

## Journal View

### Patiromer Reduces Potassium in CKD Patients Taking RAAS Inhibitors

The new oral potassium binder patiromer effectively lowers serum potassium levels in patients with chronic kidney disease (CKD) who are being treated with renin-angiotensin-aldosterone system (RAAS) inhibitors, reports a trial in the *New England Journal of Medicine*.

The multicenter study included 243

patients with stage 3 or 4 CKD who were taking RAAS inhibitors and had a serum potassium level of 5.1 to less than 6.5 mmol/L. All received 4 weeks of treatment with patiromer. The starting dose was 4.2 or 8.4 g twice daily. Patients whose potassium level decreased to the target range (3.8 to less than 5.1 mmol/L) were eligible for an 8-week

randomized withdrawal phase, with one group continuing to receive patiromer and the other switching to placebo. Changes in potassium level were compared between groups.

The mean reduction in serum potassium during the initial treatment phase was 1.01 mmol/L, and 76 percent of patients reached the target range by 4

weeks. Among 107 patients enrolled in the withdrawal phase, potassium levels increased by 0.72 mmol/L within 4 weeks for those switching to placebo, compared with no change for those continuing to receive patiromer. The rates of recurrent hyperkalemia (potassium level 5.5 mmol/L or higher) were 60

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For the control of serum phosphorus levels in patients with chronic kidney disease on dialysis

## INTRODUCING AURYXIA (FERRIC CITRATE), THE FIRST AND ONLY ABSORBABLE-IRON-BASED PHOSPHATE BINDER CLINICALLY PROVEN TO MANAGE HYPERPHOSPHATEMIA<sup>1-6</sup>

- Proven control of serum phosphorus within KDOQI guidelines (4.88 mg/dL at Week 56)<sup>7,8</sup>
- Demonstrated safety and tolerability profile over 52 weeks
- Each AURYXIA tablet contains 210 mg ferric iron, equivalent to 1 g ferric citrate

Introducing  
**Auryxia™**  
(ferric citrate) tablets

#### References:

1. Fosrenol [package insert]. Wayne, PA: Shire US, Inc.; 2014. 2. Phoslyra [package insert]. Waltham, MA: Fresenius Medical Care North America; 2011. 3. PhosLo Gelcaps [package insert]. Waltham, MA: Fresenius Medical Care North America; 2012. 4. Renegel [package insert]. Cambridge, MA: Genzyme Corporation; 2014. 5. Renvela [package insert]. Cambridge, MA: Genzyme Corporation; 2014. 6. Velphoro [package insert]. Waltham, MA: Fresenius Medical Care North America; 2014. 7. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis.* 2003;42(4 Suppl 3):S1-S201. 8. Data on File 1, Keryx Biopharmaceuticals, Inc.

a risk for spontaneous abortion, gestational diabetes, and fetal malformation. Rat studies have shown the transfer of iron into milk. There is possible infant exposure when AURYXIA is taken by a nursing woman.

**Pediatric:** The safety and efficacy of AURYXIA have not been established in pediatric patients.

**Adverse Events:** The most common adverse events with AURYXIA were diarrhea (21%), nausea (11%), constipation (8%), vomiting (7%), and cough (6%). Gastrointestinal adverse reactions were the most common reason for discontinuing AURYXIA (14%).

**Drug Interactions:** Doxycycline should be taken at least 1 hour before AURYXIA. Consider separation of the timing of the administration of AURYXIA with drugs where a reduction in their bioavailability would have a clinically significant effect on safety or efficacy.

**Please see Brief Summary on following page.**

**You may report side effects to Keryx at 1-844-44KERYX (844-445-3799).**



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## Journal View

### Patiromer

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percent versus 15 percent, respectively. During the initial treatment phase, mild to moderate constipation occurred in 11 percent of patients and hypokalemia in 3 percent.

Patiromer—a nonabsorbed polymer that binds potassium in exchange for calcium—was developed to meet the

need for effective outpatient treatments for hyperkalemia. This two-phase trial supports its effectiveness in reducing potassium levels and the rate of recurrent hyperkalemia in CKD patients taking RAAS inhibitors. Hypokalemia appears to be an infrequent and reversible event in patients taking patiromer [Weir MR, et al. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *N Engl J Med* doi: 10.1056/NEJMoa1410853]. ●

### Longer Steroid Courses Don't Affect Recurrence Rate in Nephrotic Syndrome

For children with steroid-sensitive nephrotic syndrome, extending initial steroid therapy from 3 to 6 months does not affect the subsequent relapse rate, reports a trial in *Kidney International*.

