Newsletter 2019 Vol 22 Issue 1

# The Renal Pharmacist

Vol 22

2019

Issue 1

## In this issue ...



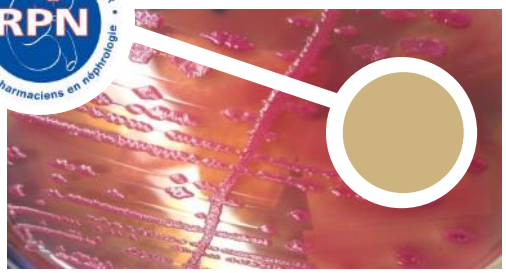
## View from the Chair

Firstly, welcome to all of our new members, and thank you to our long-term members for your continued engagement with the renal pharmacist community! 2019 has been off to a great start with The Renal Pharmacists Network. In May, we held our education event in Montreal in conjunction with the Canadian Society of Nephrology AGM. This successful event included some excellent presentations on hot, new topics in nephrology, including iron isomaltoside and new agents for hyperkalemia, as well as prevention of catheter -related infections in dialysis patients and a review of DOAC use in hemodialysis. If you were unable to attend the talks in Montreal but are interested in these topics, you can access the presentation slides through the members-only portal on the RPN website, and have a read through the summary articles in this newsletter, submitted by some of our fantastic speakers. While you're visiting the website, don't forget to check out the discussion boards; this is a great place to post clinical quandaries and questions and get input from your colleagues across the country, or share your expertise with others!

We are looking forward to hosting another RPN education event in Toronto on October 25th 2019, so mark your calendars! We will be offering education bursaries for this event; stay tuned for more details coming soon.

I would like to extend my sincere thanks to the RPN executive committee members; Judith, Jenny, Marisa, Joanne B, Jo-Anne W, Andrea, Elaine and Cliff who have been indispensable in the coordinating of our education events, maintaining the website, publishing newsletters and brainstorming new initiatives for the RPN to take on. We are always looking for colleagues to join the RPN Executive Committee, so please let us know if you are interested in joining this incredible team of passionate renal pharmacists! I look forward to serving as your chair for the rest of 2019, and hope to see many of you in Toronto in October.

*Katie Haubrich*
BScPharm, PharmD
Chair, Renal Pharmacist Network 2019

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kathryn.haubrich@cw.bc.ca

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Renal pharmacist, St. Joseph's Healthcare Hamilton
sgilbrea@stjoes.ca

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Marisa.battistella@uhn.ca

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Clinical Pharmacist - Nephrology
Sunnybrook Health Sciences Centre
Jenny.ng@sunnybrook.ca

**Education Coordinators:**
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Clinical Pharmacy Specialist - Nephrology
St. Paul's Hospital
JMarin@providencehealth.bc.ca

**Website Coordinator:**
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Vancouver General Hospital
Elaine.Cheng@vch.ca



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# Biography: Stephanie Gilbreath

Stephanie Gilbreath is the new chair elect for the Renal Pharmacist Network. She is currently the hemodialysis pharmacist at St. Joseph's Healthcare in Hamilton, Ontario. She obtained her BSc Pharm from the University of Toronto in 1998 and has worked in community pharmacy for over 15 years . She became a Certified Diabetes Educator in 2014 which has helped her provide care for her current patients. Stephanie started her hospital career in the Kidney Care clinics (now called Multicare Kidney Clinics) in 2014 at St. Joe's where she still helps to cover. Stephanie has been a yearly preceptor with the University of Toronto and University of Waterloo Pharmacy faculties since 2007 for 4th year pharmacy students. Outside of work, she volunteers with L'Arche, an organization for adults with developmental disabilities and loves music and gardening. Stephanie is excited to join the Renal Pharmacist Network!

