observed at doses up to 50 mg/kg/day (exposure 4 times those resulting with a human oral dose of 180 mg/day based on AUC comparison). Decreased fetal body weights were observed at all doses (less than 1 to 4 times a human oral dose of 180 mg/day based on AUC comparison) in conjunction with maternal toxicity (decreased food consumption and body weight gain). In pregnant female rabbits given oral gavage doses of 2, 12, 25 mg/kg/day during gestation no adverse fetal effects were observed (exposures less than with a human oral dose of 180 mg/day based on AUC comparisons). Reductions in maternal food consumption and body weight gain were seen at doses of 12 and 25 mg/kg/day. In pregnant rats given oral gavage doses of 5, 15, 25 mg/kg/day during gestation through lactation no adverse fetal or pup (post-weaning) effects were observed at 5 mg/kg/day (exposures less than with a human therapeutic dose of 180 mg/day based on AUC comparisons). Higher doses of 15 and 25 mg/kg/day (exposures 2-3 times a human oral dose of 180 mg/day based on AUC comparisons) were accompanied by maternal signs of hypocalcemia (peri-parturient mortality and early postnatal pup loss), and reductions in postnatal maternal and pup body-weight gain. Sensipar® has been shown to cross the placental barrier in rabbits. There are no adequate and well-controlled studies in pregnant women. Sensipar® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Lactating Women:** Studies in rats have shown that Sensipar® is excreted in the milk with a high milk-to-plasma ratio. It is not known whether this drug is excreted in human milk. Considering these data in rats and because many drugs are excreted in human milk and because of the potential for clinically significant adverse reactions in infants from Sensipar®, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the lactating woman. **Pediatric Use:** The safety and efficacy of Sensipar® in pediatric patients have not been established. **Geriatric Use:** Of the 1136 patients enrolled in the Sensipar® phase 3 clinical program, 26% were ≥ 65 years old, and 9% were ≥ 75 years old. No differences in the safety and efficacy of Sensipar® were observed in patients greater or less than 65 years of age (see DOSAGE AND ADMINISTRATION, Geriatric Patients).

ADVERSE EVENTS

Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease on Dialysis: In 3 double-blind placebo-controlled clinical trials, 1126 CKD patients on dialysis received study drug (656 Sensipar®, 470 placebo) for up to 6 months. The most frequently reported adverse events (incidence of at least 5% in the Sensipar® group and greater than placebo) are provided in Table 1. The most frequently reported events in the Sensipar® group were nausea, vomiting, and diarrhea.

Table 1. Adverse Event Incidence (≥ 5%) in Patients On Dialysis

Event*	Placebo n=470 (%)	Sensipar® n=656 (%)	Event*	Placebo n=470 (%)	Sensipar® n=656 (%)
Nausea	19	31	Hypertension	5	7
Vomiting	15	27	Asthenia	4	7
Diarrhea	20	21	Anorexia	4	6
Myalgia	14	15	Pain Chest, Non-Cardiac	4	6
Dizziness	8	10	Access Infection	4	5

*Included are events that were reported at a greater incidence in the Sensipar® group than in the placebo group.

The incidence of serious adverse events (29% vs. 31%) was similar in the Sensipar® and placebo groups, respectively. **12-Month Experience with Sensipar®:** Two hundred and sixty-six patients from 2 phase 3 studies continued to receive Sensipar® or placebo treatment in a 6-month double-blind extension study (12-month total treatment duration). The incidence and nature of adverse events in this study were similar in the two treatment groups, and comparable to those observed in the phase 3 studies. **Postmarketing Experience with Sensipar®:** Rash, hypersensitivity, diarrhea and myalgia have been identified as adverse reactions during post-approval use of Sensipar®. Isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia have been reported in Sensipar®-treated patients with impaired cardiac function in postmarketing safety surveillance. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. **Laboratory Values:** Serum calcium levels should be closely monitored in patients receiving Sensipar® (see PRECAUTIONS and DOSAGE AND ADMINISTRATION).