The randomized trial included 219 children with a first episode of steroid-sensitive nephrotic syndrome, enrolled at five academic hospitals in India. After 3

months of standard therapy with prednisolone, 181 children were assigned to receive 3 additional months of prednisolone or 3 months of placebo therapy. The effects of extended steroid therapy on the risk of future relapse were assessed.

The cumulative initial prednisolone dosage was about 3500 mg/m<sup>2</sup> in the 6-month group versus 2800 mg/m<sup>2</sup> in the 3-month group. On intention-to-treat analysis, the numbers of steroid-sensitive relapses during the year after randomization were 1.26 and 1.54, respectively. The difference was not significant after adjustment for sex, age, and time to initial remission. The rates of sustained remission, frequent relapses, and adverse steroid effects were similar as well.

For children with idiopathic nephrotic syndrome, multiple relapses are associated with a risk of serious complications and medication-related adverse events. Some reports have suggested that a prolonged course of initial prednisolone therapy can reduce the relapse rate, although these studies have had important limitations.

The new trial finds no reduction in relapse rate for children with steroid-sensitive nephrotic syndrome assigned to 3 months versus 6 months of initial prednisolone therapy. Although extended treatment can postpone the occurrence of initial relapse, the 1-year relapse rates are similar between groups. A Japanese trial comparing 2 months versus 6 months of prednisolone, published in the same issue (*Kidney Int* 2015; 87:225–232), reaches a similar conclusion [Sinha A, et al. Extending initial prednisolone treatment in a randomized control trial from 3 to 6 months did not significantly influence the course of illness in children with steroid-sensitive nephrotic syndrome. *Kidney Int* 2015; 87:217–224]. ●

AURYXIA™ (ferric citrate) tablets contain 210 mg of ferric iron equivalent to 1 g ferric citrate for oral use.

#### INDICATIONS AND USAGE

AURYXIA is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

#### CONTRAINDICATIONS

AURYXIA is contraindicated in patients with iron overload syndromes (eg, hemochromatosis).

#### WARNINGS AND PRECAUTIONS

**Iron Overload:** Iron absorption from AURYXIA may lead to excessive elevations in iron stores. Increases in serum ferritin and transferrin saturation (TSAT) levels were observed in clinical trials. In a 56-week safety and efficacy trial in which concomitant use of AURYXIA and IV iron was permitted, 55 (19%) patients treated with AURYXIA had a ferritin level >1500 ng/mL as compared with 13 (9%) patients treated with active control. Assess iron parameters (eg, serum ferritin and TSAT) prior to initiating AURYXIA and monitor iron parameters while on therapy. Patients receiving IV iron may require a reduction in dose or discontinuation of IV iron therapy.

**Accidental Overdose of Iron:** Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Keep this product out of the reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

**Patients with Gastrointestinal Bleeding or Inflammation:** Patients with inflammatory bowel disease or active, symptomatic gastrointestinal bleeding were excluded from clinical trials. Safety has not been established in these populations.

#### ADVERSE REACTIONS

Adverse reactions to a drug are most readily ascertained by comparison with placebo, but there is little placebo-controlled experience with AURYXIA, so this section describes adverse events with AURYXIA, some of which may be disease-related, rather than treatment-related. A total of 289 patients were treated with AURYXIA and 149 patients were treated with active control (sevelamer carbonate and/or calcium acetate) during the 52-week, randomized, open-label, active control phase of a trial in patients on dialysis.

