percent of patients are treated and released. Preventing repeat visits is important to reduce the “excruciating pain” of kidney stones and to reduce health care costs.

The findings suggest that one of nine patients makes a repeat ED visit for kidney stones. Close to one-third of these repeat visits result in hospitalization or an urgent procedure. Markers of access and quality of care may be useful targets for efforts to reduce high-cost, high-acute repeat visits for kidney stones [Scales CD Jr., et al. Emergency department revisits for patients with kidney stones in California. Acad Emerg Med 2015; 22:468-474].

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

AURYXIA™ (ferric citrate) IS THE FIRST AND ONLY ABSORBABLE-IRON–BASED PHOSPHATE BINDER CLINICALLY PROVEN TO MANAGE HYPERPHOSPHATEMIA1-6

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

References:

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.

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

©2015 Keryx Biopharmaceuticals, Inc.
01/15 PP-AUR-US-0075

Urine Test for Early Detection of Renal Cell Carcinoma?

Measuring levels of two urine proteins may provide a noninvasive approach for early detection of renal cell carcinoma (RCC), reports a study in JAMA Oncology.

Urinary specimens were obtained from a convenience sample of 720 patients undergoing abdominal computed tomography (CT) for various indications, and from 19 patients with pathologically confirmed RCC and 80 healthy control individuals. Two urine proteins—aquaporin-1 (AQP1) and perilipin-2 (PLIN2)—were evaluated as biomarkers of early RCC.

Continued on page 8

Measuring levels of two urine proteins may provide a noninvasive approach for early detection of renal cell carcinoma (RCC), reports a study in JAMA Oncology. Urinary specimens were obtained from a convenience sample of 720 patients undergoing abdominal computed tomography (CT) for various indications, and from 19 patients with pathologically confirmed RCC and 80 healthy control individuals. Two urine proteins—aquaporin-1 (AQP1) and perilipin-2 (PLIN2)—were evaluated as biomarkers of early RCC. Urine specimens were obtained from a convenience sample of 720 patients undergoing abdominal computed tomography (CT) for various indications, and from 19 patients with pathologically confirmed RCC and 80 healthy control individuals. Two urine proteins—aquaporin-1 (AQP1) and perilipin-2 (PLIN2)—were evaluated as biomarkers of early RCC.

Continued on page 8
Urine Test
Continued from page 7

Previous studies showed that these proteins are elevated in patients with RCC but not in those with nonmalignant kidney disease. Renal masses and RCC were confirmed by CT scans and postnephrectomy examination, respectively. The median urine AQP1 level was 225.0 mg/mg creatinine in patients with confirmed RCC versus 1.1 mg/mg in healthy control individuals. The values for PLIN2 were 37.8 versus 3.1 absorbance units/mg, respectively. In the screening population, the median AQP1 value was 0.5 ng/mg, and the median PLIN2 value was 0 absorbance units/mg.

For the two biomarkers alone or in combination, the area under the receiver operating characteristic curve was at least 0.990. Sensitivity was at least 95 percent and specificity at least 91 percent in comparison with control individuals and the screening population. Three patients in the screening population had biomarker levels suggesting RCC. All three had a renal mass shown by CT scan, and two had pathologically confirmed RCC.

The results validate the clinical utility of urine AQP1 and PLIN2 as biomarkers for early and noninvasive detection and screening for RCC. These proteins may also be useful for the differential diagnosis of renal masses seen on imaging studies [Montiusey JF, et al. Evaluation of urine aquaporin-1 and perilipin-2 concentrations as biomarkers to screen for renal cell carcinoma: a prospective cohort study. JAMA Oncol Published online March 19, 2015. doi:10.1001/jamaoncol.2015.0215].

Continued on page 10

BRIEF SUMMARY
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, hereditary 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, 82 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 treatment (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: amiodarone, aspirin, atorvastatin, calcitriol, clopidogrel, digoxin, doxycycline, enalapril, flavastatin, lovastatin, 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 of 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. However, data from rat studies have shown that iron absorption from 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.

CONTINUED ON PAGE 9