OVERDOSAGE

Doses titrated up to 300 mg once daily have been safely administered to patients on dialysis. Overdosage of Sensipar® may lead to hypocalcemia. In the event of overdosage, patients should be monitored for signs and symptoms of hypocalcemia and appropriate measures taken to correct serum calcium levels (see PRECAUTIONS). Since Sensipar® is highly protein bound, hemodialysis is not an effective treatment for overdosage of Sensipar®.

DOSAGE AND ADMINISTRATION

Sensipar® tablets should be taken whole and should not be divided. Sensipar® should be taken with food or shortly after a meal. Dosage must be individualized. **Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease on Dialysis:** The recommended starting oral dose of Sensipar® is 30 mg once daily. Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®. Sensipar® should be titrated no more frequently than every 2 to 4 weeks through sequential doses of 60, 90, 120, and 180 mg once daily to target iPTH consistent with the NKF-K/DOQI recommendation for CKD patients on dialysis of 150–300 pg/mL. PTH levels should be assessed no earlier than 12 hours after dosing with Sensipar®. Sensipar® can be used alone or in combination with vitamin D sterols and/or phosphate binders. During dose titration, serum calcium levels should be monitored frequently and if levels decrease below the normal range, appropriate steps should be taken to increase serum calcium levels, such as by providing supplemental calcium, initiating or increasing the dose of calcium-based phosphate binder, initiating or increasing the dose of vitamin D sterols, or temporarily withholding treatment with Sensipar® (see PRECAUTIONS).

Special Populations: Geriatric patients: Age does not alter the pharmacokinetics of Sensipar®; no dosage adjustment is required for geriatric patients. **Patients with renal impairment:** Renal impairment does not alter the pharmacokinetics of Sensipar®; no dosage adjustment is necessary for renal impairment. **Patients with hepatic impairment:** Cinacalcet exposures, as assessed by AUC_{0-48h}, in patients with moderate and severe hepatic impairment (as indicated by the Child-Pugh method) were 2.4 and 4.2 times higher, respectively, than that in normals. In patients with moderate and severe hepatic impairment, PTH and serum calcium concentrations should be closely monitored throughout treatment with Sensipar® (see CLINICAL PHARMACOLOGY, Pharmacokinetics and PRECAUTIONS). **Drug Interactions:** Sensipar® is metabolized in part by the enzyme CYP3A4. Co-administration of ketoconazole, a strong inhibitor of CYP3A4, caused an approximate 2-fold increase in cinacalcet exposure. Dose adjustment of Sensipar® may be required and PTH and serum calcium concentrations should be closely monitored if a patient initiates or discontinues therapy with a strong CYP3A4 inhibitor (e.g., ketoconazole, erythromycin, itraconazole; see CLINICAL PHARMACOLOGY, Pharmacokinetics and PRECAUTIONS).

Storage: Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F). [See USP controlled room temperature]. Rx Only: This product, or its use, may be covered by one or more US Patents including US Patent Nos. 6313146, 6211244, 6031003 and 6011068, in addition to others, including patents pending.

References: 1. National Kidney Foundation: K/DOQI clinical practice guidelines: bone metabolism and disease in chronic kidney disease. American Journal of Kidney Disease 42:S1-S201, 2003



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Renal Dietitians Chair Message

Patricia Williams, RD, CSR, LDN

RPG Chair



I want to extend a welcome to those who have joined the Renal Dietitians Dietetic Practice Group (RPG) this year or are renewed members. At the writing of this message, we are 2152 members strong. I am excited that even in tight economic times you see the value of continuing your membership in RPG.

The 2009 American Dietetic Association Food & Nutrition Conference & Expo in Denver took place in late October and I know many of you made plans to attend. I hope each of you took the opportunity to attend the session, Using the Malnutrition Inflammation Scoring System with Renal Patients presented by Deborah Benner, MA, RD, CSR and Kamyar Kalantar-Zadeh, MD, PhD, MPH, FAAP, FACP, FASN, FAHA. This session was an introduction to the Malnutrition Inflammation Scoring scale being used in the assessment of the nutritional status of patients on dialysis. This assessment tool incorporates various components to calculate an actual score that reflects the nutritional risk. Also, thanks to those who visited the RPG booth at the DPG-MIG Showcase. We enjoyed getting to meet and talk with you.

