trajectories to donation. On analysis of observed 15-year ESRD rates among living kidney donors, postdonation risks were 3.5 to 5.3 times higher than predonation risks.


Belatacept improves long-term kidney transplant outcomes

Follow-up from a previous clinical trial shows improvements in kidney graft survival and function in patients receiving belatacept-based immunosuppression compared with those receiving cyclosporin, reports a study in The New England Journal of Medicine.

The researchers presented 7-year follow-up data from the Belatacept Evaluation of Nephroprotection and Efficacy as First-line Immunosuppression Trial (BENEFIT). Kidney transplant recipients were randomly assigned to ‘primary’ immunosuppression with a more intensive belatacept-based regimen, a less intensive belatacept regimen, or a cyclosporin regimen. Patient and graft survival and eGFR were assessed at 84 months. Of 666 randomized patients, 660 received their assigned treatment. Complete follow-up data were available for 153 patients treated with the more intensive belatacept regimen, 163 patients treated with less intensive belatacept, and 131 patients treated with cyclosporin. Both the more and less intensive belatacept regimens were associated with a lower risk of death or graft loss compared with the cyclosporin regimen: hazard ratio of 0.35 in both groups.

Mean eGFR increased with both belatacept regimens but declined in the cyclosporin group. At 84 months, mean eGFR was 70.4 mL/min per 1.73 m² with more intensive belatacept and 72.1 mL/min per 1.73 m² with less intensive belatacept compared to 44.9 mL/min per 1.73 m² with cyclosporin. The three groups had similar cumulative rates of serious adverse events.

Continued on page 18

IMPROVED FORMULARY ACCESS!
Visit Auryxia.com to learn more

For the control of serum phosphorus 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 HYPERPHOSPHATEMIA

• Proven control of serum phosphorus within KDOQI guidelines (4.88 mg/dL at Week 56)³
• Demonstrated safety and tolerability profile over 52 weeks
• Each AURYXIA tablet contains 210 mg ferric iron, equivalent to 1 g ferric citrate

References:
5. Data on File 1, Keryx Biopharmaceuticals, Inc.
8. 8. Data on File 1, Keryx Biopharmaceuticals, Inc.

Drug Interactions: Doxycycline should be taken at least 1 hour before AURYXIA. Ciprofloxacin should be administered at least 2 hours before or after 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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PP-AUR-US-0173 08/15
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, 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. Avoid 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 189 patients were treated with active control (sevelamer carbonate and/or calcium acetate) during the 52-week, randomised, 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 group. 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
Doxercalciferol, enalapril, fluvastatin, levofloxacin, metoprolol, pravastatin, propranolol, sitagliptin, and warfarin. There are no empirical data on interactions with AURYXIA. Oral drugs that can be administered concomitantly with AURYXIA are: amlodipine, aspirin, atorvastatin, calcitriol, cholestyramine, digoxin, doxersalciferol, enalapril, fluvastatin, levofoxacin, 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 when 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, as such 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). There are no empirical data on the effects of AURYXIA on milk-exposed infants. In clinical trials, a case of elevated iron in the liver as confirmed by biopsy was reported in a patient administered IV iron and 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 to 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 use. Advise patients to report severe or persistent gastrointestinal symptoms to their physician. Kirkos Biopharmaceuticals, Inc. ©2015 Kirkos Biopharmaceuticals, Inc.