A total of 322 patients were treated with AURYXIA for up to 28 days in three short-term trials. Across these trials, 557 unique patients were treated with AURYXIA; dosage regimens in these trials ranged from 210 mg to 2,520 mg of ferric iron per day, equivalent to 1 to 12 tablets of AURYXIA. In these trials, adverse events reported for AURYXIA were similar to those reported for the active control group. Adverse events reported in more than 5% of patients treated with AURYXIA in these trials included diarrhea (21%), nausea (11%), constipation (8%), vomiting (7%), and cough (6%). During the 52-week active control period, 60 patients (21%) on AURYXIA discontinued study drug because of an adverse event, as compared to 21 patients (14%) in the active control arm. Patients who were previously intolerant to any of the active control treatments (calcium acetate and sevelamer carbonate) were not eligible to enroll in the study. Gastrointestinal adverse events were the most common reason for discontinuing AURYXIA (14%).

AURYXIA is associated with discolored feces (dark stools) related to the iron content, but this staining is not clinically relevant and does not affect laboratory tests for occult bleeding, which detect heme rather than non-heme iron in the stool.

#### DRUG INTERACTIONS

Doxycycline is an oral drug that has to be taken at least 1 hour before AURYXIA. Oral drugs that can be administered concomitantly with AURYXIA are: amlodipine, aspirin, atorvastatin, calcitriol, clopidogrel, digoxin, doxercalciferol, enalapril, fluvastatin, levofloxacin, metoprolol, pravastatin, propranolol, sitagliptin, and warfarin. There are no empirical data on avoiding drug interactions between AURYXIA and most concomitant oral drugs. For oral medications where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, consider separation of the timing of the administration of the two drugs. The duration of separation depends upon the absorption characteristics of the medication concomitantly administered, such as the time to reach peak systemic levels and whether the drug is an immediate release or an extended release product. Consider monitoring clinical responses or blood levels of concomitant medications that have a narrow therapeutic range.

#### USE IN SPECIFIC POPULATIONS

**Pregnancy:** Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women. It is not known whether AURYXIA can cause fetal harm when administered to a pregnant woman. Animal reproduction studies have not been conducted.

The effect of AURYXIA 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. An overdose of iron in pregnant women may carry a risk for spontaneous abortion, gestational diabetes, and fetal malformation.

**Labor and Delivery:** The effects of AURYXIA on labor and delivery are unknown.

**Nursing Mothers:** Data from rat studies have shown the transfer of iron into milk by divalent metal transporter-1 (DMT-1) and ferroportin-1 (FPN-1). Hence, there is a possibility of infant exposure when AURYXIA is administered to a nursing woman.

**Pediatric Use:** The safety and efficacy of AURYXIA have not been established in pediatric patients.

**Geriatric Use:** Clinical studies of AURYXIA included 106 subjects aged 65 years and older (33 subjects aged 75 years and older). Overall, the clinical study experience has not identified any obvious differences in responses between the elderly and younger patients in the tolerability or efficacy of AURYXIA.

#### OVERDOSAGE

No data are available regarding overdose of AURYXIA in patients. In patients with chronic kidney disease on dialysis, the maximum dose studied was 2,520 mg ferric iron (12 tablets of AURYXIA) per day. Iron absorption from AURYXIA may lead to excessive elevations in iron stores, especially when concomitant IV iron is used.

In clinical trials, one case of elevated iron in the liver as confirmed by biopsy was reported in a patient administered IV iron and AURYXIA.

#### PATIENT COUNSELING INFORMATION

**Dosing Recommendations:** Inform patients to take AURYXIA as directed with meals and adhere to their prescribed diets. Instruct patients on concomitant medications that should be dosed apart from AURYXIA.

**Adverse Reactions:** Advise patients that AURYXIA may cause discolored (dark) stools, but this staining of the stool is considered normal with oral medications containing iron.

AURYXIA may cause diarrhea, nausea, constipation, and vomiting. Advise patients to report severe or persistent gastrointestinal symptoms to their physician.

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### Surgical Robots Linked to Increased Rates of Partial Nephrectomy

Hospitals acquiring surgical robots are more likely to perform guideline-recommended partial nephrectomy in patients with renal cancer, reports a study in *Medical Care*.

The researchers used payer data from seven states to identify nearly 21,600 nephrectomies performed in 2001, 2005, and 2008. Hospital-level rates of partial nephrectomy were analyzed in relation to the hospitals' acquisition of a surgical robotic system. The association was adjusted for nephrectomy volume, year of surgery, and other hospital factors.

Hospitals performed more partial nephrectomies after acquiring surgical robots. For hospitals acquiring robots between 2001 and 2004, the proportion of

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