**Please enjoy the following articles summarizing presentations from our RPN Education Day (which was held on May 2nd 2019 in Montreal, QC).**

# DOACs in CKD- Is it Safe?

*By Marisa Battistella, PharmD*

This presentation discussed the controversies of anticoagulation for atrial fibrillation in patients on hemodialysis. The talk reviewed the literature with both warfarin and direct oral anticoagulants (DOACs) in patients on hemodialysis. Patients with atrial fibrillation on hemodialysis are at a higher risk of thromboembolism due to traditional risk factors, increased platelet activation during hemodialysis, and systemic inflammation. Moreover, they are also at an increased risk of bleeding due to platelet dysfunction secondary to uremia and use of heparin during dialysis.[1] Although the use of anticoagulants for stroke prevention in this population remains controversial, warfarin has historically been the drug of choice if anticoagulation is deemed necessary.[2]

In the general population with normal kidney function DOACs have largely replaced warfarin as the anticoagulant of choice in patients with atrial fibrillation. Randomized controlled trials comparing DOACs to warfarin have shown that they are non-inferior or superior to warfarin and confer a lower risk of bleeding.[3-6] However, patients on dialysis were excluded from these landmark DOAC trials. Despite the paucity of data regarding the efficacy and safety of DOACs in this population, observational data has shown that the use of these drugs has increased in clinical practice. Both rivaroxaban and dabigatran appear to be associated with an increased risk of bleeding, and should not be used in these patients.[7-9] The use of edoxaban should also be avoided due to its lack of data in the hemodialysis population. Although a retrospective cohort study and pharmacokinetic data has generated some promising preliminary results regarding the use of apixaban, these findings need to be further assessed with randomized controlled trials before its use can be recommended in this population. [10-13] Until additional data emerges for DOACs, warfarin remains the oral anticoagulant of choice in hemodialysis. However, due to the high risk of bleeding in this population, the real decision remains whether anticoagulation is truly needed in this patient population.

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# Iron Isomaltoside… the new iron on the block!

*By Judith Marin, PharmD*

Iron Isomaltoside (II) 1000 (Monoferric®) has been available in Canada since October 2018. It differs from other intravenous (IV) iron product as it is designed with a more complex carbohydrate shell, which improves its stability and helps to release lower level of free iron in the circulation(1). It has been studied in the gastrointestinal, gynecology, oncology and nephrology populations(2). In nephrology, II 1000 was studied in chronic kidney disease non-dialysis (CKD-ND) as well as dialysis (CKD-D) (peritoneal dialysis and intermittent hemodialysis (HD)) patients (3–8). II 1000 can be given as an intravenous (IV) bolus, with a dose up to 500 mg, or IV infusion, with a dose up to 1.5 g(2). For HD patients, it may be administered during dialysis directly into venous port of dialyzer (similar as IV bolus administration)(2).

In the CKD-ND and CKD-D patients, II 1000 showed effectiveness in improving hemoglobin (Hgb) and iron parameters (tsat and ferritin) (3–8). In CKD-ND, II 1000 was superior to oral ferrous sulfate 300 mg/d in improving Hgb and TSAT/ferritin(4). In HD patients, II 1000 is non inferior to IV iron sucrose in maintaining Hgb, TSAT/ferritin(6,8). In terms of safety, the rate of adverse drug reactions (ADRs) reported (40-60%) is comparable to rates reported in the PO iron or iron sucrose study arms, and doesn't seem to differ between the IV bolus and the IV infusion route of administration(3–8). The rate and type of serious ADRs (hypersensitivity reaction, sepsis, and unstable angina) are also comparable to what is seen with other IV iron products(3–8).

A few points need to be highlighted from these studies:

In the CKD-ND and CKD-D studies, II 1000 was dosed using the Ganzoni formula, which calculates the iron dose based on patient's weight and target Hgb(2). Most Canadian CKD programs do not use this method to calculate patient's iron need, using instead an anemia management protocol dosing iron based on Hgb and iron studies results. How II 1000 would fit or dosage recommendation into our current practice is unknown.

A transient hypophosphatemia (PO4 < 0.6 mmol/L) has been reported in 1-2% of CKD patients, with a nadir within the first week of administration. This is likely occurring because of an acute increase in FGF-23. Up to now, no symptoms have been reported linked to the hypophosphatemia(2).

