CADTH

CADTH COMMON DRUG REVIEW

Patient Input

sucroferric oxyhydroxide (Velphoro)
(Vifor Fresenius Medical Care Renal Pharma)

Indication: Hyperphosphatemia, end-stage renal disease

CADTH received patient input for this review from:
Canadian Organization for Rare Disorders

June 29, 2018

Patient Group | Canadian Organization for Rare Disorders

1. About Your Patient Group

The Canadian Organization for Rare Disorders is registered charity that provides a strong common voice to advocate for health policy and a healthcare system that works for those with rare disorders. CORD provides education and resources to patient groups to enable them to better meet their members' needs.

2. Information Gathering

This submission summarizes the perspectives of individuals and caregivers with chronic kidney disease (CKD) undergoing dialysis affected by hyperphosphatemia. Information was collected by the Canadian Organization from several sources: directly through one-on-one individual patient interviews, in-person and web-based focus groups, and email exchanges with individual patients and caregivers. We also gathered indirect patient information through interviews with clinicians and dietitians working patients with CKD on dialysis.

We could not identify a Canadian dialysis patient group (either in-person or web-based support group), and while there is a Canadian kidney association, they did not have a database specific for the dialysis community. Moreover, while there are many dialysis clinics, it was not possible within the time available to get permission to conduct interviews or surveys with patients at the clinics. Finally, because we could not identify any Canadian patients who had personal experience with sucroferric oxyhydroxide (Velphoro), we chose to solicit patients with Velphoro experience from the USA where Velphoro has been used for several years.

Starting with individual interviews with two clinicians and one dietitian in the USA, we requested referrals to individual patients with experience with Velphoro as well as other phosphate binders. We also posted requests into two Facebook groups specific to dialysis patients, asking any patient who had experience with Velphoro and or other phosphate binders (PBs) to contact CORD through our info@raredisorders.ca email account.

In Canada, we spoke with three clinicians treating dialysis patients. In addition, we interviewed six dialysis patients known to us from an Ontario complex diabetes clinic and using a "snowballing technique" were able to connect with 22 other patients, in person, by telephone or by email.

Each individual interview lasted between 15 to 60 minutes, with most lasting 20 to 30 minutes. Two small-group interviews lasted about 60 minutes.

Overall, we contacted 124 persons whose responses are included in this submission. Among these, 105 were patients on dialysis and 19 were caregivers. In terms of location, 96 were from the USA and 28 were patients living in Canada, specifically 20 in Ontario, six in BC, and two in Alberta. Patients ranged in age from 29 to 71 years and had been on hemodialysis, ranging from approximately 2 to 10 years. Overall, 60% (65) patients were males while 80% (15) of caregivers responding were female. All the patients and caregivers with direct experience with Velphoro were living in the USA while the Canadian patients had experience only with other phosphate binders. All individual and group interviews were conducted in English by the same interviewer.

Given the short timeframe that we had to locate respondents, conduct interviews, and analyze the data, we could not do a proper qualitative analysis. Instead, for each individual or small group interview, we listed all of the comments and then sorted the comments by theme: experience of dialysis, experience and perceptions about hyperphosphatemia, experience of managing diet (for phosphorous content), experience of managing phosphate binders, overall adherence to phosphate management regimen, overall impact of kidney disease and dialysis on quality of life (work, family, and social relations; independence, depression), and overall impact of phosphate medicines on quality of life.

3. Disease Experience

Because the focus of the submission is response to phosphate binders, we chose not to dwell on the respondents' experience and quality of life specific to their kidney disease and/or dialysis except as a context for our understanding of their experience in managing hyperphosphatemia and use of phosphate binders. One challenge affecting their experience of the condition is that phosphorus overload, per se, is usually not symptomatic; however associated conditions (low calcium levels) may cause symptoms that could be credited to elevated phosphorous (itching, painful sores, brittle bones). Patients were often only aware of their phosphorus levels when they were tested and received their "numbers" at clinic. The experience of their condition was the burden of managing phosphorus levels, specifically through diet and medication.

Therefore, based on our literature review and expert interviews, we asked about four issues: (1) personal knowledge about and risk for elevated phosphorus levels; (2) personal experience of elevated phosphorous levels; (3) strategies for reducing phosphorous levels (maintaining balance) through diet and mediation; and (4) success and challenges with all of the phosphate binders they have used. For patients with experience with Velphoro, we asked them to describe, separately, their experience with other phosphate binders and their experience with Velphoro (good and bad).