John F. Kennedy said, "Change is the law of life. And those who look only to the past or present are certain to miss the future." I feel like we can truly say that change has been a big part of all our lives this past year with one of the greatest changes being the recession. I don't think I had a clue that in such a short time so many people would have their lives changed so drastically. I know that many of the companies that you work for are cutting back on spending and part of the decreased budgets are in the area of

continuing professional education. I have heard some dietitians say they are unsure how they will be able to get the seventy-five hours of continuing professional education if they are not able to attend national meetings or travel to other cities or states for learning opportunities.

The *Renal Nutrition Forum* offers members the opportunity to get a minimum of twelve hours per year of continuing professional education, completed on your own time frame, without travel and at no added expense. Completion of the CPEUs is also offered online on RPG's Web site, www.renalnutrition.org. Articles are written by leaders in our profession on a wealth of topics. Our editorial staff is always looking for cutting edge topics and information to help us constantly improve our skills and widen our knowledge base.

This year the RPG will also be offering the Certified Specialist in Renal Nutrition Review Course in the winter and spring of 2010 as a series of webinars. In the past, the course had been held in one city on one day, with eight hours of intense review and one choice of review topics. The plan is to offer the same review topics, but they will be offered two at a time on three different days. This will allow you to take part in one or all three webinars no matter where you live. The webinars will cut out the need for travel, hotel, and food expenses and best of all—the dress is pajama casual (that is if you are not doing the webinar at work!). The webinar sessions will begin in February and end during the early part of April.

Yes, change is inevitable. It can be good or it can be unpleasant. I think the changes you will see in RPG will be very good changes. I am excited and I hope you are or will be as well. ◆

National Kidney Foundation (NKF)

2010 Spring Clinical Meetings

Walt Disney World Swan and Dolphin, Orlando, FL

April 13-17, 2010

Join more than 2,000 kidney health care professionals at the NKF 2010 Spring Clinical Meetings, for a carefully designed curriculum of information-filled courses, practical workshops, thought-provoking symposia and insightful debates. The Meetings' focus on clinical practice in nephrology will include important "take home" messages for daily applications in your practice setting. Engage in stimulating activities for new, non-renal and advanced practice dietitians. Don't miss the latest information on Medical Nutrition

Therapy for CKD, clinical privileging, standards of performance and the new CMS guidelines, new research including FGF-23, Nutrigenomics, Bariatric Surgery and Obesity! Catch sessions on Nephrology Medications, Alternative Medicine: Meditation/Yoga, Herbs, and AKI and CKD.

For more information regarding SCM10,
visit us online at www.nkfclinicalmeetings.org

CRN Chairperson Message

Karen Wiesen, MS, RD, LD

CRN Chair

As you read this, autumn has already arrived, but it has been a busy spring and summer. I would like to update the Renal Dietitians Dietetic Practice Group (RPG) membership on several projects on which the American Dietetic Association (ADA) Renal Dietitians Dietetic Practice Group and the Council on Renal Nutrition (CRN) have been working. Some are joint RPG/CRN efforts.

New Medicare Chronic Kidney Disease (CKD) Education

The Medicare Improvements for Patients and Providers Act of 2008 (MIPPA) includes a new benefit for individuals with Stage 4 CKD who are entitled to Medicare coverage. Effective January 1, 2010, this new benefit enables Medicare eligible individuals to participate in education to prepare for possible renal replacement therapy. Beneficiaries may receive up to six sessions of kidney disease education services. The referring physician and patient determine if the education will occur in group or individual sessions. One of the topics the Centers for Medicare & Medicaid Services (CMS) identifies for an education program is diet, fluid restrictions and medication usage. Recall under the Medical Nutrition Therapy (MNT) Act, Medicare currently covers MNT provided to qualifying beneficiaries with a glomerular filtration rate between 13-50 mL/min/1.73m².