Finally, II 1000 is a bit more expensive than iron sucrose (see table 1), but it is anticipated that the overall cost would be lower with this agent, considering that patients can get higher doses of iron at one time which may translate to less ambulatory visits for IV iron.

*Table 1. Cost comparison of different iron formulations in British Columbia (BC).*

| Iron Preparation | Dosage | BC Cost |
|---|---|---|
| PO Ferrous fumarate | 300mg/d x 100 days | $11.98 (100 capsules) |
| IV iron dextran | 300 mg | $95.98 |
| IV iron sucrose | 300 mg | $121.50 |
| IV iron Isomaltoside | 1 g | $486 ($145.80 for 300 mg) |

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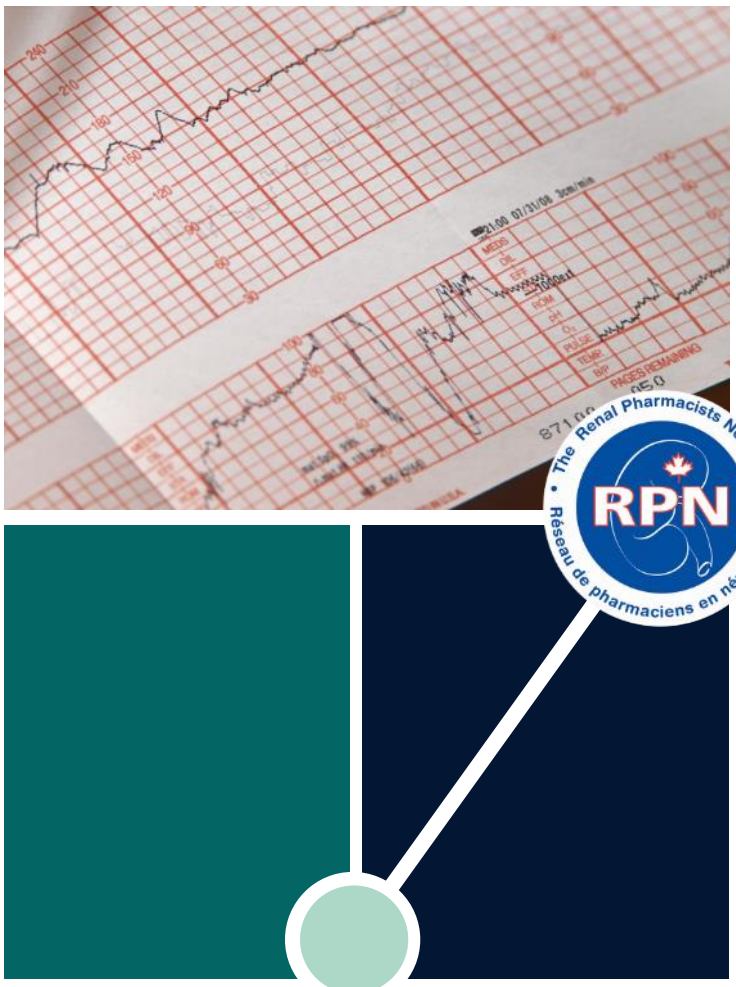
# New Therapies in Management of Hyperkalemia

*By Jenny Ng, BScPhm*

Hyperkalemia commonly occurs in people with chronic kidney disease (CKD) and is a potentially life-threatening electrolyte abnormality. In a study by Einhorn et al. it was found that there is increased risk of mortality within 1 day after a hyperkalemic event. Hyperkalemia can be related to medication use of agents such as renin-angiotensin blockers or mineralocorticoid receptor antagonists (MRAs). For outpatients, traditional approaches have included diet modification, stopping/adjusting agents contributing to hyperkalemia, non-K sparing diuretics and cation-exchange resins.




Though majority of potassium is eliminated by the kidney, 10% is absorbed via the gastro-intestinal tract (GIT). Cation-exchange resins work to bind potassium in the GIT and facilitates excretion in the feces. Currently two cation-exchange resins are available on the Canadian market, sodium polystyrene sulfonate (SPS) and calcium polystyrene sulfonate. In late 2019/early 2020, we anticipate 2 new agents to become available on the Canadian market.