We analyzed (listed, sorted, and categorized) the responses from the Canadian interviews separately from the USA responses. While there were differences in the frequency of some of the issues expressed, there were no discernible differences in the lists generated for each cohort. Similarly, there were no differences in the overarching themes and categories. The key difference was that the Canadian respondents had no experience with iron-based PBs. Finally, because the number of participants in each cohort was small and because there were no significant differences between the cohorts, we have presented their combined responses in this section.

All of the participants were aware of hyperphosphatemia (elevated phosphorous levels) as a potential consequence of their kidney disease but only one (and maybe two) had experienced serious consequences (severe chest pain and muscle cramping) that they were told could be due to phosphorous overload. About one-fifth (25) said they had experienced some symptoms that they believed were caused by high phosphorus levels. These (not in order of seriousness or frequency) included itching, tingling sensations on skin or extremities, fatigue, shortness of breath, nausea, muscle pain, muscle cramping, and "pain in the bone." They reported that these symptoms usually subsided over time or were resolved when they were paid attention to avoiding "phosphorous-rich foods" and/or taking their medicines (phosphate binders) regularly.

All participants raised concerns about the challenge of managing phosphorous levels, with about three- fourths of the comments related to the medications used to eliminate phosphate. Patients said the number of pills that needed to be taken was a "burden" and the fact that they needed to be taken at mealtime and sometimes spaced throughout the meal were added challenges. "At every single meal, I have to remember to take a pill before I start eating and then to take another during the meal and sometimes a third pill. This is really annoying when you're eating out." "My numbers kept going up and my doctor accused me of not taking my pills but I knew I was, sometimes up to six a meal. Then she asked what I was drinking and explained that I had to take a pill if I was drinking certain beverages, like Coke or waters flavored with fruit juice or bottled iced tea with lemon. Who knew." "My husband was taking upwards of 15 pills, two different kinds, three to five per meal, spaced out. If I wasn't right there, I know he just took them randomly and missed most."

Patients also complained about trying to adjust the number of pills when they varied their diet (taking more dairy, meat, soda, fruits, or other foods with high levels of phosphorous) or needing to change the quantity or frequency whenever they had their phosphorous levels checked. "The dietitian would say my levels were too high and I needed to cut back on foods with protein which also had phosphorous. That meant keeping a list, and I would try for a while but sometimes when you're with other people, it is hard not to have what they're having."

Finally, when asked about the overall burden of managing their phosphorous levels relative to managing dialysis and any other underlying health conditions, the responses varied. About one-fourth said it was a minor concern even though they realized there were potentially serious complications. "I am on dialysis three days a week for four hours at a time. Actually it takes up the whole day when you include the travel and set-up time. I can't travel very far from home. So dialysis pretty much

runs my life and my wife's life. The good news is that dialysis lowers my phosphorous levels so I don't have to be as careful about what I eat or my medicines on the days when I do dialysis. I don't know if that is really true but that is what I think."

"I had a pretty bad scare with really high phosphorous numbers a few months back and now I am always checking the phosphorous in foods and am very careful about taking my meds. I am also making sure I get enough calcium so I pretty much stick to a few foods that I know work for me."

In summary, the experience of hyperphosphatemia focused on managing phosphorus levels, primarily through diet and medication. This is analogous to the challenge for patients with diabetes except that patients do not experience any immediate symptoms if they are not adherent and they cannot immediately access their phosphorous numbers to know whether they are in range. This leads to feelings of anxiety and stress but also feelings of guilt since most acknowledge they are not totally compliant with either diet or pill

4. Experiences with Currently Available Treatments

Most patients had experience with more than one type of phosphate binder (PB). Given the heterogeneity of the respondents, we did not attempt to categorize responses by patient characteristics but summarized the responses across all patients and caregivers.

All patients were taking some form of PB at the time of the interview. About 82% (102) of all respondents (USA and Canada) had or were currently taking a calcium-based phosphate binder. Among the USA patients, about 23% (22) were taking a calcium-based PB either as their only PB or in combination with a non-calcium PB. Among Canadian patients, 68% (22) were taking a calcium PB either as single medicine or in combination with another non-calcium PB. The difference may be due to difference in practice or reflect our deliberate solicitation of patients from the USA with Velphoro experience. Among patients in the USA, 68% (62) had in the past or were currently taking Velphoro, most as the only PB but 10 patients reported they were also using something else, either at the same time or switching between the medicines. Two of the (USA) patients were taking Aruxyia (ferric citrate) but none of the other patients had any experience with this PB. Similarly, two USA patients were taking lathanum carbonate but none of the other patients reported experience with this PB.