While registered dietitians (RD) are not listed as one of the “qualified person[s]” cited in MIPAA who can provide the CKD education, an RD employed at a rural facility approved by CMS as a “provider of services,” or one of the other qualified persons could be involved in the new education program. CMS defines “qualified person” at any of the following locations that are located in a rural area, “a hospital, critical access hospital, skilled nursing facility, home health agency, and hospice program.” Dialysis units are not considered “providers” of this education. Both CRN and ADA believe that the RD should be involved in the new education program and have provided feedback to CMS in earlier conference calls and as part of the National Kidney Foundation (NKF) response. CRN and ADA also promoted increased use of the Medicare MNT benefit for these patients due to the complexity of the renal diet. RPG is working with ADA to provide comments to CMS on the proposed regulations for CKD education. CMS will release the final rules and regulations for the CKD education program in November.

Food Labeling Recommendations

In collaboration with the ADA, NKF filed a response to the Food and Drug Administration to “Advance Notice for Proposed Rulemaking on Food Labeling” under “Food Labeling: Revision of Reference Values and Mandatory Nutrients.” The recommendation is to change the Nutrition Facts Panel by adding potassium and calcium in the actual amounts consumed in a serving. This would also make listing potassium on the Nutrition Facts Label mandatory. At that time, it was decided to limit the petition to the nutrients potassium and calcium, as this is more applicable to the general population at large and had a greater probability of garnering more support.

A Clinical Guide to Nutrition Care in Kidney Disease

Work on the revision of *A Clinical Guide to Nutrition Care in Kidney Disease* is progressing and the anticipated publication date is 2011. New additions to this revision include a section on Herbal and Alternative Medicine, MNT Protocols and the Nutrition Care Process. Editors are Laura Byham-Gray, PhD, RD, CNSD, Karen Wiesen, MS, RD, LD and Jean Stover, RD, LDN.

NKF Spring Clinical Meeting

Be sure to mark your calendars, as planning is underway for the 2010 NKF Spring Clinical Meeting to be held at Walt Disney World in Orlando, Florida on April 13-17, 2010. Marianne Hutton, RD, CSR, CDE is the CRN Program Chair and she and her committee have a great program in development. Dr. Alison Steiber, PhD, RD, LD of Case Western Reserve University was recently named to a two-year appointment as the Strategies II Course Director. Strategies II is the advanced practice Spring Clinical Meeting pre-conference workshop. We welcome Dr. Steiber to the CRN Executive Committee.

Please contact me at kwiesen@dom.wustl.edu if you have questions about any of these projects. ◆

Standards of Practice and Standards of Professional Performance for RDs in Nephrology Care

are now available on the RPG Web site.

www.renalnutrition.org

2009-2010 RPG Executive Committee

Mission: Renal dietitians dietetic practice group is leading the future of dietetics by promoting and supporting its members working in nephrology nutrition.

Vision: RPG members are a valued source of expertise in nephrology nutrition.

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RNF Guidelines for Authors

Article length: Article length is determined by the Editor for each specific issue. The feature article (including abstract) is approximately 3000 words (not including tables/graphs). Other articles are usually 1000-1500 words; member highlights and reports are approximately 400-500 words.

Text format: Times New Roman font, 12 point, double space.

Tables/illustrations: Tables should be self-explanatory. All diagrams, charts and figures should be camera-ready. Each should be accompanied by a title and brief caption that clearly explains the table, chart, diagram, figure, illustration, etc.

References: References should be cited in the text in consecutive order parenthetically. At the end of the text, each reference should be listed in order of citation. The format should be the same as the *Journal of the American Dietetic Association*.

Reference citation examples:

Article in periodical:

Knower WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Eng J Med*. 2002;346:393–403.

Book:

Institute of Medicine. *Dietary Reference Intakes: Applications for Dietary Assessment*. Washington, DC.: National Academy Press; 2001.

Chapter in a book:

Walsh J. Which insulin to use and how to start. In: *Using Insulin*. San Diego, Calif.: Torry Pines Press; 2003.

Web site:

Medscape drug info. Available at www.medscape.com/druginfo. Accessed Feb. 3, 2004.

Author information: List author with first name, middle initial (if any), last name, professional suffix and affiliation below the title of the article. Also include the primary author's complete contact information including affiliation, phone, fax and email address.

All submissions for publication should be submitted to the editor as an email attachment (MS Word file). The feature articles from the Renal Nutrition Forum will be posted on the Members Only Section of the RPG website (password protected). Thus, please include a brief abstract along with feature article submissions.

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