Below is a summary table comparing some of these agents:

| Pharmacological Property | Sodium polystyrene sulfonate (SPS) | Patiromer calcium sorbitex | Sodium Zirconium cyclosilicate (ZS-9) |
|---|---|---|---|
| Brand name | Kayexalate | Veltassa | Lokelma |
| Mechanism of Action | Non-absorbed polymer. Binds potassium in the GIT and facilitates excretion in the feces | Non-absorbed polymer containing calcium-sorbitol counter ion. Binds potassium in the GIT and facilitates excretion in the feces | Non-absorbed zirconium silicate that preferentially captures potassium in exchange for hydrogen and sodium. Binds potassium in the GIT and facilitates excretion in the feces |
| Selectivity for potassium ion | Non selective. Also binds calcium and magnesium | Selective. Also binds magnesium | Highly selective. 9x binding capacity compared to SPS. Also binds ammonia. |
| Sodium content | 1500 mg sodium per 15 g dose (about 1/3 of resin sodium is delivered to the body) | No sodium content | ~ 1000 mg per 10 g dose |
| Sorbitol content | None | 4 g sorbitol per 8.4 g dose | None |
| Dosing | 15 g PO 1-4x/day | 8.4 g PO once daily with meal (titrate up to 25.2 g /day based on response) | Acute treatment: 10 g PO 3x/day with meals<br>Maintenance: 5, 10 or 15 g PO once daily with food |
| Preparation/ Administration | Powder for suspension. Mix with water | Powder for suspension. Mix with water. | White, tasteless powder for suspension. Mix with water. |
| Availability | Bottled powder (need to measure out individual doses | Available in US in sachets | Available in US in sachets |
| Efficacy | -1.04 mEq/L | -0.70 mEq/L change in potassium at 4 weeks* | -0.67 mEq/L at 48 hours[iii]* |
| Safety | GI intolerance, hypernatremia, diarrhea. Risk of intestinal necrosis. | Mild-moderate constipation, diarrhea, hypokalemia, hypomagnesemia | GI disorder, Urinary tract infection, edema, hypokalemia |
| Drug Interactions | Administer 3 hours before or 3 hours after other oral medications | Administer 3 hours before or 3 hours after other oral medications | Administer 2 hours before or 2 hours after other oral medications |
| Cost | $84 per 454 g | ? | ?<br>(Currently being reviewed by CADTH) |

*from meta-analysis of studies with significant heterogeneity

Cation-exchange resins may assist clinicians to be able to escalate doses of ACEi/ARB and MRA therapies to optimize therapy for proteinuria and heart failure. Though all these agents demonstrate efficacy in lowering potassium levels, it is important to note that there are no head to head studies to compare efficacy between these products nor dose equivalency studies. As these new agents come to the Canadian market, price, tolerability, and packaging of the powder may all play roles in clinician decision of which agent to use in management of hyperkalemia.