The types of PBs cited as previously or currently used by respondents included: calcium acetate (PhosLo or EliphosT), calcium carbonate (Tums), sevelamer (Renagel or Renvela), lathanum carbonate (Fosrenol), sucroferric oxyhydroxide (Velphoro) and ferric citrate (Auryxia), although none of the Canadian patients have had experience with either of the iron PBs (Velphoro and Auryxia).

Current therapies that are not iron-based: The issue most frequently expressed by all respondents across all types of PBs was the "pill burden", that is, the number of pills that needed to be taken daily, coupled with the disruptive schedule (before and during meals). This complaint was common for all calcium based PBs as well as sevelamer. Almost all respondents (about 90%) said they had been nonadherent to their PB regimen when they had to take more than one pill per meal (skipped one or more pills at some meals). The reason most frequently given for nonadherence was that they "forgot" either before or during the meal. "If I could just take [the PBs] once or twice a day same as the diabetes, heart, and other medications, it would be a lot easier to remember." "I sometimes notice that my husband is not taking his medicine during the meal but he gets annoyed when I remind him, especially when there are other people there."

More than half (55%) volunteered that they sometimes deliberately chose not to take their medicines. "I figure when I have just had four hours of dialysis, that should be enough to get rid of extra phosphorous, so I often don't bother on those days." "I know that when I'm eating foods, like chicken or salmon, which are high in protein but low in phosphorous, I don't need to take the [PBs] or at least not all of them for that meal."

Across all PBs, the symptoms most often mentioned were GI issues. About one-fifth of participants describing their experience with calcium-based PBs mentioned GI issues (constipation and nausea) while more than half (55%) in describing experiences with sevelamer mentioned nausea and vomiting as well as diarrhea, constipation, and stomach bloating. The number of patients who had experienced lathanum was too small to meaningfully summarize their experiences. In some

cases, GI problems were episodic. “For a while I am fine and then the next month I get regular stomach upsets and diarrhea; it doesn’t seem to have anything to do with what I eat so I don’t feel I can predict or control the problems.” About three- fourths of the patients on sevelamer who said they experienced GI side effects reported that the issues were manageable (not severe and not frequent) or they were resolved (reduced) over time. One patient who was having GI events said her physician suggested she go back to calcium carbonate and then swaps them out for sevelamer for just one meal a day. If that worked, substitute for another meal and build up to full dosage of sevelamer. And it worked; no more bloating or diarrhea.” Other patients reported that they switched from sevelamer to another PB, that is, back to calcium-based PB or to a (newly available) iron-based PB. Some patients said their physicians decided to switch them to another drug,

Other symptoms mentioned infrequently (one to five times each) were itching, fatigue; anemia, weakness but patients were not sure whether these were attributable to the PB, dialysis, or the underlying health condition.

Most patients expressed the challenge of getting the dosage right. “I don’t know how they can be working one month and then not the next.” “I doubled the number of pills at each meal and the levels still didn’t go down.” “I gradually increased to four pills per meal which seemed to work on my phosphorous levels but I had constipation much of the time. So I started taking a stool softener and then I cut back the Renvela to two pills and added two Tums. This combination seems to be working for now.”

Among the 62 patients with Velphoro experience, about 80% (50) reported they were still taking this PB, either alone or with another PB. All of the patients in the USA who had or were currently taking Velphoro remarked on the benefit of having significantly fewer pills. “It was so much easier to remember one pill at the beginning of the meal.” “I went from 9 to 12 pills a day to just 3. This I can do!” Some remarked on the consistency and flavour. “It’s easy to chew and has a nice berry flavour.” Others voiced a different response. “It breaks down into a sticky paste and sometimes sticks to your dentures for a while. If you are going out, carry a toothbrush.” “It has a rather sickly sweet berry flavour. But you get used to it.” “I don’t feel as self-conscious when I’m eating out and don’t have to explain why I’m taking pills throughout the meal.” “I feel I can leave my husband to eat on his own without constantly nagging him to take his medicines all during the meal. If I’m not there, I may just call to remind him before he eats. A lot less stress for him and for me!!”

About half of those taking Velphoro reported they had experienced some negative side effects, including itching, dry mouth, stools “as black as night”, cramps and diarrhea. For most respondents, these were usually tolerable or resolvable with other treatments (ointments or medications). About 10% complained that Velphoro did not sufficiently lower their phosphorus levels. “Even when I went up to two pills per meal, I couldn’t get the numbers down to where they used to be with Tums. It just didn’t work for me.” “I added another pill (Renvela) but it still didn’t work so I went back to Renvela and Tums. Too bad because we definitely liked the convenience of Velphoro. My physician suggests that I might try again when my levels have stabilized.”