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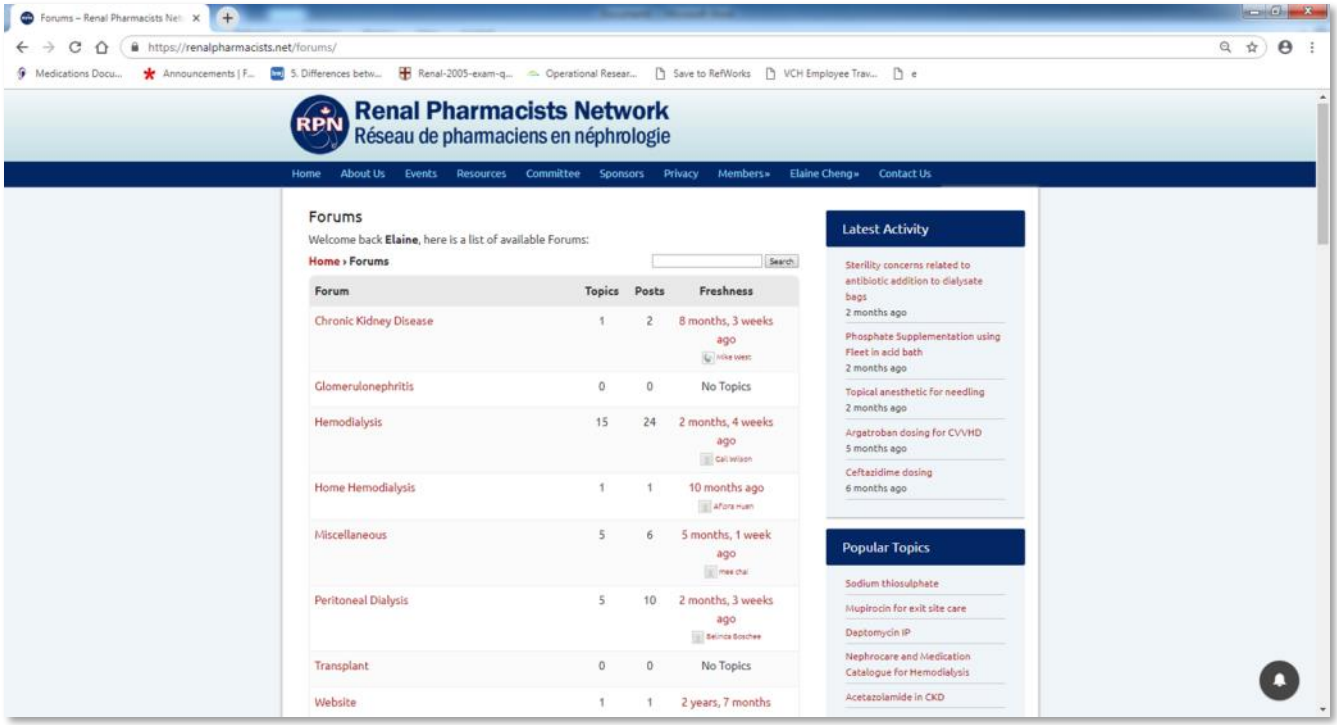
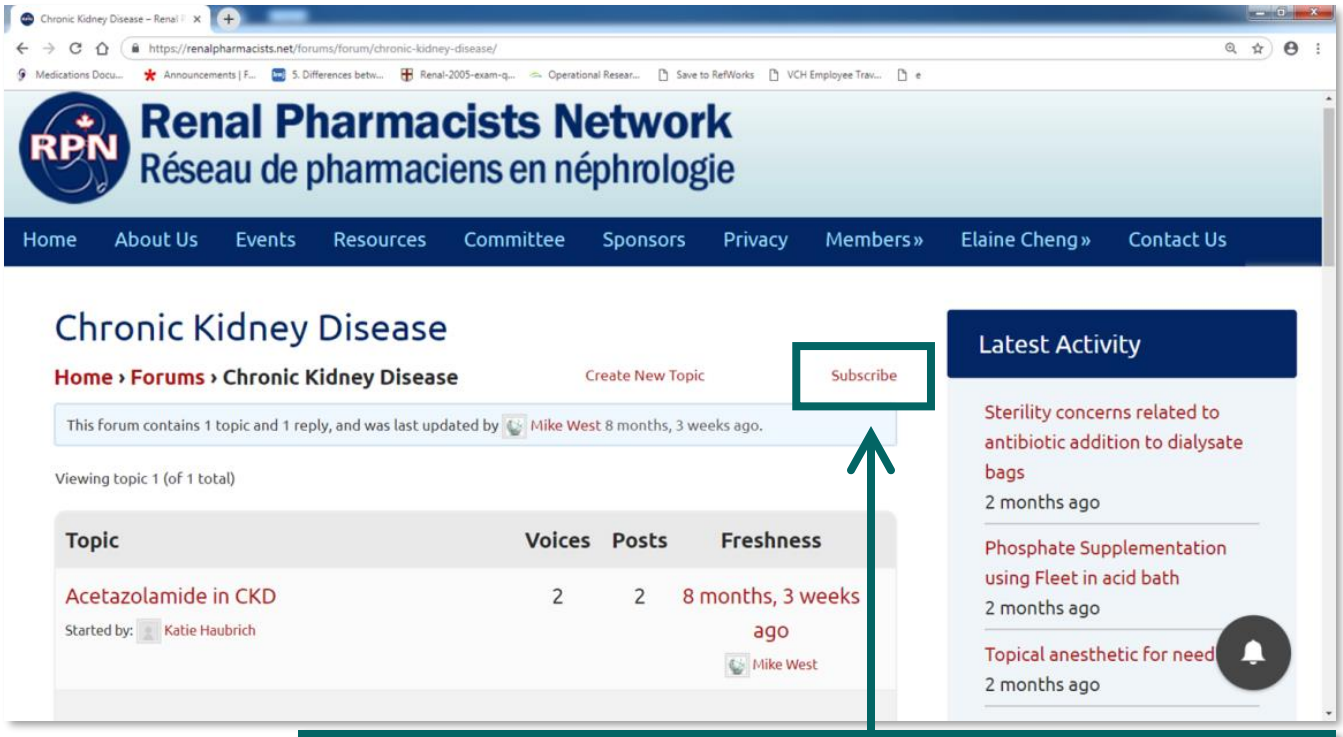
# RPN Website Discussion Forums

There are a total of 8 different discussion forums on the RPN website. Please post topics in the most relevant discussion forum. To receive email notifications of discussion forum postings, you will have to subscribe to each discussion forum separately (see instructions on the next page).



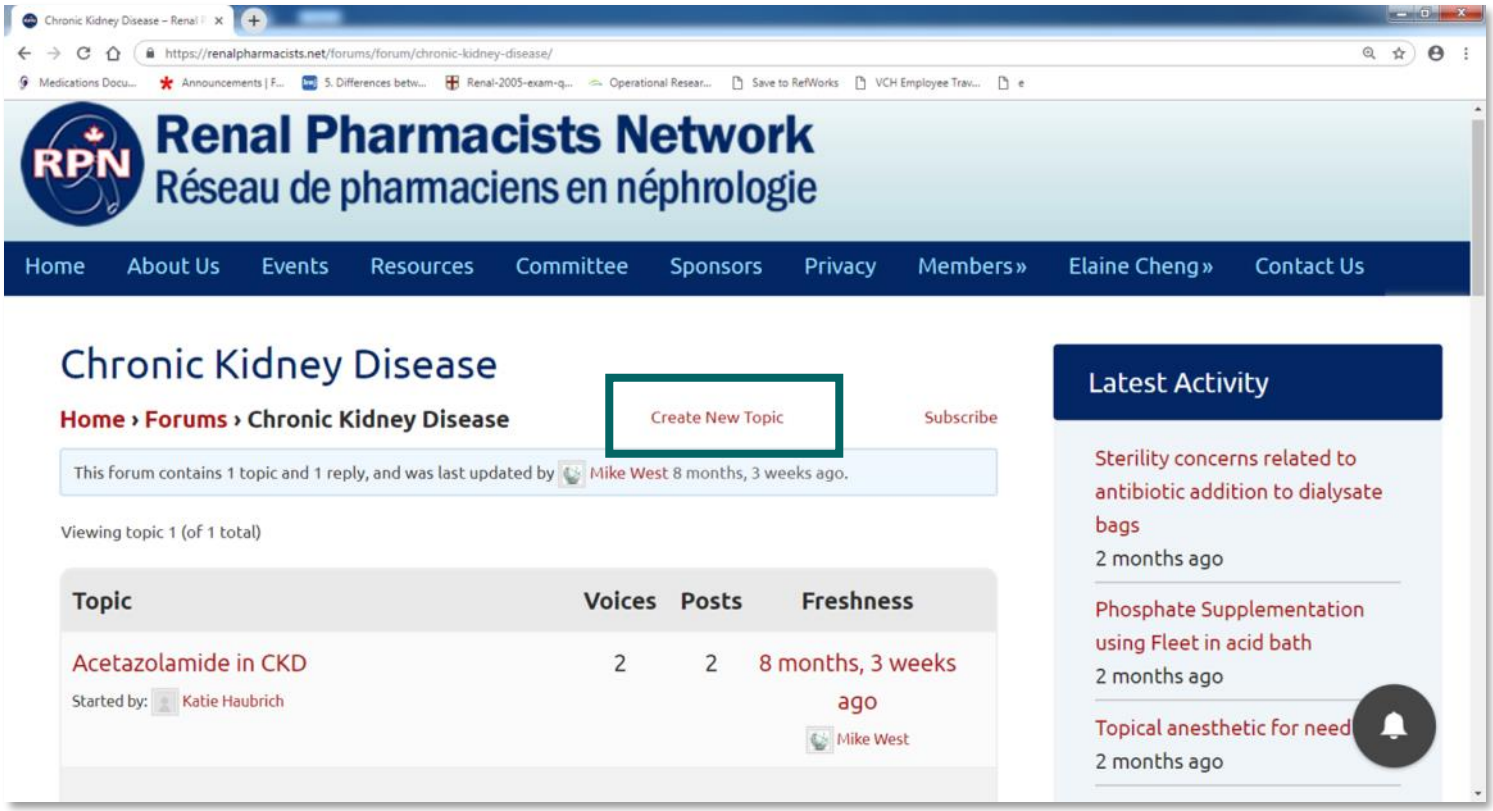

# How to Subscribe to a RPN Discussion Forum

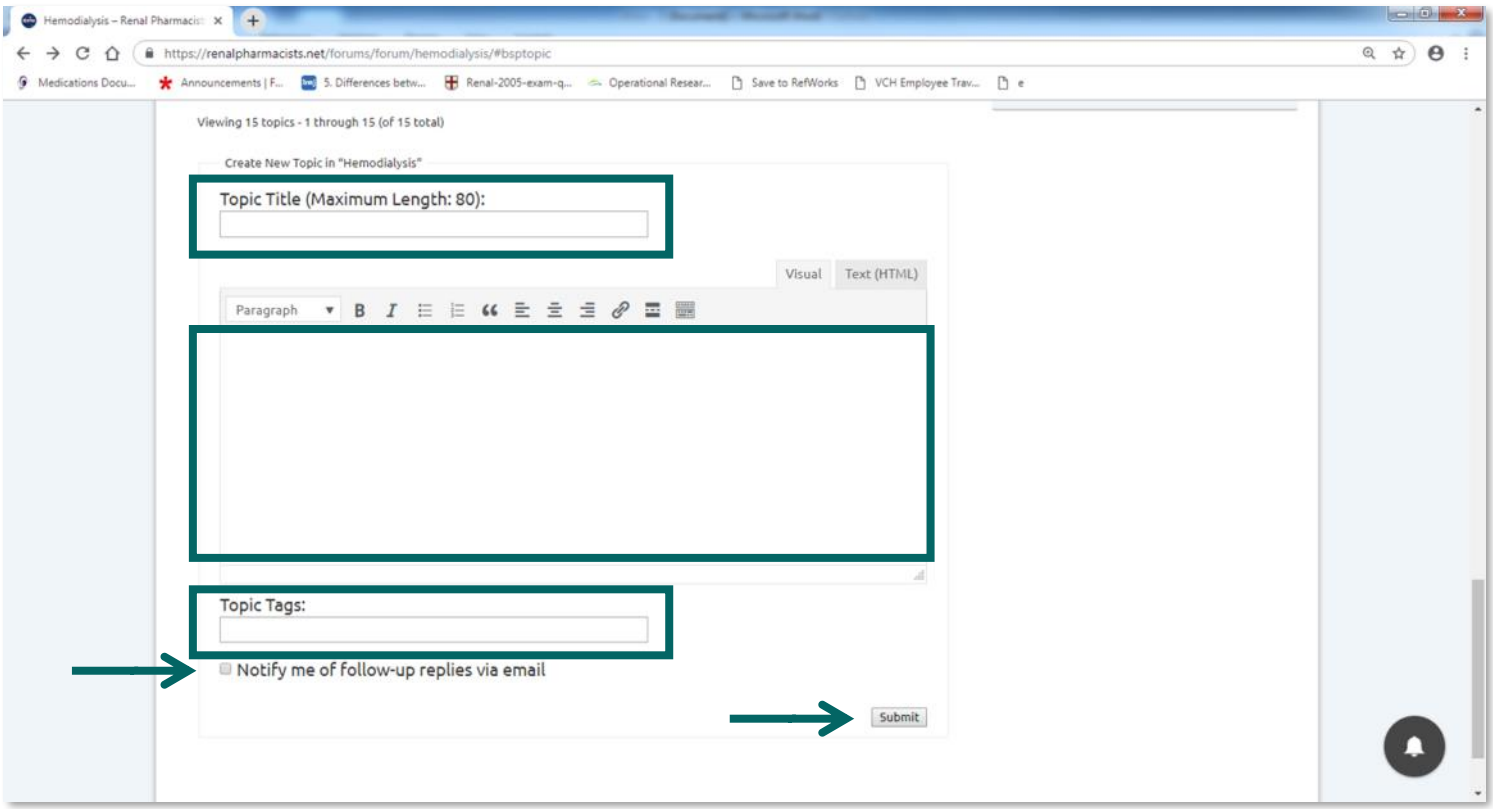



**To subscribe to the Chronic Kidney Disease discussion forum, click on "Chronic Kidney Disease" and choose "Subscribe" in the top menu bar as indicated above.**

# How to Create a Posting in a RPN Discussion Forum

To start a new discussion topic, either click on “Create New Topic” in the topic menu bar or scroll down to the bottom of the discussion forum page. Enter your topic title, body text and topic tags, and click “Submit”. If you wish to receive email notifications of responses to your posting, check off “Notify me of follow-up replies via email”.