When asked about any other changes they have experienced since they started taking Velphoro, some patients said they felt their phosphorous levels were more consistently within target. Most said that three pills a day worked for them, so they no longer had to worry about adjusting the dosage and remembering how many pills to take with each meal. Because they had more confidence in the PB, they felt they had access to a greater variety of foods and they did not have to calculate the exact phosphorous content of each item and the whole meal. “Before Velphoro, I would avoid any foods that had slightly higher phosphorous levels or I would add another pill if the count was too high. Now, I feel ‘more free’ to eat ‘food that I really like’ but had been afraid to have in the past. I still have to avoid many foods but I feel like I have a lot more options.”

Moreover, because they did not have to remember to take pills throughout the meal, participants said they actually enjoyed their meals more, had a better appetite, and ate more. “I enjoy meals with the family again.” “I am able to eat out more and I feel healthier and happier.” Finally, participants said they were less anxious because they felt their phosphorous levels and their calcium levels were “in the safe range.” “It’s just one less thing to worry about.” “I felt bad every time I had my levels checked because I knew I wasn’t eating the way I should and I wasn’t taking the pills the way I should. But I also knew if I lied about it, the doctor would just prescribe more pills and that wasn’t good. Now with Velphoro, I don’t have to lie, because I am taking my pills.”

We did not specifically probe about the cost of Velphoro but some respondents did remark on the high cost of the drug compared to their previous medicines, namely, sevelamer and calcium carbonate or acetate. While none of the patients said they stopped Velphoro because of cost, many expressed gratitude that "they (Velphoro) have a really good patient assistance program which really helps with the co-pay. Otherwise, I don't think we could do it." "It actually costs us less [out of pocket] for Velphoro than it did for Renvela."

In summary, patients on calcium-based PBs were burdened by their pill regimen, experienced relatively few GI issues but had concerns about calcium overload and anxiety about managing their phosphorous levels. Patients on sevelamer were also concerned about the pill regimen (number and dosing) and experience significant GI issues. Finally, those on Velphoro were pleased with the pill requirements, also experienced GI problems but overall reported important improvements in quality of life related to meals and stress

5. Improved Outcomes

Given that many USA patients were already on Velphoro, we decided to pose this question only to the 28 Canadian patients. Specifically, we asked them to describe what their ideal phosphate binder would be like, that is, what outcomes would they expect and specifically what would make the management easier (better or more tolerable) given the likelihood that they would have to use phosphate binders for life. If they did not mention Velphoro spontaneously, we asked whether they were aware of this drug and what their impressions were.

Among the 28 Canadian patients, 54% (15) have only had experience with calcium-based binders and the remaining 13 had in the past or currently were taking sevelamer. While all participants were aware of PBs that they did not personally have access to, only eight were aware of iron-based binders, either by name or type.

Participants said their ideal phosphate binder would be easy to manage and have few or no side effects "because dialysis is already a chore and we take a lot of other pills." "It would be great to have a pill you could take once a day, in the morning or at night when you are taking your other pills." "It would be wonderful if the pill was so effective that you wouldn't have to worry about what you were eating." "The good thing about Tums is that they are easy to take (just chew), easy to carry around, and easy to store." "Ideally, a phosphate binder should be covered by your insurance plan and any co-pay would be very little or nothing."

We provided a very brief description of Velphoro as a PB that uses iron to eliminate phosphorous, is highly effective so most people take only three pills a day (one pill before meal), has some GI side effects that are usually manageable, and has been used safely for several years by dialysis patients in other countries. All indicated this would be highly desirable and they would be interested in trying the medication. "I think the biggest difference Velphoro would make for our family is that we wouldn't feel so stressed every time we sat down to eat. It would make family dinners almost normal again, even if John couldn't eat everything."

6. Experience with Drug Under Review

None in Canada. See section 4.

7. Anything Else?

We really need to encourage companies to do clinical trials in Canada to give clinicians and patients experience with these therapies. It is a shame that this drug has taken so long to get to Canada.

Appendix: Patient Group Conflict of Interest Declaration

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No outside help was provided. CORD performed the background research, conducted the interviews, analyzed the data, and prepared the submission.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No outside help was provided.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Innomar Strategies (on behalf of Vifor Fresenius Medical Care Renal Pharma Ltd – Switzerland			x	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

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