## SAVE THE DATE – October 25th

**The RPN will be hosting an education day in Toronto on Friday October 25, 2019.**
**Final agenda and meeting details to come soon.**

**We are happy to be able to offer a few bursaries for those without funding to attend this event.**
**Further details to follow via email.**

# Future Events

## ASN Kidney Week 2019

November 5-10, 2019
Walter E. Washington Convention Center
Washington, DC, USA
For further information: https://www.asn-online.org/

Please send any articles of interest to
renalpharmacistsnetwork@gmail.com

# Recent Publications

Spoendlin J, Spoendlin J, Paik JM, Tsacogianis T, Kim SC, Schneeweiss S, Desai RJ. **Cardiovascular Outcomes of Calcium-Free vs Calcium-Based Phosphate Binders in Patients 65 Years or Older With End-stage Renal Disease Requiring Hemodialysis.** *JAMA Intern Med*. 2019 May 6. [Epub ahead of print]

WilsonJS, Tran J, Veith A, Landry D, Neville H, Kelly C, Soroka S, West K. **Medication Reimbursement Model and Cost Savings in a Canadian Ambulatory Hemodialysis Program.** *Can J Hosp Pharm* 2019; 72(2): 155-9.

Lim W, Afif W, Knowles S, Lim G, Lin Y, Mothersill C, Nistor I, Rehman F, Song C, Xendodemetropoulos T. **Canadian expert consensus: management of hypersensitivity reaction to intravenous iron in adults.** *Intern Society of Blood Transfusion*. 2019 Apr 2. [Epub ahead of print]

Perkovic V, Jardine MJ, Neal B, et al. **Canagliflozin and renal outcomes in type 2 diabetes and nephropathy** (CREDENCE). *N Engl J Med.* 2019;380:2295-306.

Berger I, Haubrich K, Ensom MH, Carr R. **RELATE: Relationship of limited sampling strategy and adverse effects of mycophenolate mofetil in pediatric renal transplant patients.** *Pediatric transplantation.* 2019 Mar;23(2):e13355.

Warady BA, Iles JN, Ariceta G, Dehmel B, Hidalgo G, Jiang X, Laskin B, Shahinfar S, Walle JV, Schaefer F. **A randomized, double-blind, placebo-controlled study to assess the efficacy and safety of cinacalcet in pediatric patients with chronic kidney disease and secondary hyperparathyroidism receiving dialysis.** *Pediatric Nephrology.* 2019 Mar 1;34(3):475-86.

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